Description of document:	**Defense Technical Information Center, Ft. Belvoir, VA, bibliographies on botulism; botulinum, February-2007**
Requested date:	08-February-2007
Released date:	21-March-2007
Posted date:	14-January-2008
Title of Document	DTIC Bibliography
Date/date range of document:	Reports cited range in date from 1941 - 2006
Source of document:	Defense Technical Information Center (DTIC-R) ATTN: FOIA Requester Service Center 8725 John J. Kingman Road, Suite 0944 Ft. Belvoir, VA 22060-6218 Phone: (703) 767-9194 FAX: (703) 767-9201 Email: foia@dtic.mil

DEFENSE TECHNICAL INFORMATION CENTER
8725 JOHN J. KINGMAN RD, STE 0944
FT. BELVOIR, VA 22060-6218

IN REPLY REFER TO:

DTIC-R (FOIA 2007-19)

MAR 2 1 2007

This is in response to your letter of February 8, 2007 requesting information under the Freedom of Information Act (FOIA). Under Department of Defense rules implementing the FOIA, published at 32 CFR 286, your request was categorized as "other."

Enclosed are computer-generated bibliographies prepared by matching the subject terms or keywords listed in your request against our database (i.e., *botulism; botulinum*). The bibliographies may contain some documents that do not apply to the specific subject area(s) in which you are interested; however, to eliminate any of the key search terms would also eliminate documents that do apply to your subject area(s) of interest.

The documents listed on enclosure 1 have been approved for public release and may be obtained from the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, VA 22161. NTIS sells such documents to the general public and, if you wish, you can order the documents by telephone at (703) 605-6000. Be sure to include the AD numbers when requesting the documents.

Enclosure 2 is a bibliography containing unclassified descriptions of classified and/or unclassified/limited distribution documents related to your request. These documents may only be released by the controlling activity. Requests for these documents should be forwarded to the controlling activity, usually identified in the Distribution Statement field of the citation. This office upon request can research documents with no controlling activity identified.

To date, the search effort related to your request has required 1 hour of professional level time at $44 per hour. It is estimated that another 2-4 hours would be required to search our manual card file. In addition, our card file contains index cards for a large

collection of documents mostly dated prior to 1960. Be aware that the bibliographies would be made up of xeroxed copies of the index cards and fees are appropriate for reproduction in excess of the 100 pages (at a rate of $.15 per page) to which you are entitled at no charge. If you still want a manual search to be conducted, please forward your willingness to pay any associated fees that may be incurred for professional time ($44 per hour) beyond the 1 hour of free search time remaining to which you are entitled and to pay for any reproduction in excess of 100 pages. This does not mean you would necessarily be charged fees; however, it would allow us to initiate the manual card file search. NOTE: Also be aware that the search could result in no records being located related to your request, however you may still be responsible for any fees incurred.

To date, there are no assessable fees for services from the Defense Technical Information Center at this time. In your letter, you request a fee waiver. Court rulings impacting on agency FOIA operations require a collection of fees when there is no public interest in the disclosure of the requested information. If you can demonstrate the ability to significantly enhance the general public's knowledge of the operations and activities of the government (along with your capability and intention to disseminate the information to the public), it is possible to qualify for a fee waiver or reduction. Be aware, however, that bibliographies tend to reveal nothing concerning the conduct of any government agency or that of their officials. They merely identify/list documents in our collection that may be related to the subject matter of your request.

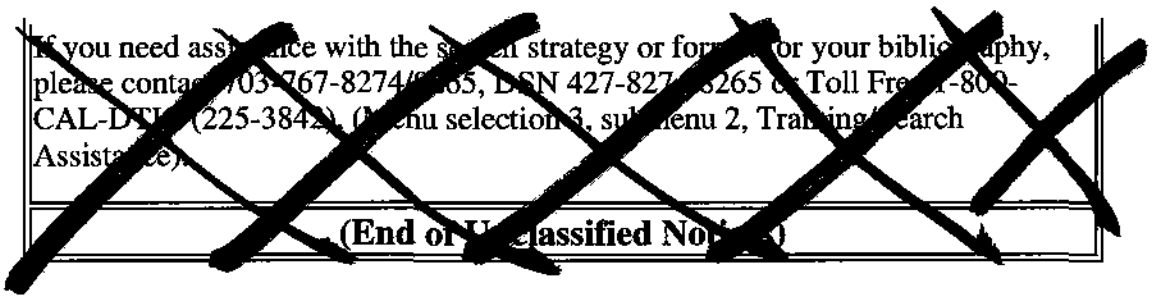
Please understand that other members of the public may submit a FOIA request for copies of FOIA requests received by this office or the names of those who have submitted requests. Should such occur, your name and, if asked for, a copy of your request will be released; however, your home address and home telephone number will not be released. Other private citizens who have obtained your name by using such a request may contact you. However, correspondence from the Defense Department about your request will be on official letterhead. Please call me at (703) 767-9194 if you have any questions.

Sincerely,

Kelly D. Akers

2 Encl

KELLY D. AKERS
FOIA Program Manager



Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA457724
Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a457724.pdf
Size: 138 KB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA457724
Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD
Unclassified Title:
(U) Multiagent Vaccines Vectored by Venezuelan Equine Encephalitis Virus Replicon Elicits Immune Responses to Marburg Virus and Protection Against Anthrax and Botulinum Neurotoxin in Mice
Descriptive Note:
Journal article
Personal Author(s):
Lee, John S
Groebner, Jennifer L
Hadjipanayis, Angela G
Negley, Diane L
Schmaljohn, Alan L
Welkos, Susan L
Smith, Leonard A
Smith, Jonathan F
Report Date:
Jan 2006
Media Count:
9 Page(s)
Report Number(s):
RPP-05-445
XA-USAMRIID
Monitor Series:
USAMRIID
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE

26 - NOT AVAILABLE IN MICROFICHE

Distribution Statement:

Approved for public release; distribution is unlimited. This document is not available from DTIC in microfiche.

Abstract:

(U) The development of multiagent vaccines offers the advantage of eliciting protection against multiple diseases with minimal inoculations over a shorter time span. We report here the results of using formulations of individual Venezuelan equine encephalitis (VEE) virus replicon-vectored vaccines against a bacterial disease, anthrax; a viral disease, Marburg fever; and against a toxin-mediated disease, botulism. The individual VEE replicon particles (VRP) expressed mature 83-kDa protective antigen (MAT-PA) from Bacillus anthracis, the glycoprotein (GP) from Marburg virus (MBGV), or the H(C) fragment from botulinum neurotoxin (BoNT H(C)). CBA/J mice inoculated with a mixture of VRP expressing BoNT H(C) serotype C (BoNT/C H (C)) and MAT-PA were 80% protected from a B. anthracis (Sterne strain) challenge and then 100% protected from a sequential BoNT/C challenge. Swiss mice inoculated with individual VRP or with mixtures of VRP vaccines expressing BoNT H(C) serotype A (BoNT/A H(C)), MAT-PA, and MBGV-GP produced antibody responses specific to the corresponding replicon-expressed protein. Combination of the different VRP vaccines did not diminish the antibody responses measured for Swiss mice inoculated with formulations of two or three VRP vaccines as compared to mice that received only one VRP vaccine. Swiss mice inoculated with VRP expressing BoNT/A H(C) alone or in combination with VRP expressing MAT-PA and MBGV GP, were completely protected from a BoNT/A challenge. These studies demonstrate the utility of combining individual VRP vaccines into multiagent formulations for eliciting protective immune responses to various types of diseases.

Abstract Classification:

Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:

ADA443596

Full Text (pdf) Availability:

View Full Text (pdf)

File: /U2/a443596.pdf

Size: 457 KB

Handle / proxy Url: http://handle.dtic.mil/100.2/ADA443596

Corporate Author:

ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD

Unclassified Title:

(U) Serotype-Selective, Small-Molecule Inhibitors of the Zinc Endopeptidase of Botulinum Neurotoxin Serotype A

Personal Author(s):

Park, Jewn G
Sill, Peter C
Makiyi, Edward F
Garcia-Sosa, Alfonso T
Millard, Charles B
Schmidt, James J

Pang, Yuan-Ping

Report Date:
Jan 2006

Media Count:
15 Page(s)

Report Number(s):
XA-USAMRIID

Contract Number:
DAAD19-01-1-0322

Monitor Series:
USAMRIID

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE

Distribution Statement:
Approved for public release; distribution is unlimited.

Abstract:
(U) Botulinum neurotoxin serotype A (BoNTA) is one of the most toxic substances known. Currently there is no antidote to BoNTA. Small molecules identified from high-throughput screening reportedly inhibit the endopeptidase - the zinc-bound, catalytic domain of BoNTA - at a drug concentration of 20 M. However, optimization of these inhibitors is hampered by challenges including the computational evaluation of the ability of a zinc ligand to compete for coordination with nearby residues in the active site of BoNTA. No improved inhibitor of the endopeptidase has been reported. This article reports the development of a serotype-specific small-molecule inhibitor of BoNTA with Ki of 12 m. it suggests that multiple molecular dynamics simulations using the cationic dummy atom approacb are useful to structure-based design of zinc protease inhibitors.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA449190

Full Text (pdf) Availability:
View Full Text (pdf)

File: /U2/a449190.pdf

Size: 382 KB

Handle / proxy Url: http://handle.dtic.mil/100.2/ADA449190

Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD

Unclassified Title:
(U) Expression and Purification of Clostridium botulinum Type B Light Chain

Descriptive Note:
Journal article

Personal Author(s):
Gilsdorf, Janice

Gul, Nizamettin
Smith, Leonard A

Report Date:
26 Oct 2005

Media Count:
14 Page(s)

Report Number(s):
RPP-05-293
XA-USAMRIID

Contract Number:
RIID 02-4-3U-064

Monitor Series:
USAMRIID

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE

Distribution Statement:
Approved for public release; distribution is unlimited.

Abstract:
(U) A full-length synthetic gene encoding the light chain of botulinum neurotoxin serotype B, approximately 50kDa (BoNT/B LC), has been cloned into a bacterial expression vector pET24a+. BoNT/B LC was expressed in Escherichia coli BL21.DE3.pLysS and isolated from the soluble fraction. The resultant protein was purified to homogeneity by cation chromatography and was determined to be >98% pure as assessed by SDS-polyacrylamide gel stained with SilverXpress and analyzed by densitometry. Mass spectroscopic analysis indicated the protein to be 50.8kDa, which equaled the theoretically expected mass. N-terminal sequencing of the purified protein showed the sequence corresponded to the known reported sequence. The recombinant BoNT/B light chain was found to be highly stable, catalytically active, and has been used to prepare antisera that neutralizes against BoNT/B challenge. Characterization of the protein including pH, temperature, and the stability of the protein in the presence or absence of zinc is described within. The influence of pH differences, buffer, and added zinc on secondary and tertiary structure of BoNT/B light chain was analyzed by circular dichroism and tryptophan fluorescence measurements. Optimal conditions for obtaining maximum metalloprotease activity and stabilizing the protein for long term storage were determined. We further analyzed the thermal denaturation of BoNT/B LC as a function of temperature to probe the pH and added zinc effects on light chain stability. The synthetic BoNT/B LC has been found to be highly active on its substrate (vesicle associated membrane protein-2) and, therefore, can serve as a useful reagent for BoNT/B research.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA449700

Full Text (pdf) Availability:
View Full Text (pdf)

File: /U2/a449700.pdf
Size: 107 KB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA449700

Corporate Author:
WALTER REED ARMY INST OF RESEARCH WASHINGTON DC DIV OF EXPERIMENTAL THERAPEUTICS

Unclassified Title:
(U) Application of Sirna Technology to Manipulate Factors Involved in Acetylcholine Exocytosis and Botulinum Toxicity

Personal Author(s):
Ishida, Hiroshi
Erickson, Kelly
Ray, Prabhati

Report Date:
01 Oct 2005

Media Count:
6 Page(s)

Report Number(s):
XA-WRAIR

Monitor Series:
WRAIR

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE

Distribution Statement:
Approved for public release; distribution is unlimited.

Abstract:
(U) We demonstrated that the RhoB signaling pathway, regulates ACh release via actin cytoskeletal reorganization and that botulinum toxin type A (BoNT) inhibits neuroexocytosis by targeting the RhoB pathway in nerve growth factor-differentiated PC12 cells. To confirm these facts, small interfering RNA (siRNA) was used to knockout the expression of RhoB. Transfection of PC12 cells by the siRNA resulted in about 70% reduction of both mRNA and RhoB expression. This siRNA-induced RhoB suppression totally inhibited ACh release actin reorganization. The results of these studies strongly suggest that RhoB is involved in ACh exocytosis, likely that RhoB is a target of BoNT.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA436372

Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a436372.pdf
Size: 168 KB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA436372

Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD DIV OF TOXINOLOGY AND AEROBIOLOGY

Unclassified Title:
(U) Characterization of Botulinum Progenitor Toxins by Mass Spectrometry

Personal Author(s):
Hines, Harry B
Lebeda, Frank
Hale, Martha
Brueggemann, Ernst E

Report Date:
Aug 2005

Media Count:
11 Page(s)

Report Number(s):
RPP-04-370
XA-USAMRIID

Monitor Series:
USAMRIID

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE

Distribution Statement:
Approved for public release; distribution is unlimited.

Abstract:
(U) Botulinum toxin analysis has renewed importance. This study included the use of nanochromatography-nanoelectrospray-mass spectrometry/mass spectrometry to characterize the protein composition of botulinum progenitor toxins and to assign botulinum progenitor toxins to their proper serotype and strain by using currently available sequence information. Clostridium botulinum progenitor toxins from strains Hall, Okra, Stockholm, MDPH, Alaska, Langeland, and 89 representing serotypes A through G, respectively, were reduced, alkylated, digested with trypsin, and identified by matching processed product ion spectra of the tryptic peptides to proteins in accessible databases. All proteins known to be present in progenitor toxins from each serotype were identified. Additional proteins, including flagellins, ORF-X1, and neurotoxin binding protein, not previously reported to be associated with progenitor toxins, were present also in samples from several serotypes. Protein identification was used to assign toxins to a serotype and strain. Serotype assignments were accurate, and strain assignments were best when either sufficient nucleotide or amino acid sequence data were available. Minor difficulties were encountered using neurotoxin-associated protein identification for assigning serotype and strain. This study found that combined nanoscale chromatographic and mass spectrometric techniques can characterize C. botulinum progenitor toxin protein composition and that serotype/strain assignments based upon these proteins can provide accurate serotype and, in most instances, strain assignments using currently available information. Assignment accuracy will continue to improve as more nucleotide/amino acid sequence information becomes available for different botulinum strains.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA442476
Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a442476.pdf
Size: 570 KB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA442476
Corporate Author:
ARMY MEDICAL RESEARCH INST OF CHEMICAL DEFENSE ABERDEEN PROVING GROUND MD
Unclassified Title:
(U) Primary Cell Culture for Evaluation of Botulinum Neurotoxin Antagonists
Descriptive Note:
Open literature
Personal Author(s):
Sheridan, Robert E
Smith, Theresa J
Adler, Michael
Report Date:
Jan 2005
Media Count:
7 Page(s)
Report Number(s):
USAMRICD-P00-026
XA-USAMRICD
Monitor Series:
USAMRICD
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Distribution Statement:
Approved for public release; distribution is unlimited.
Abstract:
(U) The actions of botulinum neurotoxin (BoNT) were studied on evoked release of the neurotransmitter glycine in primary mouse spinal cord cells. 3[H]-glycine was taken up by cells in physiological solution and released by depolarization with 56 mM K + in the presence of 2 mM Ca2+. Release of 3 [H]-glycine was found to be inhibited by BoNT serotypes A, B and E with similar potency ratios to those observed in the acutely isolated mouse diaphragm muscle. When spinal cord cultures were exposed to BoNT/A for 24 h, inhibition of 3[H]-glycine release was detected at toxin concentrations as low as 10-14 M, and complete inhibition was observed at concentration >10-12 M. Preincubation of BoNT/A with polyclonal equine antiserum led to antagonism of toxin-induced inhibition of 3[H]-glycine release in spinal cord cells and to protection of mice from the lethal effects of BoNT/A. It is concluded that spinal cord neurons are a useful model for studying botulinum intoxication and for evaluating BoNT antagonists.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA437753
Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a437753.pdf
Size: 19 MB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA437753
Corporate Author:
MASSACHUSETTS UNIV NORTH DARTMOUTH
Unclassified Title:
(U) Protein Receptor(s) of Botulinum Neurotoxin
Descriptive Note:
Final rept. 19 Dec 2001-18 Dec 2004
Personal Author(s):
Singh, Bal R
Report Date:
Jan 2005
Media Count:
361 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-02-C-0001
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Distribution Statement:
Approved for public release; distribution is unlimited.
Abstract:
(U) Seven serotypes of botulinum neurotoxin (BoNT) are a group of water-soluble large proteins that act on the presynaptic nerve cells of the neuro-muscular junctions. BoNTs act intracellulary to block acetylcholine neurotransmitter release leading to the flaccid muscle paralysis in the dreaded botulism disease. In order to enter the neuronal cells, BoNTs bind to as yet to be clearly identified protein receptor(s), whicb could be targeted to develop proper antidotes. The aim of this research has been to identify protein receptor(s) of BoNTs by purifying them from neuronal tissues, and characterize its binding mechanism with the neurotoxins, including the effects of low pH and membrane lipid interactions. During the past three years, we have made major strides in discovering the domain of receptor that binds to the BoNT/A and /E, a novel form of BoNT/E, interaction of native and purified BoNTs to the a potential receptor protein, GT1b-induced structural changes in purified BoNT/E and its light chain, role of receptor in the translocation of the toxin, differential binding of the identified receptor with different serotypes of BoNT, identification of a component within BoNT complex that effectively binds to nerve membrane, and a surprise survival of quahogs with exposure to heavy doses of BoNT. In addition, we have improved methodologies to examine structural changes in BoNT proteins. These results have

been communicated through 8 published article, 2 pending publications, and over 35 conference presentations.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA434855
Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a434855.pdf
Size: 652 KB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA434855
Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD
Unclassified Title:
(U) Conformational Sampling of the Botulinum Neurotoxin Serotype A Light Chain: Implications for Inhibitor Binding
Personal Author(s):
Burnett, James C
Schmidt, James J
McGrath, Connor F
Nguyen, Tam L
Hermone, Ann R
Panchal, Rekha G
Vennerstrom, Jonathan L
Kodukula, Krishna
Zaharevitz, Daniel W
Gussio, Rick
Bavari, Sina
Report Date:
11 Nov 2004
Media Count:
11 Page(s)
Report Number(s):
XA-USAMRIID
Monitor Series:
USAMRIID
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
26 - NOT AVAILABLE IN MICROFICHE
Distribution Statement:
Approved for public release; distribution is unlimited., Availability: This document is not available from DTIC in microfiche.
Abstract:

(U) Botulinum neurotoxins (BoNTs) are the most potent of the known biological toxins, and consequently are listed as category A biowarfare agents. Currently, the only treatments against BoNTs include preventative antitoxins and long-term supportive care. Consequently, there is an urgent need for therapeutics to counter these enzymes--post exposure. In a previous study, we identified a number of small, nonpeptidic lead inhibitors of BoNT serotype A light chain (BoNT/A LC) metalloprotease activity, and we identified a common pharmacophore for these molecules. In this study, we have focused on how the dynamic movement of amino acid residues in and surrounding the substrate binding cleft of the BoNT/A LC might affect inhibitor binding modes. The X-ray crystal structures of two BoNT/A LCs (PDB refcodes=3BTA and 1E1H) were examined. Results from these analyses indicate that the core structural features of the examined BoNT/A LCs, including alpha-helices and beta-sheets, remained relatively unchanged during 1ns dynamics trajectories. However, conformational flexibility was observed in surface loops bordering the substrate binding clefts in both examined structures. Our analyses indicate that these loops may possess the ability to decrease the solvent accessibility of the substrate binding cleft, while at the same time creating new residue contacts for the inhibitors. Loop movements and conformational/positional analyses of residues within the substrate binding cleft are discussed with respect to BoNT/A LC inhibitor binding and our common pharmacophore for inhibition. The results from these studies may aid in the future identification/development of more potent small molecule inhibitors that take advantage of new binding contacts in the BoNT/A LC.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA428643
Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a428643.pdf
Size: 886 KB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA428643
Corporate Author:
CALIFORNIA UNIV SAN DIEGO LA JOLLA
Unclassified Title:
(U) Combinatorial Strategies and High Throughput Screening in Drug Discovery Targeted to Channel of Botulinum
Descriptive Note:
Annual rept. 1 Sep 2003-31 aug 2004
Personal Author(s):
Montel, Mauricio
Report Date:
Sep 2004
Media Count:
17 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:

DAMD17-02-C-0106

Monitor Series:
USAMRMC

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE

Abstract:
(U) This program examines innovative approaches and powerful new technologies to identify selective and potent agents directed to prevent or relieve the neuroparalytic toxic actions of botulinum toxin A (BoNTA)1. The focus is on the ion channel forming activity pf BoNTs as a validated target to screen for inhibitors of the translocation of the light chain into the cytosol and therefore to attenuate the BoNT neurotoxicity. The key of the program is based on our discovery that the heavy chain (HC) of BoNT acts as both a channel and a transmembrane chaperone for the light chain (LC) to ensure a trans location competent conformation during its transit from the acidic endosome into the cytosol - its site of action. This is an exciting time to focus on innovative technologies to uncover lead compounds that may represent a potential new generation of useful and safe antidotes for BoNTs.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA428309

Full Text (pdf) Availability:
View Full Text (pdf)

File: /U2/a428309.pdf

Size: 5 MB

Handle / proxy Url: http://handle.dtic.mil/100.2/ADA428309

Corporate Author:
RAND GRADUATE SCHOOL SANTA MONICA CA

Unclassified Title:
(U) An Investigation of the Factors Influencing Breastfeeding Patterns

Descriptive Note:
Dissertation

Personal Author(s):
Jacknowitz, Alison

Report Date:
May 2004

Media Count:
134 Page(s)

Report Number(s):
RAND/RGSD-182
XD-XD

Monitor Series:
XD

Report Classification:

Unclassified

Distribution Limitation(s):

01 - APPROVED FOR PUBLIC RELEASE

Abstract:

(U) There are well-established short- and long-term benefits of breastfeeding to mothers and children. Research has shown that breastfeeding is associated with health, cognitive, and educational benefits for children. For example, studies in the United States (U.S.) and abroad have found evidence that children who are breastfed have lower rates of urinary tract infections, respiratory tract infections, diarrhea, allergic diseases, otitis media, bacterial meningitis, botulism, bacteremia, and necrotizing enterocoloitis. In addition to the physiological health benefits, human milk may benefit children's cognitive development. Studies also suggest that breastfeeding is beneficial for the mother's health. The list of beneficial maternal health outcomes includes lowered risk of breast and ovarian cancers, decreased incidence of long-term osteoporosis and pregnancy-induced obesity, more rapid return to the prepartum state, and reduced menstrual blood loss. Some evidence also demonstrates an improved sense of maternal self-esteem, bonding with infant, and success with mothering. Both individuals and society accrue large benefits from breastfeeding. For example, one study finds that medical expenditures were 20 percent less for fully-breastfed infants compared to never-breastfed infants (Hoey and Ware 1997). In addition, an analysis by the U.S. Department of Agriculture's Economic Research Service estimates at least $3.6 billion in annual savings if the prevalence of exclusive breastfeeding was increased to those levels recommended by the Surgeon General (Weimer 2001). This figure reflects $3.1 billion in savings attributable to preventing premature deaths and $0.5 billion in savings associated with reduced medical expenses and indirect costs of time and earnings savings to parents. These estimates should be considered conservative as they only include the costs of three common infant illnesses..

Abstract Classification:

Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:

ADA419148

Full Text (pdf) Availability:

View Full Text (pdf)

File: /U2/a419148.pdf

Size: 2 MB

Handle / proxy Url: http://handle.dtic.mil/100.2/ADA419148

Corporate Author:

CALIFORNIA UNIV SAN DIEGO LA JOLLA

Unclassified Title:

(U) Combinatorial Strategies and High Throughput Screening in Drug Discovery Targeted to the Channel of Botulinum Neurotoxin

Descriptive Note:

Annual rept. 1 Sep 2002-31 Aug 2003

Personal Author(s):

Montal, Mauricio

Report Date:

Sep 2003

Media Count:
27 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-02-C-0106
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) The ultimate goal of this program is to discover selective and potent drugs targeted to prevent or relieve the neurotoxic actions of botulinum neurotoxin (BoNT) A. A major goal of this program is the identification of open channel blockers as a single class of drugs that would be effective against all BoNT isoforms. The major focus thus far has been the implementation of a reliable and robust high-throughput screen for blockers specific for BoNT. This facet of the program involves the use of the VIPR(Trademark) Voltage/Ion Probe Reader, a proven strategy for high-throughput screening, using nerve growth factor-differentiated pheochromocytoma PC12 cells in which BoNTA forms channels with similar properties to those previously characterized in lipid bilayers. The fidelity of the assay relies on fluorescence measurements of membrane potential changes as an index of open BoNT channels and increased cation conductance. The immediate task is to select mixtures from synthetic combinatorial libraries with high blocking activity to deconvolute and identify the most potent compounds. We consider the BoNT channel as a validated target for intervention aimed to inhibit the translocation of the light chain into the cytosol and therefore to attenuate the BoNT neurotoxicity.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA421172
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/a421172.pdf
Size: 630 KB
Corporate Author:
ARMY MEDICAL RESEARCH INST OF CHEMICAL DEFENSE ABERDEEN PROVING GROUND MD
Unclassified Title:
(U) A Capillary Electrophoresis Technique for Evaluating Botulinum Neurotoxin B Light Chain Activity
Descriptive Note:
Open literature
Personal Autbor(s):
Adler, Michael

Shafer, Harlan F
Manley, Heather A
Hackley, Brennie E , Jr
Nicholson, James D

Report Date:
Jul 2003

Media Count:
9 Page(s)

Report Number(s):
USAMRICD-P03-004
XA-USAMRICD

Monitor Series:
USAMRICD

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY

Distribution Statement:
Availability: Pub. in Journal of Protein Chemistry, v22 n5 p441-448, Jul 2003. Available only to DTIC users. No copies furnished by NTIS.

Abstract:
(U) Botulinum neurotoxin B (BoNT/B) produces muscle paralysis by cleaving synaptobrevin/vesicle- associated membrane protein (VAMP), an 18-kDa membrane-associated protein located on the surface of small synaptic vesicles. A capillary electrophoresis (CE) assay was developed to evaluate inhibitors of the proteolytic activity of BoNT/B with the objective of identifying suitable candidates for treatment of botulism. The assay was based on monitoring the cleavage of a peptide that corresponds to residues 44-94 of human VAMP-2 (V5 1) following reaction with the catalytic light chain (LC) of BoNT/B. Cleavage of V51 generated peptide fragments of 18 and 33 amino acids by scission of the bond between Q76 and F77. The fragments and parent peptide were clearly resolved by CE, allowing accurate quantification of the BoNT/B LC-mediated reaction rates. The results indicate that CE is suitable for assessing the enzymatic activity of BoNT/B LC.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA411069

Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/a411069.pdf
Size: 695 KB

Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD

Unclassified Title:
(U) Fluorigenic Substrates for the Protease Activities of Botulinum Neurotoxins, Serotypes A, B,

and F
Personal Author(s):
Schmidt, James J
Stafford, Robert G
Report Date:
Jan 2003
Media Count:
8 Page(s)
Report Number(s):
XA-USAMRIID
Monitor Series:
USAMRIID
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY
Distribution Statement:
Availability: Pub. in Applied and Environmental Microbiology, v69 n1 p297-303, Jan 2003. Available only to DTIC users. No copies furnished by NTIS.
Abstract:
(U) The seven botulinum neurotoxins (BoNTs) are zinc metalloproteases that cleave neuronal proteins involved in neurotransmitter release and are among the most toxic natural products known. High-throughput BoNT assays are needed for use in antibotulinum drug discovery and to characterize BoNT protease activities. Compared to other proteases, BoNTs exhibit unusually stringent substrate requirements with respect to amino 0 acid sequences and polypeptide lengths.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA412928
Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a412928.pdf
Size: 3 MB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA412928
Corporate Author:
WISCONSIN UNIV-MADISON
Unclassified Title:
(U) Interagency Botulism Research Coordinating Committee
Descriptive Note:
Conference proceedings, 22-25 Oct 2002
Personal Author(s):
Johnson, Eric A
Report Date:
Nov 2002

Media Count:
55 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-02-P-1115
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA409546
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/a409546.pdf
Size: 633 KB
Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD
Unclassified Title:
(U) Free-Energy Contributions to Complex Formation Between Botulinum Neurotoxin Type B and Synaptobrevin Fragment
Personal Author(s):
Olson, Mark A
Armendinger, Timothy L
Report Date:
31 May 2002
Media Count:
6 Page(s)
Report Number(s):
XA-USAMRIID
Monitor Series:
USAMRIID
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY
Distribution Statement:
Availability: Pub. in Protein Engineering, v15 n9 p739-743, 2002. Available only to DTIC users. No copies furnished by NTIS.
Abstract:
(U) Free-energy terms that contribute to complex formation between the catalytic domain of botulinum neurotoxin type B (BoNT/B-Lc) and a 36-residue synaptobrevin fragment were

estimated by using a combination of microscopic simulations and continuum methods. The complex for a non-hydrolyzed substrate was calculated by optimizing an energy function applied to the X-ray co-crystal structure of BoNT/B-Lc bound with reaction products from a cleaved synaptobrevin peptide, refined to high crystallographic thermal factors. The estimated absolute binding affinity of the simulation structure is in good qualitative agreement with the experimental free energy of Michaelis complex formation, given the approximations of the model calculations. The simulation structure revealed significant complex stabilization from the hydrophobic effect, while the electrostatic cost of releasing water molecules from the interface determined to be highly unfavorable. By partitioning the total electrostatic and hydrophobic terms into residue free-energy contributions, a binding-affinity signature' for synaptobrevin was developed from the optimized conformation. The results demonstrate the effect of substrate length on complex formation and identify a peripheral high-affinity binding site near the N-terminal region that might initiate cooperative activation responsible for the large minimal substrate length requirement. The so-called SNARE motif is observed to contribute negligible free energy of binding.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA407696
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/a407696.pdf
Size: 720 KB
Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD
Unclassified Title:
(U) Antibody Response to a Delayed Booster Dose of Anthrax Vaccine and Botulinum Toxoid
Personal Author(s):
Pittman, Phillip R
Hack, Dallas
Mangiaflco, Joseph
Gibbs, Paul
McKee, Kelly T , Jr
Report Date:
Jan 2002
Media Count:
11 Page(s)
Report Number(s):
XA-USAMRIID
Monitor Series:
USAMRIID
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE

20 - JOURNAL ARTICLES; DTIC USERS ONLY

Distribution Statement:

Availability: Pub. in Vaccine, v20 i16, p2107-2115,2002. Available only to DTIC users. No copies furnished by NTIS.

Abstract:

(U) We evaluated the prevalence and concentration of serum antibodies 18-24 months after primary inoculation with anthrax and botulinum vaccines, and assessed the reactogenicity and immunogenicity of a signifcantly delayed booster dose of these vaccines. Five Hundred & eight male active-duty military personnel received one, two or three inoculations with anthrax vaccine &/or botulinum toxoid in 1990/1991 in preparation for Operations Desert Shield/Desert Storm. Subjects were vaccinated with the licensed anthrax vaccine, adsorbed (AVA) & pentavalent (ABCDE) botulinum toxoid (PBT)BB-IND 3723. Anthrax protective antigen (PA) IgG antibody was measured in serum using an immunocapture enzyme-linked immunosorbent assay (ELISA). A mouse neutralization test was used to determine the titer of Clostridium botulinum type A antitoxin in serum samples. The prevalence of anti-PA IgG was 30% in individuals 18-24 months after respond. The prevalence of antibodies against botulinum toxin type A was 28% 18-24 months after initial priming. Following boosting, 99% of volunteers had serum titers >0.02 lU/ml, and 97% responded with titers >0.25IU/ml. Systemic reactions to booster vaccinations could not be specifically ascribed to one or the other vaccine, but were generally mild and of brief duration. Forty-five percent of volunteers reported one or more systemic reactions over the course of 7 days. Injection site reactions of any kind occurred in 25% of AVA recipients and in 16% of PBT recipients; persistence of local reactions beyond 7 days was infrequent. While the kinetics and durability of immune response must be studied, these findings suggest that booster doses of anthrax vaccine and botulinum toxoid sufficient to stimulate a robust anamnestic response may be given at times distant from receipt of the primary inoculations.

Abstract Classification:

Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:

ADA400463

Full Text (pdf) Availability:

View Full Text (pdf)

File: /U2/a400463.pdf

Size: 5 MB

Handle / proxy Url: http://handle.dtic.mil/100.2/ADA400463

Corporate Author:

CALIFORNIA UNIV SAN DIEGO LA JOLLA

Unclassified Title:

(U) Combinatorial Strategies and Hypothesis-Based Drug Design in Drug Discovery Targeted to the Protease and Channel Activities of Botulinum Toxin A

Descriptive Note:

Final rept. 1 Jul 1998-31 Dec 2001

Personal Author(s):

Montal, Mauricio

Report Date:

Jan 2002

Media Count:
83 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-98-C-8040
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) The ultimate goal of this program is to understand in detail the mechanisms by which botulinum neurotoxins (BoNT) abrogate neurotransmitter release. One facet is focused on the channel-forming domain of the heavy chain (HC). The aim is to identify open channel blockers as a single class of drugs that would be effective against all BoNT isoforms. A major objective is to seek direct demonstration that the HC acts as the molecular conduit for the light chain (LC) thereby allowing the protease activity to reach the cytosol where it acts. Accordingly, purified HC is first reconstituted in lipid bilayers and the direct translocation of isolated LC through the HC channel is measured by single channel recordings and also by direct analytical determination of the LC protease activity. A second facet of the program involves the concept that the peptide products of substrate proteolysis by BoNTs uncouple excitation from secretion pointing to new means of intervention. This notion, discovered for BoNT A, appears to be valid for other BoNT isoforms thereby yielding a diverse repertoire of peptide sequences that may provide insights into the molecular interactions between partner proteins involved in membrane fusion. It is anticipated that this concerted and focused approach will uncover lead compounds that may be developed into selective drugs targeted to prevent or relieve the neurotoxic actions of BoNT.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA407982
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/a407982.pdf
Size: 463 KB
Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD
Unclassified Title:
(U) Development of Sensitive Colorimetric Capture ELISAs for Clostridium Botulinum Neurotoxin Serotypes E and F
Personal Author(s):
Poli, Mark A
Rivera, Victor R
Neal, Dwayne

Report Date:
Jan 2002
Media Count:
7 Page(s)
Report Number(s):
XA-USAMRIID
Monitor Series:
USAMRIID
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY
Distribution Statement:
Availability: Pub. in Toxicon, v40 p797-802, 2002. Available only to DTIC users. No copies furnished by NTIS.
Abstract:
(U) Sensitive and specific enzyme-linked immunosorbent assays (ELISAs) were developed to detect Clostridium botulinum neurotoxin serotypes E (BoNT E) and F (BoNT F) in assay buffer and human serum. The assay is based upon affinity-purified horse polyclonal antibodies directed against the 50kD C-fragments of each toxin. Standard curves were linear over 0.5- 10 ng/ml (BoNT E) or 2-20 ng/ml (BoNT F). Accurate measurements were achieved at 0.5 ng/ml (BoNT E) or 2 ng/ml (BoNT F) in assay buffer and 10% human serum. Variation between triplicates was typically 5-10%. Less than 1% cross-reactivity occurred between other serotypes A, B, E or F). When tested against toxins complexed to their neurotoxin-associated proteins, interference was absent for BoNT F. However, pure BoNT E and that complexed to associated proteins demonstrated significant quantitative differences. We believe these differences arise from trypsin activation of the toxin. These assays demonstrated sensitivities close to that of the mouse bioassay, without the use of animals, in a much simpler format than other reported assays of similar sensitivity. a 2002 Elsevier Science Ltd. All rights reserved.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA386472
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/a386472.pdf
Size: 1 MB
Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD
Unclassified Title:
(U) Development of Vaccines for Prevention of Botulism
Personal Author(s):
Byrne, Michael P
Smith, Leonard A

Report Date:
02 Feb 2001
Media Count:
13 Page(s)
Report Number(s):
XA-USAMRIID
Monitor Series:
USAMRIID
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY
Distribution Statement:
Availability: Pub. in Biochimie, v82, p955-966, 2000. Available only to DTIC users. No copies furnished by NTIS.
Abstract:
(U) Botulism is a potentially lethal disease caused by one of seven homologous neurotoxic proteins usually produced by the bacterium, Clostridium botulinum. This neuromuscular disorder occurs through an exquisite series of molecular events, ultimately ending with the arrest of acetylcholine release and hence, flaccid paralysis. The development of vaccines that protect against botulism dates hack to the 194Os. Currently, a pentavalent vaccine that protects against BoNT serotypes A-E and a separate monovalent vaccine that protects against BoNT serotype F are available as Investigational New Drugs. However, due to the numerous shortcomings associated with the toxoid vaccines, several groups have efforts towards developing next-generation vaccines. Identifying a synthetic peptide that harbors a neutralizing epitope is one approach to a BoNT vaccine, while another employs the use of a Venezuelan equine encephalitis virus replicon vector to produce protective antigens in vivo against BoNT. The strategy used in our laboratory is to design synthetic genes encoding non-toxic, carboxy-terminal fragments of the C. botulinum, neurotoxins (rBoNT(H)). The gene products are expressed in the yeast, Pichia pastoris and purified to greater than 98% with yields typically ranging from 200-500 mg per kg of wet cells. Protective immunity to the purified products against high-level challenges of neurotoxin is elicited in mice and in non-human primates. A pre-Investigational New Drug meeting was held with the Food and Drug Administration, and the next milestone for the vaccine candidates will be clinical trials. % 2000 Societe francaise de biochimie et biologie moleculaire / Editions scientifiques et medicales Elsevier SAS
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADB270793
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/b270793.pdf
Size: 4 MB
Corporate Author:

LONDON UNIV (UNITED KINGDOM)

Unclassified Title:
(U) Development of Targeted Therapeutic Agents for Botulism

Descriptive Note:
Final rept. 25 Aug 1997-24 Jan 2001

Personal Author(s):
Dolly, Oliver J
Foran, Patrick G
Mohammed, Nadiem

Report Date:
Feb 2001

Media Count:
81 Page(s)

Report Number(s):
XA-USAMRMC

Contract Number:
DAMD17-97-C-7060

Monitor Series:
USAMRMC

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE

Abstract:
(U) The neuroparalytic symptoms of human botulism, resulting from inhibition of acetylcholine release by type A botulinum neurotoxin (BoNTIA), are life threatening and last for up to 2 years. Thus, development of a fast and effective treatment for the forces exposed to this threat warrants the highest priority. Initial experiments focussed on developing an avid inhibitor of the BoNTIA protease that cleaves SNAP-25 - a SNARE essential for transmitter release. The inhibitors prepared were toxin-resistant mutants of the full-length substrate that retained ability to mediate exocytosis. This vital advance created a means of overcoming the poisoning by transfecting cultured neuroendocrine cells with these SNAP-25 genes. Importantly, the constructs encoding several non-cleavable SNAP-25s rescued exocytosis in BoNTlA-blocked cells, providing an innovative, efficient and rapid therapy for botulism wbich can be adopted for humans. Moreover, the observed iuability of wild-type SNAP-25 to counteract the toxin's action, even at 3 weeks after intoxication, revealed the amazing longevity of type A protease.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA387280

Full Text (pdf) Availability:
View Full Text (pdf)

File: /U2/a387280.pdf

Size: 13 MB

Handle / proxy Url: http://handle.dtic.mil/100.2/ADA387280

Corporate Author:
BATTELLE MEMORIAL INST COLUMBUS OH
Unclassified Title:
(U) A Medical Research and Evaluation Facility (MREF) and Studies Supporting the Medical Chemical Defense Program. Protection of Guinea Pigs by Passive Immunization With Human Botulinum Immune Globulin Obtained Post Primary Series and Post Six-Month Booster Immunizations
Descriptive Note:
Final rept.
Personal Author(s):
Olson, Carl T
Hunt, Robert E
Starner, Rebekah A
Clagett, Michelle L
Niemuth, Nancy A
Report Date:
Oct 2000
Media Count:
383 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-89-C-9050
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) Studies (MREF Tasks 95-39, 96-45, 97-51, and 97-52) have previously demonstrated a high degree of correlation between circulating neutralizing antibody titers and protection against high doses of all botulinum toxin serotypes in the guinea pig model. Neutralizing antibodies have been proposed to the FDA as a serological marker for human protection since efficacy for This vaccine cannot be directly demonstrated in traditional human clinical trials. Task 97-53 establishes the level of passive protection conferred in the guinea pig model by pretreatment with botulism immune globulin (BIG) isolated and purified from human volunteers immunized with one-of-two different Pentavalent Botulinum Toxoid Adsorbed (PBT) vaccine lots (arbitrarily designated A or B).
Abstract Classification:
Unclassified

Tecbnical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA395305
Full Text (pdf) Availability:
View Full Text (pdf)

File: /UL/a395305.pdf
Size: 553 KB

Corporate Author:
ARMY MEDICAL RESEARCH INST OF CHEMICAL DEFENSE ABERDEEN PROVING GROUND MD

Unclassified Title:
(U) Anomalous Enhancement of Botulinum Toxin Type A Neurotoxicity in the Presence of Antitoxin

Descriptive Note:
Journal article

Personal Author(s):
Sheridan, R E
Deshpande, S S
Amersdorfer, P
Marks, J D
Smith, T

Report Date:
02 Jun 2000

Media Count:
8 Page(s)

Report Number(s):
XA-USAMRICD

Monitor Series:
USAMRICD

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY

Distribution Statement:
Availability: Pub. in Toxicon, v39 p651-657, 2001. Available only to DTIC users. No copies furnished by NTIS.

Abstract:
(U) The neutralization of botulinum toxin serotype A with polyclonal equine antitoxin was studied in isolated mouse hemidiaphragms and compared to the same action in live mice. The hiological activity of the toxin in the isolated muscle could be markedly reduced with excess antitoxin, estimated as 3:1 molar ratios of IgG Ab:toxin or better. Toxin neutralization in vivo required higher ratios of Ab:toxin, ranging from 30:1 at high toxin doses and increasing to 100:1 at 10 x LD50 toxin. At equimolar Ah to toxin ratios in the isolated muscle, the biological activity of the toxin underwent a statistically significant increase. This paradoxical effect of the polyclonal antisera was serotype selective and independent of the presence or absence of hemagglutinin in the toxin. The enhancement of toxin activity was subsequently localized to occupancy of one of four epitopes on the toxin using monoclonal antibodies to mimic the effect of the antitoxin. The enhancement of toxin activity suggests that botulinum toxin may undergo a conformational change upon binding antibodies to certain domains. This phenomenon could contribute to the observed concentration dependent changes in neutralization efficacy with antitoxin in vivo.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADB252915
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/b252915.pdf
Size: 3 MB
Corporate Author:
IMPERIAL COLL OF SCIENCE TECHNOLOGY ANDMEDICINE LONDON (UNITED KINGDOM)
Unclassified Title:
(U) Development of Targeted Therapeutic Agents for Botulism
Descriptive Note:
Annual rept. 25 Aug 1998-24 Aug 1999
Personal Author(s):
Dolly, Oliver J
Report Date:
Sep 1999
Media Count:
53 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-97-C-7060
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) Botulinum neurotoxin (BoNT) types A and B selectively block transmitter release by cleavage of SNAP-25 and synaptobrevin, respectively; many months are required for full recovery from the resultant neuromuscular paralysis. To decipher the molecular basis for such prolonged poisoning, intoxication of adreno-chromaffin cells was monitored over 2 months. Exocytosis in BoNT/B-treated cells resumed after 56 days due to the appearance of intact synaptobrevin. However, inhibition continued in BoNT/A-treated cells, over the same interval, due to the persistence of cleaved SNAP-25 (1-197). when recovery of exocytosis was attenipted by transfection of poisoned cells with the gene encoding full-length SNAP-25 (1-206), no restoration of exocytosis ensued even 3 weeks post intoxication. To ascertain if this failure was due to the persistence of the toxin's protease activity, the cells were transfected with genes encoding mutated forms of SNAP-25, engineered (via point-mutations at residues Q197 and/or R198) to be highly resistant to BoNT/A protease. Importantly, expression of these mutants yielded complete rescue of exocytosis, even 3 weeks after the initial exposure to BoNT/A. Thus, this unusually long-term persistence of protease activity is a major contributing factor to the extended duration of BoNT/A poisoning. These novel findings establish the proof of principle for fast and complete rescue from BoNT/A intoxication by an innovative and straightforward transfection process. Moreover, such a fundamental advance provides the realistic potential of a

new and effective therapy for botulism, particularly, because the technology for gene targeting is available.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA368202
Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a368202.pdf
Size: 7 MB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA368202
Corporate Author:
CALIFORNIA UNIV BERKELEY
Unclassified Title:
(U) Three Dimensional Structure Determination of Botulinum Neurotoxin
Descriptive Note:
Final rept. 1 Aug 93-30 Jun 99
Personal Author(s):
Stevens, Raymond C
Report Date:
Jul 1999
Media Count:
103 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-93-C-3118
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) The immediate goals of the contract on the structure and function relationship of botulinum neurotoxin are: (1) Determine the three-dimensional structure of botulinum neurotoxin at atomic resolution by x-ray crystallography. (2) Based on the structure of the neurotoxin, understand the toxins mechanism of action. We have accomplished the first goal of determining the three-dimensional structure of the 150 kD botulinum neurotoxin serotype A. The toxin is Y-shaped, with a very long alpha-helical translocation domain forming the backbone of the structure. The translocation domain is composed almost entirely of helices, 2 of which are 95 A in length and form a pseudo-coiled coil. The binding domain and catalytic domain are more globular in shape, located at two different ends of the translocation domain. The overall dimensions of the protein are 120 A x 80 A x 40 A. A complete description of the three-dimensional structure is described in the report. Refinement and analysis of the structure are also included. To date, a total of 8

manuscripts have been published, and 3 Ph.D. thesis generated.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA374545

Full Text (pdf) Availability:
View Full Text (pdf)

File: /UL/a374545.pdf

Size: 553 KB

Corporate Author:
ARMY MEDICAL RESEARCH INST OF CHEMICAL DEFENSE ABERDEEN PROVING GROUND MD

Unclassified Title:
(U) Evaluation of Phosphoramidon and Three Synthetic Phosphonates for Inhibition of Botulinum Neurotoxin B Catalytic Activity

Descriptive Note:
Open literature publication

Personal Author(s):
Adler, Michael
Nicholson, James D
Starks, David F
Kane, Charles T
Comille, Fabrice

Report Date:
Jan 1999

Media Count:
8 Page(s)

Report Number(s):
USAMRICD-P99-010
XA-USAMRICD

Monitor Series:
USAMRICD

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY

Distribution Statement:
Availability: Pub. in Journal of Applied Toxicology , v19 pS5-S11, 1999. Available only to DTIC users. No copies furnished by NTIS.

Abstract:
(U) Three putative metalloprotease inhibitors were synthesized and tested for their ability to inhibit the catalytic activity of botulinum neurotoxin B light chain (BoNT/B LC). The compounds were designed to emulate the naturally occurring metalloprotease inhibitor phosphoramidon, which has been reported to he a weak antagonist of BoNT/B action. All three

analogs contained the dipeptide Phe-Glu in place of Leu-Trp of phosphoramidon and possessed a phenyl, ethyl or methyl group in place of the rhamnose sugar of the parent compound. The inhibitors were evaluated in a cell-free assay based on the detection of a fluorescent product following cleavage of a 50-mer synaptohrevin peptide (Pya88 S 39-88) hy BoNT/B LC. This peptide corresponds to the hydrophilic core of synaptobrevin-2 and contains a fluorescent analog L- pyrenylalanine (Pya) in place of Tyr88. Cleavage of Pya88 S 39-88 by BoNT/B LC gives rise to fragments of 38 and 12 amino acid residues. Quantification of BoNT/B-mediated substrate cleavage was achieved by separating the 12-mer fragment (FFTSAAKLKRK-Pya) that contains the C-terminal fluorophore and measuring fluorescence at 377 nm. The results indicate that the phenyl-substituted synthetic compound ICD 2821 was slightly more active than phosphoramidon, but analogs with methyl or ethyl substitutions were relatively inactive. These findings suggest that phosphonate monoesters may be useful for providing insights into the structural requirement of BoNT/B protease inhibitors.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA374526
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/a374526.pdf
Size: 407 KB
Corporate Author:
ARMY MEDICAL RESEARCH INST OF CHEMICAL DEFENSE ABERDEEN PROVING GROUND MD
Unclassified Title:
(U) Comparison of In Vitro and In Vitro Mouse Bioassays for Botulinum Toxin Antagonists
Descriptive Note:
Open literature publication
Personal Author(s):
Apland, J P
Biser, J A
Adler, M
Ferrer-Montiel, A V
Montal, M
Report Date:
Jan 1999
Media Count:
5 Page(s)
Report Number(s):
USAMRICD-P98-039
XA-USAMRICD
Monitor Series:
USAMRICD
Report Classification:
Unclassified

Distribution Limitation(s):

01 - APPROVED FOR PUBLIC RELEASE

20 - JOURNAL ARTICLES; DTIC USERS ONLY

Distribution Statement:

Availability: Pub. in Journal of Applied Toxicology, v19 pS23-S26, 1999. Available only to DTIC users. No copies furnished by NTIS.

Abstract:

(U) Botulinum neurotoxin serotypes A and E (BoNT/A and BoNT/E) block neurotransmitter release, presumably by cleaving SNAP-25, a protein involved in docking of synaptic vesicles with the presynaptic plasma membrane. Three excitation-secretion uncoupling peptides (ESUPs), which mimic the carboxy-terminal domain of SNAP-25 and span or adjoin the cleavage sites for BoNT/A and BoNT/E, also inhibit transmitter release from permeabilized bovine chromaffin cells. In this study, these peptides were tested for effects on acetylcholine (ACh) release at an identified cholinergic synapse in isolated buccal ganglia of Aplysia Californica. The presynaptic neuron was stimulated electrically to elicit action potentials. The postsynaptic neuron was voltage-clamped, and evoked inhibitory postsynaptic currents (IPSCs) were recorded. The ESUPs were pressure-injected into the presynaptic neuron, and their effects on the amplitude of the IPSCs were studied. Acetylcholine release from presynaptic cells, as measured by IPSC amplitudes, was gradually inhibited by the ESUPs. All three peptides caused ca. 40% reduction in IPSC amplitude in 2 h. Random-sequence peptides of the same amino acid composition had no effect. Injection of BoNT/E, in contrast, caused ca. 50% reduction in IPSC amplitude in 30 min and almost complete inhibition in 2 h. These results are the first demonstration that ESUPs block neuronal cholinergic synaptic transmission. They are consistent with the concept that ESUPs compete with the intact SNAP-25 for binding with other fusion proteins, thus inhibiting stimulus-evoked exocytosis of neurotransmitter.

Abstract Classification:

Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:

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Full Text (pdf) Availability:

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File: /UL/a359637.pdf

Size: 777 KB

Corporate Author:

ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD

Unclassified Title:

(U) Purification, Potency, and Efficacy of the Botulinum Neurotoxin Type A Binding Domain from Pichia pastoris as a Recombinant Vaccine Candidate.

Descriptive Note:

Scientific Paper

Personal Author(s):

Byrne, Michael P

Smith, Theresa J

Montgomery, Vicki A

Smith, Leonard A

Report Date:
Oct 1998
Media Count:
7 Page(s)
Report Number(s):
XA-USAMRIID
Monitor Series:
USAMRIID
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY
Distribution Statement:
Availability: Pub. in Infection and Immunity, p4817-4822, Oct 98. Available only to DTIC users. No copies furnished by NTIS.
Abstract:
(U) Recombinant botulinum neurotoxin serotype a binding domain BoNT/A(Hc), expressed in Pichia pastoris, was developed as a vaccine candidate for preventing botulinum neurotoxin type A (BoNT/A) intoxication. After fermentation and cell disruption, BoNT/A(Hc) was purified by using a three-step chromatographic process consisting of expanded-bed chromatography, Mono S cation-exchange chromatography, and hydrophobic interaction chromatography. Two pools of immunogenic product was separated on the Mono S column and processed individually. Both products were more than 95% pure and indistinguishable by sodium dodecyl sulfate-polyacrylamide gel electrophoresis, Western blot analysis, and enzyme-linked immuuosorbent assay (ELISA). Each protein was assayed for potency in mice at immunogen doses ranging from 2.4 ng to 10 ug, followed by challenge with I,000 mouse intraperitoneal 50% lethal doses (i.p. LD50) of BoNT/A. The calculated 50% effective dose for both peaks was approxiniately 0.1 ug/mouse. Peak 1 was evaluated further in a mouse efficacy assay. Mice were injected either one, twice, or three times at five different doses and subsequently challenged with 100,000 mouse i.p. LD50 of BoNT/A. In general, multiple injections protected better than one, with complete or nearly complete protection realized at doses of >- 0.5 ug/mouse. Serum neutralization and ELISA titers were also determined. Tellingly, 82 of 83 mice with antibody titers of >- 1,600, as measured by ELISA, survived, but only 6 of 42 mice with titers of <- 100 survived. This work shows that the purified BoNT/A(Hc) produced was highly effective immunogen, able to protect against a high challenge dose of neurotoxin.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA360768
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/a360768.pdf
Size: 774 KB
Corporate Author:

ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD

Unclassified Title:
(U) Identifying the Principal Protective Antigenic Determinants of Type A Botulinum Neurotoxin.

Descriptive Note:
Scientific Paper

Personal Author(s):
Bavari, S
Pless, Dorothy D
Torres, Edna R
Lebeda, Frank J
Olson, Mark A

Report Date:
Jan 1998

Media Count:
8 Page(s)

Report Number(s):
XA-USAMRIID

Monitor Series:
USAMRIID

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY

Distribution Statement:
Availability: Pub. in Vaccine, v16 n19, p1850-1856, 1998. Available only to DTIC users. No copies furnished by NTIS.

Abstract:
(U) The neurotoxins from Clostridium botulinum (BoNT serotype A-G) exert their lethal effect by preventing the release of acetylcholine at the neuromuscular junction. As with tetanus toxin, immunization with a non-toxic fragment, the 50 kDa C-terminal portion of BoNT/A (Hc; residues 861-1296), protects mice against lethal challenges with the intact toxin. To locate the neutralizing epitopes, several protective monoclonal antibodies (mAbs) against BoNT/A-Hc were isolated and cloned. Specific binding of the mAbs to BoNT/A-Hc was demonstrated by surface plasmon resonance, with Kds in the range of 10-11 M. These antibodies recognized a genetically engineered polypeptide (1150-1289) that was previously shown to induce protective immunity. Prior to the determination of the X-ray crystal structure of the tetanus neurotoxin Hc fragment, molecular modelling studies indicated that it contained two highly solvent-exposed loops. Based on these predictions, two 25-mer Hc-peptides corresponding to these two regions were synthesized and were demonstrated to bind the neutralizing mAbs. Mice immunized with the Hc-peptides had high levels of antibodies that recognized BoNT/A-Hc. However, immunizations with only one of the Hc peptides protected when mice were challenged with BoNT/A. On the basis of these analyses, it should be possible to develop small peptides that could be useful in the design of future vaccines against these neurotoxins.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA359623
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/a359623.pdf
Size: 914 KB
Corporate Author:
ARMY MEDICAL RESEARCH AND MATERIEL COMMAND FORT DETRICK MD
Unclassified Title:
(U) Development of Recombinant Vaccines for Botulinum Neurotoxin
Personal Author(s):
Smith, Leonard A
Report Date:
Jan 1998
Media Count:
11 Page(s)
Report Number(s):
XA-USAMRMC
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY
Distribution Statement:
Availability: Pub. in Toxicon v36 n11 p1539-1548, 1998. Available only to DTIC users. No copies furnished by NTIS.
Abstract:
(U) Synthetic genes encoding non-toxic, carboxyl-terminal regions (^5O kDa) of botulinum neurotoxin (BoNT) serotype A and B (referred to as fragment C or Hc) were constructed and cloned into the methylotropic yeast, Pichia Pastoris. Genes specifying BoNTA(Hc) and BoNTB (Hc) were expressed as both intracellular and secreted products. Recombinants, expressed intracellularly, yielded products with the expected molecular weight as judged by SDS-PAGE and Western blot (immunoblot) analysis, while secreted products were larger due to glycosylation. Gene products were used to vaccinate mice and evaluated for their ability to elicit protective antibody titers in vivo.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADB231856
Full Text (pdf) Availability:
View Full Text (pdf)

File: /UL/b231856.pdf
Size: 837 KB
Corporate Author:
PROMEGA MADISON WI
Unclassified Title:
(U) The Design and Synthesis of Orally Active Inhibitors of Botulinum Toxin Metalloproteases
Descriptive Note:
Final rept. 25 Nov 1996-24 May 1997
Personal Author(s):
Zdanovsky, Alexey G
Report Date:
Jun 1997
Media Count:
18 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-97-C-7026
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) Our goal was to design, synthesize and screen noval organic chemicals designed to inhibit all or several of the known botulinum toxin (BoNT)-metalloproteases. We have succeeded in demonstrating the feasibility of our approach to the design of botulinum inhibitors based on using the weak activity of captopril as a lead compound. We report the first prototype compounds that exceed our captopril lead compound by at least an order of magnitude in inhibitory properties. Such activity could be substrantially enhanced by the resolution of the stereo enteriomeric compounds into the optical isomer possessing the biological activity.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA328904
Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a328904.pdf
Size: 2 MB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA328904
Corporate Author:
CALIFORNIA UNIV DEPT OF ENERGY
Unclassified Title:
(U) Three-Dimensional Structure Determination of Botulinum Toxin.

Descriptive Note:
Annual rept. 1 Aug 95-31 May 97,
Personal Author(s):
Stevens, Ray C
Report Date:
May 1997
Media Count:
45 Page(s)
Report Number(s):
DAMD17-93-C-3118
XA-USAMRMC
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) The immediate goals of the contract on the structure and function relationship of botulinum neurotoxin are: 1) Determine the three-dimensional structure of botulinum neurotoxin at atomic resolution by x-ray crystallography. 2) Based on the structure of the neurotoxin, understand the toxins mechanism of action. We have accomplished the first goal of determining the three-dimensional structure of the 150 kD botulinum neurotoxin serotype A. The toxin is Y-shaped, with a very long alpha-helical translocation domain forming the backbone of the structure. The translocation domain is composed almost entirely of helices, 2 of which are 9s A in length and form a pseudo-coiled coil. The binding domain and catalytic domain are more globular in shape, located at two different ends of the translocation domain. The overall dimensions of the protein are 120 A x 80 A x 40 A. A complete description of the three- dimensional structure is described in the report. Refinement and analysis of the structure are presently in progress.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA339466
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/a339466.pdf
Size: 749 KB
Corporate Author:
ARMY MEDICAL RESEARCH INST OF CHEMICAL DEFENSE ABERDEEN PROVING GROUND MD
Unclassified Title:
(U) Structural Features of Aminoquinolines Necessary for Antagonist Activity Against Botulinum Neurotoxin.
Descriptive Note:
Open literature

Personal Author(s):
Sheridan, R E
Deshpande, S S
Nicholson, J D
Adler, M
Report Date:
Jan 1997
Media Count:
14 Page(s)
Report Number(s):
USAMRICD-P96-038
XA-USAMRICD
Monitor Series:
USAMRICD
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY
Distribution Statement:
Availability: Pub. in Toxicon, v35 n9 p1439-1451, 1997. Available only to DTIC users. No copies furnished by NTIS.
Abstract:
(U) R. E. Sheridan, S. S. Deshpande, J. D. Nicholson and M. Adler. Structural features of aminoquinolines necessary for antagonist activity against botulinum neurotoxin. Toxicon 35, 1439-1451, 1997. Certain aminoquinoline antimalarial compounds, such as chloroquine, antagonize the paralytic actions of botulinum neurotoxins (BoNT). These studies have been extended to determine the critical structural groups necessary for synthetic aminoquinolines to have antagonist activity against BoNT. Isolated mouse hemidiaphragms were maintained at 360C and indirectly stimulated; the resulting isometric twitch tensions were recorded as a measure of synaptic function. The muscles were exposed to the test compounds before being treated with a challenge concentration of BoNT (typically 0.2 nM of serotype A). The time to onset of 50% muscle paralysis due to BoNT was used to assess quantitatively the (J efficacy of the test compounds, which were then ranked on the basis of the concentrations necessary to delay paralysis by a specified time increment. Of the compounds tested, those having a 7-chloro-4-aminoquinoline configuration, similar to chloroquine (or the structurally similar 6-chloro-9-amino acridine group in quinacrine), were most effective. Truncation of the alkyl-amino-alkyl group from chloroquine and conversion of the 4-amino-nitrogen to a primary amine did not significantly alter its effectiveness as a BoNT antagonist. However, the 6-chloro- or 8-chloro-isomers of chloroquine were essentially ineffective.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA313747
Full Text (pdf) Availability:

View Full Text (pdf)
File: /U2/a313747.pdf
Size: 303 KB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA313747

Corporate Author:
VETERANS ADMINISTRATION MEDICAL CENTER PITTSBURGH PA

Unclassified Title:
(U) X-Ray Crystallography of Botulinum Neurotoxins.

Descriptive Note:
Final rept. 1 May 93-30 Apr 96,

Personal Author(s):
Sax, Martin

Report Date:
May 1996

Media Count:
8 Page(s)

Report Number(s):
XA-USAMRMC

Monitor Series:
USAMRMC

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE

Abstract:
(U) Botulinum neurotoxin E is understudy crystallographically. Preliminary crystal data have been collected and a heavy atom derivative search is in progress. The structural information is relevant for applications in the development of vaccines and in the improvement of therapeutic uses of the neurotoxin.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA314749

Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/a314749.pdf
Size: 425 KB

Corporate Author:
ARMY MEDICAL RESEARCH INST OF CHEMICAL DEFENSE ABERDEEN PROVING GROUND MD

Unclassified Title:
(U) Protonophore Antagonism of Botulinum Toxin in Mouse Muscle,

Personal Author(s):
Sheridan, R E

Report Date:

28 Feb 1996

Media Count:
8 Page(s)

Report Number(s):
USAMRICD-P95-017
XA-USAMRICD

Monitor Series:
USAMRICD

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY

Distribution Statement:
Availability: Pub. in Toxicon, v34 n8 p849-855 1996. Available only to DTIC users. No copies furnished by NTIS.

Abstract:
(U) R. E. Sheridan. Protonophore antagonism of botulinum toxin in mouse muscle. Toxicon 34, 849-855 1996.-Botulinum neurotoxins (BoNT) are thought to enter cells through endocytotic vesicles where acidification is required for release of these toxins into the cytoplasm. Two ionophores, nigericin and monensin, that increase membrane permeability to H and K or H +, Na and K +, respectively, block vesicle acidification by acting as H shunts to neutralize pH gradients. Nanomolar concentrations of nigericin or monensin delayed development of blockade in BoNT-A or BoNT-B treated muscles two- to threefold over onset times in unprotected muscles. However, higher concentrations of the ionophores directly blocked synapses. Thus, nigericin and monensin could delay onset of BoNT paralysis only over a narrow range of concentrations. Copyright C' 1996 Elsevier Science Ltd

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA306803

Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/a306803.pdf
Size: 872 KB

Corporate Author:
ARMY MEDICAL RESEARCH INST OF CHEMICAL DEFENSE ABERDEEN PROVING GROUND MD

Unclassified Title:
(U) Effect of 3,4-Diaminopyridine on Rat Extensor Digitorum Longus Muscle Paralyzed by Local Injection of Botulinum Neurotoxin,

Personal Autbor(s):
Adler, Michael
Sellin, Douglas A
Gerlad, Lawrence C

Parker, W

Report Date:
Jan 1996

Media Count:
15 Page(s)

Report Number(s):
USAMRICD-P94-015-637
XA-USAMRICD

Monitor Series:
P94-015-637
USAMRICD

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY

Distribution Statement:
Availability: Pub. in Toxicon, v34 n2 p237-249, 1996. Available only to DTIC users. No copies furnished by NTIS.

Abstract:
(U) M. Adler, D. A. Macdonald, L. C. Seilin and G. W. Parker. Effect of 3,4.diaminopyridine on rat extensor digitorum longus muscle paralyzed by local injection of botulinum neurotoxin. Toxicon 34, 237-249, 1996.-The actions of the K channel blocker, 3,4-diaminopyridine (3A-DAP), were studied in the rat extensor digitorum longus (EDL) muscle following local inhibition of neuromuscular transmission by botulinum neurotoxin (BoNT). Local paralysis of the EDL muscle was induced by s.c. injections of BoNT serotypes A, B, E or F over the anterior tibialis muscle. One to 14 days later, the rats were anesthetized with urethane, and isometric twitch tensions following stimulation of the peroneal nerve were measured in situ. Muscles were paralyzed within 24 hr of administration of 5 mouse LD50 units (U) of BoNT/A and remained inhibited for the entire 14-day period of observation. Similar levels of inhibition, but of shorter duration, were observed after local injection of 20 U of BoNT/E, 104 U of BoNT/B or 20 U of BoNT/F. 3,4-DAP (4 mg/kg, i.v.) potentiated twitch tensions markedly in BoNT/A intoxicated muscle. The increase in tension developed rapidly (half. time = 5.81 +/- 0.6 min), persisted for approximately 1 hr, then decayed slowly with a halftime of 25.2 +/- 4.6 min. Subsequent administration of 3,4-DAP restored tensions to the original maxima, and this procedure could be repeated up to eight times with no decrement. The action of 3,4-DAP was comparable when given 1, 2, 3 or 7 days after BoNT/A and enhanced when administered 14 days after toxin injection. 3,4-DAP was less effective in reversing BoNT/E-induced muscle paralysis and nearly ineffective in antagonizing the paralytic actions of BoNT/B or BoNT/F.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA303514

Full Text (pdf) Availability:
View Full Text (pdf)

File: /U2/a303514.pdf
Size: 378 KB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA303514
Corporate Author:
VETERANS ADMINISTRATION MEDICAL CENTER PITTSBURGH PA
Unclassified Title:
(U) X-Ray Crystallography of Botulinum Neurotoxins.
Descriptive Note:
Annual rept. 1 May 93-30 Sep 95,
Personal Author(s):
Sax, Martin
Report Date:
Oct 1995
Media Count:
7 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
MIPR-93MM3557
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) Botulinum neurotoxin, type E (Bot E) was purified to evaluate the affects of purity on crystallization. It was found that purification of the product from PHLS/CAMR Proton, Salisbury, VK did not improve crystal quality significantly. Accordingly, the product was used as supplied in further crystallization experiments. Diffraction quality crystals were grown by VAMC personnel at Fort Detrick, but the crystal which were transported in sealed capillary tubes deteriorated in transportation. To overcome this problem, a safe and secure laboratory was set up in the Pittsburgh VAMC (UD) in compliance with Federal regulations to handle Bot E neurotoxin. Crystals were grown which diffracted to 3.A, and a set of intensity data was collected from it. Work is progressing with the aim of getting more mature and derivative data.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA299943
Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a299943.pdf
Size: 723 KB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA299943
Corporate Author:

EDGEWOOD RESEARCH DEVELOPMENT AND ENGINEERING CENTER ABERDEEN PROVING GROUND MD

Unclassified Title:
(U) Antibody-Based Detection of Toxins of Biological Origin.

Descriptive Note:
Final rept. Oct 92-Sep 93,

Personal Author(s):
Menking, Darrel E
Thompson, Roy G
Heitz, Jonathon M
Anis, Nabil A

Report Date:
Sep 1995

Media Count:
22 Page(s)

Report Number(s):
ERDEC-TR-279
XA-ERDEC

Monitor Series:
ERDEC

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE

Abstract:
(U) A Fiber optic evanescent fluorosensor was used to detect the presence of toxins of biological origin. A direct competition assay was used for cholera toxin and staphylococcus entertoxin B, and an indirect competition assay for cholera, botulinum toxoid A and ricin. Detection of toxins for both methods was in the nanomolar range.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA325467

Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/a325467.pdf
Size: 449 KB

Corporate Author:
NAVAL MEDICAL RESEARCH UNIT NO 3 FPO NEW YORK 09527

Unclassified Title:
(U) Experience with the Use of an Investigational F(ab')2 Heptavalent Botulism Immune Globulin of Equine Origin During an Outbreak of Type E Botulism in Egypt,

Personal Author(s):
Hibbs, Richard G
Weber, J T

Corwin, Andrew
Allos, Ban M
Rehim, Mohammed S

Report Date:
Aug 1995

Media Count:
6 Page(s)

Report Number(s):
XB-USAMRMC

Monitor Series:
USAMRMC

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY

Distribution Statement:
Availability: Pub. in Clinical Infectious Diseases, v23 p337-340 1996. Available only to DTIC users. No copies furnished by NTIS.

Abstract:
(U) During an outbreak of type E foodborne botulism in Cairo in 1991, an investigational equine F(ab')2 'despeciated' heptavalent botulism immune globulin (dBIG) was provided to the Egyptian Ministry of Health by the U.S. Army. Of 54 patients known to have been treated with antitoxins, 4 received commercially available trivalent antitoxins, 45 received dBIG, and 5 received both commercial antitoxin and dBIG. Herein we summarize our experience with the use of dBIG during this massive outbreak.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA299771

Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a299771.pdf
Size: 1 MB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA299771

Corporate Author:
CALIFORNIA UNIV BERKELEY

Unclassified Title:
(U) Three-Dimensional Structure Determination of Botulinum toxin.

Descriptive Note:
Annual rept.,

Personal Author(s):
Stevens, Raymond C

Report Date:
01 Ang 1995

Media Count:
19 Page(s)
Report Number(s):
44123-2799
XA-USAMRMC
Contract Number:
DAMD17-93-C-3118
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) The immediate goals on structure and function relationship studies of botulinum neurotoxin are: (1) Determine the three-dimensional structures of botulinum neurotoxins isolated Heavy chain, Light chain and holo-neurotoxin at atomic resolution by x-ray crystallography. (2) Based on the structure of the isolated chains and holo-neurotoxin, understand the toxins mechanism of action.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA294146
Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a294146.pdf
Size: 1 MB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA294146
Corporate Author:
BAYLOR COLL OF MEDICINE HOUSTON TX
Unclassified Title:
(U) Immunological Protection Against Botulinum Neurotoxin by a Synthetic Vaccine.
Descriptive Note:
Midterm rept.,
Personal Author(s):
Atassi, M Z
Report Date:
10 Apr 1995
Media Count:
27 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-93-C-3159
Monitor Series:

USAMRMC

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE

Abstract:
(U) Botulism due to food toxin is caused mainly by seven known serotypes of protein neurotoxins, botulinum neurotoxins (BoNt) produced by clostridium botulinum. BoNts are the most potent toxins and poisons known. The purpose of this work is to design a synthetic peptides vaccine for protection against BoNt. Regions of BoNt/A will be selected for synthesis, based on a number of sequence and conformational parameters and their immunological activities towards anti-BoNt/A antibodies and T cells determined. The immunodominant epitopes will be used as immunogens and those peptides which stimulate BoNt/A-cross reactive antibody and/or T cell responses will then be investigated for their capacity to provide active and passive immunity against BoNt/A challenge. The epitopes that are most protective when employed individually as immunogens will be used, in a mixture and in a multiepitope- carrier conjugate, as a vaccine for both active and passive protection of mice. The synthetic vaccine against BoNt/A will be used as a prototype to prepare synthetic vaccines containing the regions of the other serotypes that are counterparts to the regions found to be most protective on BoNt/A.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA301326

Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/a301326.pdf
Size: 452 KB

Corporate Author:
ARMY MEDICAL RESEARCH INST OF CHEMICAL DEFENSE ABERDEEN PROVING GROUND MD

Unclassified Title:
(U) A Study of Zinc-Dependent Metalloendopeptidase Inhibitors as Pharmacological Antagonists in Botulinum Neurotoxin Poisoning,

Personal Author(s):
Deshpande, Sharad S
Sheridan, Robert E
Adler, Michael

Report Date:
Jan 1995

Media Count:
8 Page(s)

Report Number(s):
USAMRICD-P94-001
XA-USAMRICD

Monitor Series:

USAMRICD

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY

Distribution Statement:
Availability: Pub. in Toxicon, v33 n4 p551-557 1995. Available only to DTIC users. No copies furnished by NTIS.

Abstract:
(U) S. S. Deshpande, R. E. Sheridan and M. Adler. A study of zinc-dependent metalloendopeptidase inhibitors as pharmacological antagonists in botulinum neurotoxin poisoning. Toxicon 33, 551-557, 1995. Zinc-dependent metallo- protease inhibitors phosphoramidon, captopril and a peptide hydroxamate were studied as potential pretreatment compounds by examining their ability to delay the onset or to prolong the time to 50% block of nerve-elicited muscle twitch tension in the mouse phrenic-nerve diaphragm (in vitro at 360C) after botulinum neurotoxin serotypes A and B (BoNT-A, BoNT-B). Addition of BoNT-A or BoNT-B (1 >c l0%lO M) produced 50% block of the twitch response at 56 + 9 min and 76 + 4 min, respectively. Preincubation (45 min) of muscles with phosphoramidon (0.2 mM) prolonged the time to 50% block by 15 min in BoNT-B-poisoned muscles with no effect on the time-course of paralysis in BoNT-A exposed muscles. When the same quantities of BoNT-A or BoNT-B (equivalent to 1 x l0-Io M bath concentration) were preincubated for 2 hr with phosphoramidon (equivalent to 0.2 mM final bath concentration), and the incubation mixture was added to the muscle chamber, the times to 50% block were prolonged by 38 min and 18 min for BoNT-B and BoNT-A, respectively. Preincubation of diaphragms with captopril (up to 10 mM) or peptide hydroxamate (75 ptM) failed to antagonize BoNT-A or BoNT-B- induced neuromuscular block. Among the three metalloprotease inhibitors examined here, only phosphoramidon showed a significant protection against both serotypes of BoNT. A search for better inhibitor compounds specifically tailored to match the active site on BoNT molecule deserves attention.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA346800

Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a346800.pdf
Size: 4 MB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA346800

Corporate Author:
CENTERS FOR DISEASE CONTROL ATLANTA GA

Unclassified Title:
(U) Summary of Notifiable Diseases, United States, 1993.

Personal Author(s):
Koo, Denise T
Dean, Andrew G

Slade, Ruth W
Knowles, Carol M
Adams, Deborah A

Report Date:
21 Oct 1994

Media Count:
96 Page(s)

Report Number(s):
XJ-XD

Monitor Series:
XD

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE

Abstract:
(U) As of January 1, 1994, 49 infectious diseases were designated as notifiable at the national level. A notifiable disease is one for which regular, frequent, and timely information on individual cases is considered necessary for the prevention and control of the disease. This section briefly summarizes the history of national notifiable disease reporting in the United States. In 1878, Congress authorized the U.S. Public Health Service (PHS) to collect morbidity reports on cholera, smallpox, plague, and yellow fever from U.S. consuls overseas; this information was to be used for instituting quarantine measures to prevent the introduction and spread of these diseases into the United States. In 1879, a specific Congressional appropriation was made for the collection and publication of reports of these notifiable diseases. The authority for weekly reporting and publication was expanded by Congress in 1893 to include data from states and municipal authorities. To increase the uniformity of the data, Congress enacted a law in 1902 directing the Surgeon General to provide forms for the collection and compilation of data and for the publication of reports at the national level. In 1912, state and territorial health authorities-in conjunction with PHS-recommended weekly telegraphic reporting of five infectious diseases and monthly reporting by letter of 10 additional diseases. The first annual summary of The Notifiable Diseases in 1912 included reports of 10 diseases from 19 states, D.C., and Hawaii. By 1928, all states, the D.C., Hawaii, and Puerto Rico were participating in national reporting of nearly 30 specified conditions. At their meeting in 1950, the State and Territorial Health Officers authorized a conference of state epidemiologists whose purpose was to determine which diseases should be reported to PHS. CDC assumed responsibility for the collection and publication of data on nationally notifiable diseases in 1961.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA288960

Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a288960.pdf
Size: 3 MB

Handle / proxy Url: http://handle.dtic.mil/100.2/ADA288960
Corporate Author:
JEFFERSON MEDICAL COLL PHILADELPHIA PA
Unclassified Title:
(U) Neuropharmacological Characterization of Botulinum Neurotoxin.
Descriptive Note:
Final rept. 30 Mar 90-31 Dec 93,
Personal Author(s):
Simpson, Lance L
Report Date:
22 Sep 1994
Media Count:
76 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-90-C-0048
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) Studies have been done in three general areas: (i) study of the mechanism of action of botulinum neurotoxin, (ii) identification of drugs that antagonize botulinum neurotoxin action, and (iii) extension of basic science studies on toxin action to the human nervous system. The two principal tissue preparations used were the mouse phrenic nerve-hemidiaphragm and the human pyramidalis muscle. The major findings were: (i) stimulation of transglutaminase activity is not likely to be relevant to clostridial toxin action, (ii) zinc chelators, such as TPEN, are intracellular antagonists of all clostridial neurotoxins, (iii) inihibitors of vascuolar adenosine triphosphatase, such as bafilomycin, antagonize all clostridial neurotoxins but not phospholipase A2 neurotoxins, and (iv) human neuromuscular junctions are sensitive to all botulinum serotypes associated with natural poisoning (e.g. , A, B, and E), and they are also sensitive to one serotype that is not typically associated with natural poisoning (e.g., C).
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA285295
Corporate Author:
CALIFORNIA UNIV BERKELEY SPONSORED PROJECTS OFFICE
Unclassified Title:
(U) Three Dimensional Structure Determination of Botulinum Neurotoxin
Descriptive Note:
Annual rept. 1 Aug 1993-31 Jul 1994

Personal Author(s):
Stevens, Raymond C
Report Date:
01 Aug 1994
Media Count:
28 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-93-C-3118
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) To determine the 3-dimensional structure of botulinum neurotoxins and their isolated domains. The following specifications are listed in the contract section C-Statement of Work: Crystallization of the 150 kDs holo-botulinum neurotoxins. Serotype A has been crystallized previously and crystallization conditions will be refined as necessary. Serotype B will be crystallized. Determination of the 3-dimensional structure of serotype A. Heavy atom derivative screening is underway. Once 2 or 3 'acceptable' derivatives are known, data collection and processing of native and derivative data will be completed. The phases of the x-ray diffraction pattern will be phased, electron density maps calculated, and the structure will be determined
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA269079
Corporate Author:
WALTER REED ARMY INST OF RESEARCH WASHINGTON DC
Unclassified Title:
(U) Botulinum Toxin A Inhibits Acetylcholine Release from Cultured Neurons in Vitro
Descriptive Note:
Journal article
Personal Author(s):
Ray, Prabhati
Report Date:
Jun 1993
Media Count:
7 Page(s)
Report Number(s):
WR-080-93
XA-USAMRDC
Monitor Series:

USAMRDC

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY

Distribution Statement:
Availability: Pub. in In Vitro Cellular and Developmental Biology, v29A p456-460 Jun 93. Available only to DTIC users. No copies furnished by NTIS.

Abstract:
(U) Clostridium botulinum type toxin A (BoTx) blocks stimulus-induced acetylcholine (ACh) release from presynaptic nerve terminals at peripheral neuromuscular junctions. However, the detailed mechanism of this effect remains elusive. One obstacle in solving this problem is the lack of a suitable in vitro homogenous cholinergic neuronal model system. We studied the clonal pheochromocytoma PC12 cell line to establish such a model. PC12 cells were differentiated in culture by treatment with 50 ng/ml nerve growth factor (NGF) for 4 days to enhance cellular ACh synthesis and release properties. Stimulation of these cells with high K+ (80 mM) in the perfusion medium markedly increased calcium-dependent (3H)ACh release compared to undifferentiated cells. Stimulated 3Hach release was totally inhibited by pretreatment of cells with 2 nM BoTx for 2 h. BoTx inhihition of (3H)ACh release was time- and concentration-dependent. A 50% inhibition was obtained after 2h incubation with a low (0.02 nM) toxin concentration. The time required for 2 nM BoTx to cause a measurable inhibition (I8%) of stimulated (3H)ACh release was 30 min. Botulinum toxin inhibition of stimulated ACh release was prevented hy toxin antiserum and heat treatment, suggesting the specificity of the toxin effect. Our results show that by differentiation with NGF, PC12 cells can be shifted from an insensitive to a sensitive state with respect to BoTx inhibition of stimulated ACh release. This cell line, therefore, may serve as a valuable in vitro cholinergic model system to study the mechanism of action of BoTx. PCI2 cells; Nerve growth factor; Botulinum toxin A; Acetylcholine.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA267I27

Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a267127.pdf
Size: I4 MB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA267I27

Corporate Author:
IMPERIAL COLL OF SCIENCE AND TECHNOLOGYLONDON (UNITED KINGDOM) DEPT OF BIOCHEMISTRY

Unclassified Title:
(U) Exploitation of Botulinum Neurotoxins for Research and Clinical Purposes

Descriptive Note:
Midterm rept. 1 Aug 199I-30 Apr 1993

Personal Author(s):
Dolly, J O
Report Date:
Jun 1993
Media Count:
59 Page(s)
Report Number(s):
XA-USAMRDC
Contract Number:
DAMD17-91-Z-1035
Monitor Series:
USAMRDC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) The major long-term goal of this contract is to develop a novel and effective treatment for human botulism by producing a drug, capable of neutralising the intracellular neuroparalytical action of botulinum neurotoxin (BoNT), and delivering this inside cholinergic neurons via a innocuous transporter form of the toxins. Towards this end, our multi-disciplinary research has demonstrated that BoNTs target to murine motor nerve endings by interaction with distinct ecto-acceptors uniquely located thereon; this 'productive' binding requires a conformation of the toxin's heavy chain (HC) that is maintained by its 'natural' association with the light chain (LC), even in the absence of the inter-chain disulphide. The subsequent acceptor-mediated uptake step could be monitored by high-resolution electron-microscopy of motor endplates labelled with BoNT-gold-conjugate, and from measurement of the inhibition of transmitter release produced by the resultant internalised LC. Importantly, experiments with modified forms of BoNT and its constituent chains revealed that the inter-chain S-S hond or its balf-cyst-ines are essential for neuronal membrane translocation whereas neither the latter nor any of the toxin's free cysteines are necessary for intracellular hlockade of transmitter release; in fact, alkylation of LC did not alter its ability to block acetylcholine release when administered intraneuronally.... Botulism, Botulinum neurotoxins, Tetanus toxin, Ectoacceptors for clostridial toxins, Neuronal internalisation of botulinum neurotoxins, Exocytosis, Neurotransmitter release, Monoclonal antibodies to botulinum neurotoxin, Chromaffin cells, Pancreatic acini, Synaptobrevin, Neutral metalloproteases, Inhibitors of Zn2+-dependent proteases, Cholinergic targetted transporter.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADP008892
Corporate Author:
WALTER REED ARMY INST OF RESEARCH WASHINGTON DC
Unclassified Title:
(U) A Novel Insight into the Mechanism of Action of Botulinum Toxin in a Cholinergic Neuronal Cell Culture Model.

Personal Author(s):
Ray, Prabhati
Berman, Johnathan D
Middleton, Wilbert
Brendle, James
Report Date:
13 May 1993
Media Count:
8 Page(s)
Report Number(s):
XA-USAMRDC
Monitor Series:
USAMRDC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) Botulinum neurotoxin type A (BoTx), which is an identified biological threat agent acts by blocking the Ca 2(+) -dependent release of the neurotransmitter acetylcholine (ACh) from presynaptic nerve terminals at neuromuscular junctions. There is no effective antidote against this deadly poison primarily due to a lack of understanding of the exact sequence of events leading to the neuromuscular blockade. We studied this mechanism in an in vitro cholinergic neuronal pheochromocytoma PC 1 2 cell line model. Cultured monolayer PC12 cells were differentiated by treatment with 50 ng/ml nerve growth factor (NGF) for 4 to 5 days to enhance cellular ACh synthesis and release. Stimulation of these cells with high K(+) (80 mM) in the perfusion medium caused a marked increase (3-4X) in 3Hach release in a Ca 2(+) -dependent manner. K(+)-stimulated (3H)ACh release was totally inhibited by pretreatment of cells with BoTx (2 nM) for 2 h. High K(+) also stimulated the release of arachidonic acid ((3H)ACh from the cell membrane, which was inhibited by BoTx (2 nM). Addition of quinacrine, a phospholipase A2 (PLA2) inhibitor, to the perfusion medium inhibited K(+)stimulated (3H)ACh and (3H)AA release in a dose-dependent manner. Inclusion of exogenous AA, the PLA(2), activator mellitin or PLA, itself prevented the effect of BoTx. These results demonstrate that in NGF differentiated PC12 cells, AA release is associated with ACh release, BoTx inhibits both processes, and increased AA can protect against BoTx. Drugs that can modulate PLA(2) activity or the level of intracellular AA or its metabolites may therefore be prospective countermeasures against BoTx poisoning.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA266203
Corporate Author:
NAVAL MEDICAL RESEARCH UNIT NO 3 FPO NEW YORK 09527
Unclassified Title:
(U) A Massive Outbreak of Type E Botulism Associated with Traditional Salted Fish in Cairo

Descriptive Note:
Publication rept.
Personal Author(s):
Weber, J T
, Richard G
Darwish, Ahmed
Mishu, Ban
Corwin, Andrew L
Report Date:
Jan 1993
Media Count:
6 Page(s)
Report Number(s):
NAMRU-3-20/93
NAMRU-3-ACN-1742
XB-NMRDC
Monitor Series:
NMRDC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY
Distribution Statement:
Availability: Pub. in Jnl. of Infectious Diseases, v167 p451-454 1993. Available only to DTIC users. No copies furnished by NTIS.
Abstract:
(U) In April 1991, 91 hospitalized patients in Cairo were reported to the Egyptian Ministry of Health with botulism intoxication. To define the spectrum of illness and identify a food vehicle, 45 patients were interviewed and a case- control investigation was conducted among families of 5 hospitalized patients. Clinical specimens and specimens of implicated food were tested for toxin and cultured for Clostridium botulinum. Hospitalized patients had symptoms consistent with botulism; 18 (20%) of 91 reported patients died. Illness was associated with eating faseikh (uneviscerated, salted mullet fish; lower 95% confidence limit of odds ratio = 6.6, P < .001). All 5 case-families purchased faseikh from one shop. Very high levels of type E botulinal toxin were detected in faseikh reported to be purchased from the implicated shop; C botulinum type E was isolated from cultures of clinical specimens and from the faseikh. This is the first documented outbreak of botulism in Egypt and the largest type E outbreak ever reported.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA253554
Corporate Author:
DEFENCE RESEARCH ESTABLISHMENT SUFFIELD RALSTON (ALBERTA)
Unclassified Title:

(U) Vaccines, Passive Immune Approaches and Treatment of Biological Agents.

Descriptive Note:
Special rept.,

Personal Author(s):
Cherwonogrodzky, John W
Di Ninno, Vincent L

Report Date:
May 1992

Media Count:
41 Page(s)

Report Number(s):
DRES-SP-155

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE

Abstract:
(U) Brief summaries are given on examples of bacteria (Bacillus anthracis, Francisella tularensis, Brucella spp., Coxiella burnetii.), viruses (Venezuelan equine encephalitis, smallpox, Rift Valley fever), and toxins (botulinum, ricin, staphylococcal enterotoxin B) that are of medical importance. Descriptions, morbidity and mortality, vaccine availability, value of passive immune approaches, recommended therapy, suggested priority for further development and references are given for these examples. Bacillus anthracis, Francisella tularensis, Brucella spp., Coxiella burnetii, Venezuelan equine encephalitis, Variola, Rift Valley fever, Botulinum toxin, Ricin, Staphylococcal enterotoxin B.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA248724

Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a248724.pdf
Size: 3 MB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA248724

Corporate Author:
JEFFERSON MEDICAL COLL PHILADELPHIA PADEPT OF MEDICINE

Unclassified Title:
(U) A Core Facility for the Study of Neurotoxins of Biological Origin

Descriptive Note:
Annual rept. 15 May 1990-15 Jan 1992

Personal Author(s):
Simpson, Lance L

Report Date:
15 Feb 1992

Media Count:

86 Page(s)
Report Number(s):
XA-USAMRDC
Contract Number:
DAMD17-86-C-6161
Monitor Series:
USAMRDC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) Studies have been done on the variety of toxins that affect the nervous system. The toxins of major interest have been dendrotoxin, tetrotoxin, saxitoxin, botulinum neurotoxin, tetanus toxin and crotoxin. Experiments have been conducted mainly on three types of tissue preparations: (1) brain synaptosomes, (2) phrenic nerve-hemidiaphragm and (3) cells grown in tissue culture, including neuroblastoma cells and adrenal medullary tumor cells. The major accomplishments have been: (1) isolation of homogeneous preparations of dendrotoxin, (2) partial characterization of dendrotoxin binding sites, (3) partial characterization of tetrotoxin and saxitoxin binding properties using channels inserted into lipid membranes, (4) further characterization of the intracellular actions of clostridial toxins, (5) development of binding assays for clostridial toxins, and (6) study of structure-function relationships in clostridial neurotoxins and snake neurotoxins. Neurophysiology, Toxin, RAI, Central Nervous system mechanism.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA246495
Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a246495.pdf
Size: 1 MB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA246495
Corporate Author:
MARYLAND UNIV BALTIMORE SCHOOL OF MEDICINE
Unclassified Title:
(U) Mechanism of Action of the Presynaptic Neurotoxins Tetanus Toxin
Descriptive Note:
Rept. for 1 Jul 1990-30 Dec 1991
Personal Author(s):
Rogers, Terry B
Report Date:
25 Jan 1992
Media Count:
24 Page(s)
Report Number(s):

XA-USAMRDC
Contract Number:
DAMD17-90-Z-0043
Monitor Series:
USAMRDC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) During the past year a number of enzymatic systems have been investigated as possible targets for the action of the Clostridial neurotoxins. A cultured cell system, PC12 cells, was used as a model to exam specific systems. We have examined the effects of tetanus toxin on protein kinase C levels in such cells and have found that there is no significant inhibition during intoxication. Further, we have initiated studies to look at the effects of botulinum and tetanus toxins on cyclicnucleotide phosphodiesterase systems. We have fractioned the PDE activity by ion exchange chromatography and have found that there are multiple forms in PC12 cells and that treatment with nerve growth factor causes a marked shift or change in the pattern of PDE expression along with the growth factor induced differentiation. These studies provide the basis for future studies that will examine the effects of toxins on these specific enzyme subtypes.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA252400
Corporate Autbor:
PORTON PRODUCTS LTD WASHINGTON DC
Unclassified Title:
(U) Purification and Radiolaheling of Clostridium botulinum Type F neurotoxin
Descriptive Note:
Journal article
Personal Author(s):
Shone, Clifford C
Tranter, Howard S
Alexander, Frances C
Report Date:
Jan 1992
Media Count:
16 Page(s)
Report Number(s):
XA-USAMRDC
Contract Number:
DAMD17-88-C-8098
Monitor Series:
USAMRDC
Report Classification:

Unclassified

Distribution Limitation(s):

01 - APPROVED FOR PUBLIC RELEASE

20 - JOURNAL ARTICLES; DTIC USERS ONLY

Distribution Statement:

Availability: Pub. in Methods in Neurosciences, v8 p165-179 1992. Available only to DTIC users. No copies furnished by NTIS.

Abstract:

(U) Botulism, a frequently fatal disease affecting both humans and animals, is caused by any one of seven antigenically different neurotoxins (types A-G) produced by various strains of the bacterium Clostridium botulinum. Botulinum F neurotoxin, a typical representative of this family of potent neuroparalytic agents, is a protein of molecular mass approximately 155 kDa consisting of heavy (ca. 105 kDa) and light (ca. 55 kDa) subunits linked by a disulfide bridge. The primary site of action of all the botulinum neurotoxins is the neuromuscular junction where, following a binding step in which toxin molecules interact with acceptor sites on the presynaptic nerve surface, they enter the nerve ending and block the calcium-dependent release of neurotransmitter. Not all the botulinum neurotoxins appear to recognize the same type of acceptor molecule on the presynaptic nerve surface and once inside the nerve ending not all the toxin types appear to block the transmitter release process by the same mechanism.

Abstract Classification:

Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:

ADA243156

Full Text (pdf) Availability:

View Full Text (pdf)

File: /U2/a243156.pdf

Size: 3 MB

Handle / proxy Url: http://handle.dtic.mil/100.2/ADA243156

Corporate Author:

IMPERIAL COLL OF SCIENCE AND TECHNOLOGYLONDON (UNITED KINGDOM)

Unclassified Title:

(U) Novel Treatments for Botulism: Development of Antagonists for Identified Steps in the Action of Botulinum Neurotoxins

Descriptive Note:

Final rept. 18 Jan 88-17 Apr 91

Personal Author(s):

Dolly, J O

Report Date:

20 Sep 1991

Media Count:

79 Page(s)

Report Number(s):

XA-USAMRDC

Contract Number:

DAMD17-88-C-8008

Monitor Series:
USAMRDC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) Using a combination of electrophysiological and biochemical techniques, the action of botulinum neurotoxin (BoNT) was shown conclusively to involve (1) binding/ targetting to ecto-acceptors on cholinergic neurons, (2) acceptor-mediated uptake and, (3) block of Ca24-dependent release of transmitters. Domains/chains in BoNT responsible for each step were identified. One useful antagonist of the toxin's binding was developed, in addition to a monoclonal antibody capable of neutralizing the intracellular poisoning. Insights into the molecular action of BoNT were gained, particularly involvement of microtubules in the base of B and, possible, a large phosphorylated protein concerned with exocytosis. Equivalent experiments on tetanus toxin, and chimeric mixtures of both toxins, yielded valuable information for possible future targetting of agents to cholinergic and non-cholinergic neurons. A more detailed summary is included in the report.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA233710
Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a233710.pdf
Size: 1 MB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA233710
Corporate Author:
VIRGINIA UNIV CHARLOTTESVILLE
Unclassified Title:
(U) Neurotoxin and Epitope Structural Studies
Descriptive Note:
Final rept. 28 Sep 1987-27 Sep 1990
Personal Author(s):
Hunt, Donald F
Report Date:
25 Jan 1991
Media Count:
40 Page(s)
Report Number(s):
XA-USAMRDC
Contract Number:
DAMD17-87-C-7188
Monitor Series:
USAMRDC

Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) Neurotoxins of botulinum clostridium are scientifically interesting for two reasons. First, they are extremely toxic. Second, they can be used as models for three important biological phenomena, selective recognition by a target cell, transport through the plasma membrane and toxic activity. All three activities are situated on one polypeptide of approx. 150 kDa. Whereas the complete gene sequences of neurotoxins A and C1 were published very recently only parts of the neurotoxin E sequence is known. By using mass spectrometry, supported by automated Edman degradation we were able to deduce approx. 5Q kDa of well established sequence information. Additionally, we also found approx. 30Q kDa of preliminary sequence information.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA245629
Corporate Author:
IMPERIAL COLL OF SCIENCE AND TECHNOLOGYLONDON (UNITED KINGDOM)
Unclassified Title:
(U) Microtubule-Dissociating Drugs and A23187 Reveal Differences in Inhibition of Synaptosomal Transmitter Release by Botulinum Neurotoxins Types A and B
Personal Author(s):
Ashton, Anthony C
Dolly, J O
Report Date:
Jan 1991
Media Count:
10 Page(s)
Report Number(s):
XA-USAMRDC
Contract Numher:
DAMD17-88-C-8008
Monitor Series:
USAMRDC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY
Distribution Statement:
Availability: Pub. in Jnl. of Neurochemistry, v56 n3 p827-835 1991. Available only to DTIC users. No copies furnished by NTIS.
Abstract:
(U) The inhibitory effects of botulinum neurotoxins types A and B on Ca2+-dependent evoked

release of 3Hnoradrenaline from rat cerebrocortical synaptosomes were compared and their molecular basis investigated. A23187, a Ca2+ ionophore, proved more efficacious in reversing the blockade produced by type A than that by B, whereas the actions of neither were changed by increasing intraterminal cyclic GMP levels using 8-bromo-cyclic GMP or nitroprusside. Disruption of the actin-based cytoskeleton with cytochalasin D not alter the inhibition seen subsequently with either toxin. However, prior disassembly of microtubules with colchicine, nocodazole, or griseofulvin reduced the potency of type B toxin, but not that of type A toxin, stabilization of the microtubules with taxol counteracted this effect of colchicine. Because colchicine treatment of synaptosomes did not interfere with the measureable binding of type B toxin or its apparent uptake, it appears to act intracellularly. Collectively, these data suggest that botulinum neurotoxins types A and B inactivate transmitter release by interaction at different sites in the process.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA245625

Corporate Author:
IMPERIAL COLL OF SCIENCE AND TECHNOLOGYLONDON (UNITED KINGDOM)

Unclassified Title:
(U) Light Chain of Botulinum Neurotoxin Is Active in Mammalian Motor Nerve Terminals When Delivered via Liposomes

Personal Author(s):
DE Paiva, Anton
Dolly, J O

Report Date:
Dec 1990

Media Count:
5 Page(s)

Report Number(s):
XA-USAMRDC

Contract Number:
DAMD17-88-C-8008

Monitor Series:
USAMRDC

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY

Distribution Statement:
Availability: Pub. in FEBS Letters, v277 n1/2 p171-174 Dec 1990. Available only to DTIC users. No copies furnished by NTIS.

Abstract:
(U) Liposomal encapsulation of the individual light and heavy chain of botulinum neurotoxin A was used to investigate their intracellular effects on synaptic transmissions at the murine

neuromuscular junction. Bath-application to phrenic nerve-hemidiaphragms of liposomes containing heavy chain (up to 75 nM) caused no alteration in neurally-evoked muscle tension. In contrast, liposomes with entrapped light chain (9-20 nM fmal concentration) gave a pre-synaptic blockade of neuromuscular transmission that could be relieved temporarily by 4- aminopyridine, as for the dichain toxin. Any contribution from contaminating intact toxin was excluded both by purity and minimal toxicity in mice of the light chain preparations used, and by the lack of neuromuscular paralysis seen with liposomes containing the maximum amount of native toxin that could have been present in the light chain liposomes. As bath-application os high concentrations of light chain in the absence of liposomes failed to affect neurotransmitter release, it is concluded that this chain alone can mimic the action of the whole toxin inside mammalian motor nerve endings, it s predominant site of action. Thus, light chain could provide a more effective probe for an intra-cellular component concerned with Ca2+ dependent secretion.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA231729

Corporate Author:
ARMY ENGINEER WATERWAYS EXPERIMENT STATION VICKSBURG MS ENVIRONMENTAL LAB

Unclassified Title:
(U) Assessment of Avian Botulism Control Pilot Project at the Dike 14 Confined Dredged Material Disposal Facility, Cleveland, Ohio.

Descriptive Note:
Final rept.,

Personal Author(s):
Simmers, John W
Apfelbaum, Steven I

Report Date:
Dec 1990

Media Count:
86 Page(s)

Report Number(s):
WES/MP/EL-90-23
XA-WES

Monitor Series:
WES

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE

Abstract:
(U) The Dike 14 Confined Dredged Material Disposal Facility (CDF) at Cleveland, OH, was the site of an avian botulism outbreak in 1986. At that time the use of noise making devices was not successful in preventing the use of the CDF by shorebirds, wading birds, and waterfowl susceptible to botulism. The Buffalo District of the U.S. Army Corps of Engineers identified the

problem as one requiring a generic solution that could be applied at other operational CDFs. In a pilot project, plant propagules were planted at the CDF prior to the disposal operations so that a vegetative cover would rapidly appear as the CDF dewatered after disposal operations. The vegetation on the dewatering dredged material was expected to make the CDF unattractive to shorebirds, wading birds, and waterfowl. The pilot project was a qualified success in the prevention of a 1987 outbreak of avian botulism. The duration of the disposal operation and the depth of the dredged material placed in the CDF limited the anticipated vegetation establishment. However, the final elevation of the dredged material relative to the level of Lake Erie allowed the site to dewater and the vegetation that emerged attracted a terrestrial avifauna. The observed botulism abatement was the result of both additional filling and vegetation establishment. The procedures used to establish vegetation were feasible, compatible with dredging and disposal schedules, and cost-effective. A unique combination of equipment was required, but all of the components were relatively available.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Numher:
ADA245628
Corporate Author:
IMPERIAL COLL OF SCIENCE AND TECHNOLOGYLONDON (UNITED KINGDOM)
Unclassified Title:
(U) Ca(2+)-Dependent Noradrenaline Release from Permeabilised PC12 Cells Is Blocked by Botulinum Neurotoxin A or Its Light Chain
Descriptive Note:
Reprint
Personal Author(s):
McInnes, Colin
Dolly, J O
Report Date:
Feb 1990
Media Count:
5 Page(s)
Report Number(s):
XA-USAMRDC
Contract Number:
DAMD17-88-C-8008
Monitor Series:
USAMRDC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY
Distribution Statement:
Availability: Pub. in FEBS Letters, v261 n2 p323-326 Feb 1990. Available only to DTIC users. No copies furnished by NTIS.

Abstract:

(U) Permeabilisation of PC12 cells with digitonin allowed a direct study of the intracellular action of botulinum neurotoxin A, one of a group of dichain proteins produced by Clostridium botulinum that causes the fatal neuroparalytic condition, botulism. Release of 3Hnoradrenaline from these permeabilised cells could be evoked by Ca2+ and this was inhibited specifically by the neurotoxin in a dose-dependent manner (half-maximal dose 2nM under the conditions used). Inclusion of the reducing agent dithiothreitol (up to 10 mM) had no effect on the level of inhibition. Moreover, electrophoretic analysis showed that this treatment of the toxin in the native state caused negligible reduction of inter- chain disulphide bonds. Toxin-induced blockade of neurotransmitter releases was incomplete and could not be overcome by increased Ca2+ concentration (100 uM). The observed toxin-insensitivity of the release from intact PC12 cells must result from inefficient toxin uptake, relative to that in peripheral cholinergic neurones. Refolded light chain alone inhibited exocytosis to the same degree and with similar potency to that of the intact neurotoxin, and effect not altered by the heavy chain.

Abstract Classification:

Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:

ADA246130

Corporate Author:

IMPERIAL COLL OF SCIENCE AND TECHNOLOGYLONDON (UNITED KINGDOM)

Unclassified Title:

(U) Inhibition of Neurotransmitter Release by Botulinum Neurotoxins and Tetanus Toxin at Aplysia Synapses: Role of the Constituent Chains

Personal Author(s):

Poulain, Bernard
Mochida, Sumiko
Wadsworth, Jonathan D
Weller, Ulrih
Habermann, Ernst

Report Date:

Jan 1990

Media Count:

16 Page(s)

Report Number(s):

XA-USAMRDC

Contract Number:

DAMD17-88-C-8008

Monitor Series:

USAMRDC

Report Classification:

Unclassified

Distribution Limitation(s):

01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY

Distribution Statement:

Availability: Pub. in J. Physiol., v84 p247-261 1990. Available only to DTIC users only. No copies furnished by NTIS.

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA246151
Corporate Author:
IMPERIAL COLL OF SCIENCE TECHNOLOGY ANDMEDICINE LONDON (UNITED KINGDOM) DEPT OF BIOCHEMISTRY
Unclassified Title:
(U) Clues to the Multi-Phasic Inhibitory Action of Botulinum Neurotoxins on Release of Transmitters
Personal Author(s):
Dolly, J O
Ashton, A C
McInnes, C
Wadsworth, J D
Poulain, B
Report Date:
Jan 1990
Media Count:
11 Page(s)
Report Number(s):
XA-USAMRDC
Contract Number:
DAMD17-88-C-8008
Monitor Series:
USAMRDC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY
Distribution Statement:
Availability: Pub. in Jnl. de Physiologie, v84 n3 p237-247 1990. Availahle only to DTIC users. No copies furnished hy NTIS.

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA215346
Corporate Author:
IMPERIAL COLL OF SCIENCE AND TECHNOLOGY LONDON (ENGLAND)
Unclassified Title:

(U) Novel Treatments for Botulism: Development of Antagonists for Identified Steps in the Action of Botulinum Neurotoxins.

Descriptive Note:
Rept. for 18 Jan 88-17 Jul 89,

Personal Author(s):
Dolly, J O

Report Date:
07 Nov 1989

Media Count:
52 Page(s)

Contract Number:
DAMD17-88-C-8008

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE

Abstract:
(U) With the aim of identifying domains in botulinum neurotoxin (BoNT) responsible for blockade of transmitter release, a prerequisite for developing treatments for botulism, the heavy (HC) and light (LC) chains of types A and B were purified to homogeneity, renatured, or reconstituted to give a di-chain toxic species; controlled proteolysis of BoNT A followed by chromatographic procedures yielded pure fragments (H2L, intact toxin minus the C-terminal half of HC (H1); H2, N-terminal portion of HC). These were tested, alone or in combination, for inhibitory effects on neurally-evoked transmitter release from mouse nerve diaphragm and Aplysia ganglionic neurons. The latter allowed extra- or intra-neuronal administration of toxin samples, with quantitation of quantal release by voltage-clamp analysis of pairs of pre- and post-synaptic cells. Examination of an intracellular action of BoNT was, also, accomplished by digitonin-permeabilisation of cultured PC-12 cells, with retention of the exocytosis process. For monitoring the toxins's molecular action, nerve terminals or synaptic vesicles were isolated from brain. Keywords: Botulism; Botulinum neurotoxin; Botulinum neurotoxin acceptors; Internalisation; Antibodies; ADP-ribosylation; Exocytosis; Neuromuscular junction; Acetylcholine; Noradrena-line; G-proteins. (AW)

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA220814

Full Text (pdf) Availability:
View Full Text (pdf)

File: /U2/a220814.pdf

Size: 786 KB

Handle / proxy Url: http://handle.dtic.mil/100.2/ADA220814

Corporate Author:
JEFFERSON MEDICAL COLL PHILADELPHIA PA

Unclassified Title:
(U) Therapeutic Approaches to the Treatment of Botulism

Descriptive Note:
Annual rept. 1 Sep 1988-5 Jul 1989
Personal Author(s):
Simpson, Lance L
Report Date:
01 Oct 1989
Media Count:
26 Page(s)
Report Number(s):
XA-USAMRDC
Contract Number:
DAMD17-85-C-5285
Monitor Series:
USAMRDC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) Pharmacological methods are being sought to prevent or reverse the effects of botulinum neurotoxin. During the past year, emphasis has been placed on drugs that interact with potassium channels. Work during the past year has focused on three problems: i) aminopyridines and their analogues, ii) dendrotoxin, and iii) rubidium flux. The work on aminopyridines cofirms that they are very narrow in their utility as anti-botulism agents. The studies on dendrotoxin resulted in the provocative finding that the agent did not antagonize any clostridial neurotoxin, nor could it reverse the effects of low calcium or high magnesium. The final aspect of the research was to establish a protocol for studying rubidium flux. This may represent a rational approacb for finding clostridial toxin antagonists. Keywords: Botulinum neurotoxin; Neuromuscular blockade; Experimental therapeutics; RA1.
Abstract Classification:
Unclassified

Tecbnical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA220725
Corporate Author:
JEFFERSON MEDICAL COLL PHILADELPHIA PA
Unclassified Title:
(U) Therapeutic Approaches to the Treatment of Botulism
Descriptive Note:
Final rept. 1 Sep 1985-5 Jul 1989
Personal Author(s):
Simpson, Lance L
Report Date:
01 Oct 1989
Media Count:
40 Page(s)

Report Number(s):
XA-USAMRDC
Contract Number:
DAMD17-85-C-5285
Monitor Series:
USAMRDC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) Research has been conducted in four areas that pertain to the development of antagonists of botulinum neurotoxin, as follows: 1) Studies on monoclonal antibodies indicate that they are useful research tools, but they appear to have little therapeutic potential. 2) Research on aminopyridines and their analogues shows that they possess anti-botulinum activity, but only of a narrow utility. 3) Experiments with dendrotoxin have resulted in the provocative finding that this agent does not antagonize any clostridial toxin, nor does it reverse the effects of low calcium or high magnesium. 4) Initial studies on rubidium flux indicate that this may represent a rational approach for finding clostridial toxin antagonists. Keywords: Botulinum neurotoxin; Neuromuscular blockade; Experimental therapeutics.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA246091
Corporate Author:
JOHNS HOPKINS UNIV BALTIMORE MD DEPT OF NEUROLOGY
Unclassified Title:
(U) Neurotransmission Regulates Stability of Acetylcholine Receptors at the Neuromuscular Junction
Personal Author(s):
Avila, Orlando L
Drachman, Daniel B
Pestronk, Alan
Report Date:
Aug 1989
Media Count:
6 Page(s)
Report Number(s):
XA-USAMRDC
Contract Number:
DAMD17-85-C-5069
Monitor Series:
USAMRDC
Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY
Distribution Statement:
Availability: Pub. in The Jnl. of Neuroscience, v9 n8 p2902-2906 Aug 1989. Available only to DTIC users. No copies furnished by NTIS.

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA229063
Corporate Author:
FLORIDA UNIV GAINESVILLE COLL OF VETERINARY MEDICINE
Unclassified Title:
(U) Receptor Binding and Membrane Transport of Botulinum Toxins.
Descriptive Note:
Annual rept. 1 Apr 88-31 Mar 89,
Personal Author(s):
Dankert, John R
Report Date:
Mar 1989
Media Count:
12 Page(s)
Contract Numher:
DAMD17-86-C-6062
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) The goal of this research is to characterize the interaction of the botulinum type neurotoxins with target membranes and seeks to add to the field of study of toxin/cell interactions. Also, this research project seeks to determine any similarity between the mechanism of action of botulinum toxins and a number of other protein toxins whose mechanism of action has been more clearly defined. Through the utilization of antibodies to a series of diverse protein toxins and an artificial liposome target system for the botulinum toxin, it is hoped that the mechanism of action of the toxin can be better defined. Also, this will allow us to gain an understanding of how to inhibit the action of this toxin. Keywords: Protein/lipid interaction, Artificial botulinum inhibitor. (JS)
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA208732

Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD PATHOLOGY D IV
Unclassified Title:
(U) Evaluation of Neutralizing Antibodies to Types A, B, E, and F Botulinum Toxins in Sera from Human Recipients of Botulinum Pentavalent (ABCDE) Toxoid.
Descriptive Note:
Interim rept.,
Personal Author(s):
Siegel, Lynn S
Report Date:
28 Feb 1989
Media Count:
11 Page(s)
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) There are seven types of Clostridium botulinum, designated A-G, each type producing a pharmacologically similar but immunologically distinct neurotoxin. Immunization with botulinum toxoid has been used for over 40 years to protect laboratory personnel at risk for botulism due to contact with the neurotoxins. The botulinum toxoid currently distributed by the Centers for Disease Control is pentavalent, containing Formalin-inactivated botulinum toxins of types A, B, C, D, and E, adsorbed to aluminum phosphate. Twenty-five sera from personnel immunized with botulinum pentavalent toxoid (ABCDE) had titers of neutralizing antibodies to type A (5.7-51.6 international units (IU)/ml), type B (0.75-18 IU/ml), and to type E (0.61-10 IU/ml) botulinum toxins. Titers for one type could not be used to predict titers for another type in individuals receiving the toxoid. Cross-neutralizing antibodies to type F botulinum toxin were not detected (0.01251V/ML). (AW)
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADB141387
Corporate Author:
MINNESOTA UNIV MINNEAPOLIS
Unclassified Title:
(U) Research and Preparation of an Equine Heptavalent Botulinal Antitoxin
Descriptive Note:
Final rept. 1 Apr 1982-31 Jul 1983
Personal Author(s):
Condie, Richard M
Report Date:
Feb 1989
Media Count:

97 Page(s)
Report Number(s):
XA-USAMRDC
Contract Number:
DAMD17-82-C-2119
Monitor Series:
USAMRDC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) The following report describes the immunization and proprietary plasmapheresis methods used to produce equine hyperimmune botulinal antitoxin plasma. Also included are proprietary methods used for large scale production of an equine botulinal antitoxin with the highest specific neutralizing activity, the lowest potential for sensitization, and consisting of over 95% equine (F (ab')2 immunoglobulin. Finally, this report describes the proprietary large scale production and testing of two preparations of equine heptavalent botulinal antitoxin, FFA1-3-45-4x1 and FFA2-3-45-4xl. Keywords: RAI; New heptavalent F(ab')2 botulinal antitoxin equine; Toxin; Immunology; Antitoxin; Neurotoxin; Toxicology.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA245626
Corporate Author:
IMPERIAL COLL OF SCIENCE AND TECHNOLOGYLONDON (UNITED KINGDOM)
Uuclassified Title:
(U) Inhibition of Transmitter Release by Botulinum Neurotoxin A: contribution of Various Fragments to the Intoxication Process
Personal Author(s):
Poulain, Bernard
Wadsworth, Jonathan D
Maisey, E A
Shone, Clifford C
Melling, Jack
Report Date:
Jan 1989
Media Count:
8 Page(s)
Report Number(s):
XA-USAMRDC
Contract Number:
DAMD17-88-C-8008
Monitor Series:
USAMRDC

Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY
Distribution Statement:
Availability: Pub. in European Jnl. of Biochemistry, v185 p197-203 1989. Available only to DTIC users. No copies furnished by NTIS.
Abstract:
(U) The contribution of a proteolytic fragment (H2L) of botulinum neurotoxin type A (comprised of the amino-terminal region of the heavy chain disulphide linked to the light chain) to inhibition of neurotransmitter release was investigated, using central cholinergic synapses of Aplysia, rodent nerve- diaphragm preparations and cerebrocortical synaptosomes. No reduction in neurotransmitter release was observed following external application to these preparations of highly purified H2L or after intracellular injection into Aplysia neurons. The lack of activity was not the result of alteration in the light chain of H2L during preparation of the latter because (a) renaturation of this light chain with intact heavy chain produced a toxic di-chain form and (b) simultaneous application of heavy chain and light chain from H2L inhibited transmitter release in Aplysia. Bath application of H2L and heavy chain together inhibited release of transmitter; however, at the neuromuscular junction the potency of this mixture was much lower than that of native toxin. A similar blockade resulted when heavy chain was applied intracellularly and H2L added to the bath, demonstrating that H2L is taken up into cholinergic neurons of Aplysia.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA246097
Corporate Author:
JOHNS HOPKINS UNIV BALTIMORE MD DEPT OF NEUROLOGY
Unclassified Title:
(U) Neural Regulation of mRNA for the alpha-Subunit of Acetylcholine Receptors: Role of Neuromuscular Transmission
Personal Author(s):
Lipsky, Naomi G
Drachman, Daniel B
Pestronk, Alan
Shih, Po-Jen
Report Date:
Jan 1989
Media Count:
7 Page(s)
Report Number(s):
XA-USAMRDC
Contract Number:
DAMD17-85-C-5069
Monitor Series:

USAMRDC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY
Distribution Statement:
Availability: Pub. in Experimental Neurology, v105 p171-176 1989. Available only to DTIC users. No copies furnished by NTIS.
Abstract:
(U) Levels of mRNA for acetylcholine receptor (AChR) subunits are relatively low in innervated skeletal muscles. Following denervation they rise rapidly, leading to increased AChR synthesis. The mechanism by which motor nerves normally regulate these mRNA levels is not yet known. In order to determine the possible role of synaptic transmission this process, we have compared the effect of blockade of cholinergic ACh transmission with that of surgical denervation. Blockade of quantal ACh transmission was produced by injection of type A botulinum toxin into the soleus muscles of rats.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA206612
Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a206612.pdf
Size: 853 KB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA206612
Corporate Author:
JEFFERSON MEDICAL COLL PHILADELPHIA PA
Unclassified Title:
(U) Therapeutic Approaches to the Treatment of Botulism
Descriptive Note:
Annual rept. 1 Sep 1987-31 Aug 1988
Personal Author(s):
Simpson, Lance L
Report Date:
01 Oct 1988
Media Count:
22 Page(s)
Report Number(s):
XA-USAMRDC
Contract Number:
DAMD17-85-C-5285
Monitor Series:
USAMRDC
Report Classification:

Unclassified

Distribution Limitation(s):

01 - APPROVED FOR PUBLIC RELEASE

Abstract:

(U) Work during the past year has focused on three problems: i) defining the conditions that maximize the binding of toxin to nerve endings. ii) evaluating possibility that botulinum is a mitochondrial poison, and iii) studying the interaction between botulinum neurotoxin and a series of monoclonal antibodies. The work on toxin binding suggests that the approach currently used by most biochemists is flawed. Their approach maximizes binding, but this binding does not appear to involve relevant receptors. The work on mitochondrial function indicates that botulinum neurotoxin is not a mitochondrial poison. If it does affect mitochondrial function, that effect is indirect. The work on monoclonals has shown that type E botulinum neurotoxin can be substantially detoxified by antibodies directed against both the heavy and light chains. It also shows that antigenic determinants on the toxin continue to be exposed after the toxin has bound to nerve endings. Keywords: Neuromuscular blockade, Experimental therapeutics, RA 1, Pharmacological antagonists, Antidotes, Antitoxins, Binding sites.

Abstract Classification:

Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:

ADA197882

Full Text (pdf) Availability:

View Full Text (pdf)

File: /U2/a197882.pdf

Size: 1 MB

Handle / proxy Url: http://handle.dtic.mil/100.2/ADA197882

Corporate Author:

ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD PATHOLOGY DIV

Unclassified Title:

(U) Human Immune Response to Botulinum Pentavalent (ABCDE) Toxoid, Determined by a Neutralization Test and by an ELISA

Personal Author(s):

Siegel, Lynn S

Report Date:

04 May 1988

Media Count:

30 Page(s)

Report Number(s):

XA-USAMRDC

Monitor Series:

USAMRDC

Report Classification:

Unclassified

Distribution Limitation(s):

01 - APPROVED FOR PUBLIC RELEASE

Abstract:

(U) To determine the immune status of persons receiving Botulinum Pentavalent (ABCDE) Toxoid and to evaluate the effectiveness of the vaccine, we surveyed immunized individuals for neutralizing antibodies to type A and to type B botulinum toxins. Just prior to the first annual booster, 10 to 21 people (48%) and 14 of 21 (67%) lacked a detectable titer for type A and type B, respectively. After the first booster, all individuals tested had a demonstrable titer to both types A and B. There was a wide range of antibody levels among individuals at the same point in the immunization scheme. Results from an ELISA, with purified type A or type B neurotoxin as the capture antigen, were compared to neutralization test results on 186 serum samples for type A and 168 sera for type B. Due to the wide dipersion of values obtained, using ELISA test results to predict neutralizing antibody levels is unwarranted. Keywords: Bioassay, ELISA.

Abstract Classification:

Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:

ADA199226

Full Text (pdf) Availability:

View Full Text (pdf)

File: /U2/a199226.pdf

Size: 1 MB

Handle / proxy Url: http://handle.dtic.mil/100.2/ADA199226

Corporate Author:

JEFFERSON MEDICAL COLL PHILADELPHIA PA

Unclassified Title:

(U) Therapeutic Approaches to the Treatment of Botulism

Descriptive Note:

Annual rept. 1 Sep 1986-31 Aug 1987

Personal Author(s):

Simpson, Lance L

Report Date:

01 Oct 1987

Media Count:

35 Page(s)

Report Number(s):

XA-USAMRDC

Contract Number:

DAMD17-85-C-5285

Monitor Series:

USAMRDC

Report Classification:

Unclassified

Distribution Limitation(s):

01 - APPROVED FOR PUBLIC RELEASE

Abstract:

(U) In vitro experiments have been done on isolated phrenic nerve- hemidiaphragm preparations. The purpose of the experiments was twofold: firstly, to evaluate a host of drugs as potential

botulinum neurotoxin antagonists; and secondly, to evaluate the possibility that botulinum neurotoxin is an ADP- ribosyltransferase. The drugs that were tested included aminopyridines, guanidine, calcium, theophylline, forskolin, isobutylmethylxanthine, and cholera toxin. Various of the drugs had effects on neuromuscular transmission, and some had narrow spectrum utility as clostridial toxin antagonists, but none had the broad spectrum utility that would be needed for a clinically useful drug. In related experiments, a series of studies were conducted to determine whether the toxins have ADP-ribosyltransferase activity. The data did not support the hypothesis, though additional work needs to be done.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA192856

Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD

Unclassified Title:
(U) Ineffectiveness of 3,4-Diaminopyridine as a Therapy for Type C Botulism

Personal Author(s):
Siegel, Lynn S
Price, Jessie I

Report Date:
Jan 1987

Media Count:
5 Page(s)

Report Number(s):
XA-USAMRIID

Monitor Series:
USAMRIID

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY
23 - AVAILABILITY: DOCUMENT PARTIALLY ILLEGIBLE

Distribution Statement:
Availability: Pub. in Toxicon, v25 n9 p1015-1018 1987. Available only to DTIC users. No copies furnished by NTIS., Availahility: Document partially illegible.

Abstract:
(U) Clostridium botulinum neurotoxins inhibit acetylcholine release at neuromuscular junctions. Agents stimulating neurotransmitter efflux, such as 3, 4-diaminopyridine (3,4-DAP), could be useful for botulism therapy. Treatment with 3,4-DAP (8 mg/kg hourly, beginning 3 hr after toxin injection) failed to increase the survival times of mice receiving 10, 20 or 40 LD50 type C, but did prolong the survival of those receiving 20 LD50 type A. This difference in 3,4- DAP efficacy may reflect variations in the molecular mechanism of action of types A and C botulinum neurotoxins.

Abstract Classification:

Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA190176
Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a190176.pdf
Size: 853 KB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA190176
Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD PATHOLOGY DIV
Unclassified Title:
(U) Efficacy of 3,4-Diaminopyridine as a Therapy for Type C Botulism
Personal Author(s):
Siegel, Lynn S
Price, Jessie I
Report Date:
09 Dec 1986
Media Count:
18 Page(s)
Report Number(s):
XA-USAMRIID
Monitor Series:
USAMRIID
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) Botulism is caused solely by the protein neurotoxins produced by Clostridium botulinum. These toxins act by inhibiting acetylcholine release at neuromuscular junctions. Agents which stimulate the efflux of neutrotransmitter, such as 3,4-diaminopyridine 93,4-DAP), could be useful in the treatment of botulism. Type C botulism affects a variety of species, but is especially severe in waterfowl, causing massive die-offs each year. To evaluate 3,4-DAP as a potential therapy for type C botulism, mice were injected i.p. with 10, 20 or 40 LD50 of type C toxin. After 3 hr, when symptoms of botulism were apparent, therapy with 3,4-DAP was begun for half of each group of mice. Mice were injected i.p. with 8 mg/kg of the drug hourly. This treatment with 3,4-DAP did not significantly increase the survival times of mice receiving type C toxin. However, therapy with 3,4-DAP, administered at the same concentration and according to the same dosage schedule, significantly prolonged the survival times of mice that had received 20 LD50 of type A botulinum neurotoxin. This difference in the effectiveness of 3,4-DAP against type A and C botulinum toxins may be due to variations in the mechanism of action of these neurotoxins at the molecular level.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA181603
Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a181603.pdf
Size: 651 KB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA181603
Corporate Author:
JEFFERSON MEDICAL COLL PHILADELPHIA PADEPT OF MEDICINE
Unclassified Title:
(U) Therapeutic Approaches to the Treatment of Botulism
Descriptive Note:
Annual rept. 1 Sep 1985-31 Jul 1986
Personal Author(s):
Simpson, Lance L
Report Date:
01 Oct 1986
Media Count:
14 Page(s)
Report Number(s):
XA-USAMRDC
Contract Number:
DAMD17-85-C-5285
Monitor Series:
USAMRDC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) In vitro experiments have been done on isolated phrenic nerve- hemidiaphragm preparations. The purpose of the experiments was to evaluate aminopyridines as putative therapeutic agents in the treatment of botulism and to develop monoclonal antibodies that would neutralize botulinum toxin and tetanus toxin. The work demonstrates that aminopyridines are active against type A botulinum toxin. Research on antibodies is still in progress. Keywords: Antidotes; Botulism; Food poisoning.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:

ADA338093
Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a338093.pdf
Size: 3 MB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA338093
Corporate Author:
JOINT PUBLICATIONS RESEARCH SERVICE ARLINGTON VA
Unclassified Title:
(U) China Report, Agriculture.
Report Date:
08 Aug 1986
Media Count:
73 Page(s)
Report Number(s):
JPRS-CAG-86-030
XJ-XD
Monitor Series:
XD
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) This document contains information on Agricultural Issues in the Peoples Republic of China.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA177585
Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a177585.pdf
Size: 236 KB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA177585
Corporate Author:
WISCONSIN UNIV-MADISON FOOD RESEARCH INST
Unclassified Title:
(U) Exploration of Binding and Toxic Site of Botulinum Neurotoxin
Descriptive Note:
Annual rept 1 Feb 1984-31 Jul 1985
Personal Author(s):
DasGupta, B R
Report Date:
30 Jan 1986
Media Count:

6 Page(s)

Report Number(s):
XA-USAMRDC

Contract Number:
DAMD17-83-C-3034

Monitor Series:
USAMRDC

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE

Abstract:
(U) Roles of the heavy and light chains of the neurotoxin (NT) in neuroparalysis were examined in two systems. (1) The heavy chin first binds to the specific sites (receptors) on the nerve terminals. This binding is necessary for the light chain to be fixed at these specific sites. Then the light chain (or combination of the light and heavy chain) induces paralysis through a mechanism very similar to that of the parent dichain nt. (2) The isolated heavy chain forms channels in planar bilayer membranes. These channels have pH and voltage dependent gating properties. Planter - lunbrical of the hind paw of the mouse were introduced as neuromuscular preparation for studying botulinum nt induced paralysis.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA163060

Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a163060.pdf
Size: 678 KB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA163060

Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD

Unclassified Title:
(U) ELISA (Enzyme-linked Immunosorbent Assay) to Detect Humoral Antibodies Specific for Clostridium botulinum Type A Neurotoxin

Descriptive Note:
Interim rept.

Personal Author(s):
Lewis, George E , Jr
Kulinski, Salvatore S
Metzger, Joseph F
Higbee, Glen A

Report Date:
19 Nov 1985

Media Count:
19 Page(s)

Report Number(s):
XA-USAMRIID
Monitor Series:
USAMRIID
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) The enzyme-linked immunosorbent assay (ELISA) was modified for the rapid detection of human humoral antibodies (IgG) that are specific for Clostridium botulinum type a toxoid. The ELISA was useful for the rapid evaluation of immunization results and for distinguishing (95%) immune from nonimmune individuals. ELISA values, when compared with standard in vivo toxin neutralization test values, paralleled the anamnestic response to booster immunization in 25 to 25 individuals.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
ADA158873
Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/a158873.pdf
Size: 1 MB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA158873
Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD
Unclassified Title:
(U) Effect of 3,4-Diaminopyridine on the Survival of Mice Injected with Botulinum Neurotoxin Type A, B, E, or F,
Personal Author(s):
Siegel, L S
Johnson-Winegar, A D
Sellin, L C
Report Date:
16 Aug 1985
Media Count:
26 Page(s)
Report Number(s):
XA-USAMRIID
Monitor Series:
USAMRIID
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE

Abstract:

(U) To determine the efficacy of 3,4-diaminopyridine (3,4-DAP) as a potential Treatment for botulism, its effect on the survival times of mice injected with type A, B, E, or F botulinum toxin (BoTx) was examined. Mice were injected ip with 10, 20 or 40 LD50 of BoTx. Three hr later, when the mice displayed symptoms of botulism, half of each group of mice was treated with 3, 4DAP, and agent which increases nerve-evoked transmitter release. At each dose of type A BoTx tested, 3,4-Dap definitely prolonged survival. In contrast, treatment with the drug did not significantly increase the survival time of mice injected with type B, E, or F BoTx. The differences in efficacy of 3,4-DAP against the four serotypes of BoTx may reflect differences in the molecular mechanism of action among the neurotoxins. (Author)

Abstract Classification:

Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:

ADA138462

Corporate Author:

ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD

Unclassified Title:

(U) Botulism -- An Update

Personal Author(s):

Sellin, Lawrence C

Report Date:

Jan 1984

Media Count:

6 Page(s)

Report Number(s):

XA-USAMRIID

Monitor Series:

USAMRIID

Report Classification:

Unclassified

Distribution Limitation(s):

01 - APPROVED FOR PUBLIC RELEASE

20 - JOURNAL ARTICLES; DTIC USERS ONLY

Distribution Statement:

Availability: Pub. in Military Medicine, v149 p12-16 Jan 84.. Available only to DTIC users. No copies furnished by NTIS.

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:

ADA129823

Full Text (pdf) Availability:

View Full Text (pdf)
File: /U2/a129823.pdf
Size: 520 KB
Handle / proxy Url: http://handle.dtic.mil/100.2/ADA129823
Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD
Unclassified Title:
(U) Foodborne Illness
Personal Author(s):
Beisel, William R
Report Date:
Feb 1983
Media Count:
7 Page(s)
Report Number(s):
XA-USAMRIID
Monitor Series:
USAMRIID
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Distribution Statement:
Approved for public release; distribution is unlimited.

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
AD0690059
Corporate Author:
ALBERT EINSTEIN MEDICAL CENTER PHILADELPHIA PA RESEARCH LABS
Unclassified Title:
(U) ISOLATION OF TOXIC SUBUNITS FROM TWO MURINE-TOXIC PROTEINS FROM PASTEURELLA PESTIS,
Personal Author(s):
Montie,Thomas C
Montie,Diane B
Leon,Shalom A
Kennedy,Carole A
Ajl,Samuel J
Report Date:
24 Sep 1968
Media Count:
8 Page(s)
Report Number(s):
AFOSR-69-1653TR
Contract Number:
AF-AFOSR-1343-68

NSF-GB-6162
Monitor Series:
69-1653TR
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY
Distribution Statement:
Availability: Pub. in Biochemical and Biophysical Research Communications, v33 n3 p423-429 1968.
Abstract:
(U) Two mouse-toxic proteins, Toxin A (240,000 molecular weight) and Toxin B (120,000 molecular weight), were dissociated in sodium dodecyl sulfate to small molecular weight subunits. Subunit size from 10,000 to 12,000 molecular weight is proposed based on gel electrophoresis, ultracentrifugation and dialysis experiments. The subunits retained approximately 60% of the toxic activity of the large molecular weight toxins. (Author)
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
AD0627996
Corporate Author:
CHEMICAL RESEARCH AND DEVELOPMENT LABS EDGEWOOD ARSENAL MD
Unclassified Title:
(U) BOTULINUM ANTITOXIN AS A THERAPEUTIC AGENT IN MONKEYS WITH EXPERIMENTAL BOTULISM.
Descriptive Note:
Technical rept., Jan 63-Aug 64,
Personal Author(s):
Oberst ,Fred W
Cresthull ,Paul
Crook ,James W
House,Michael J
Report Date:
Oct 1965
Media Count:
16 Page(s)
Report Number(s):
CRDLR-3331
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Abstract:
(U) Antitoxin administered soon after the appearance of the first toxic signs in monkeys given

2.5 to 5.0 LD50's of botulinum toxin resulted in complete recovery in 11 out of 15 animals when liquid food and fluids were forced during the period of aphagia. When no supportive treatment was applied, only one out of six survived. The survivor had received 2.5 LD50's of toxin. It is concluded that most monkeys given 2.5 to 5.0 LD50s of botulinum toxin intravenously can be saved when the antitoxin is administered soon after the first toxic signs are detected and when daily, supplemental, intragastric feedings, vitamins and antibiotics are given. (Author)

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
AD0618867

Corporate Author:
ARMY BIOLOGICAL LABS FREDERICK MD

Unclassified Title:
(U) DETECTION OF BOTULIN TOXIN IN CANNED FOOD WITH THE HELP OF THE INDIRECT HEMAGGLUTINATION REACTION AFTER BOYDEN,

Personal Author(s):
BAYAR,G A

Report Date:
Jan 1965

Media Count:
4 Page(s)

Report Number(s):
TRANSLATION-1053
TT-65-62801

Monitor Series:
65-62801

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE

Abstract:
(U) The indirect hemagglutination reaction after Boyden with Konikova's modification was used with the aim of detecting botulin toxin in canned foods. Based on the results of the biological test, the activity of botulin toxin in the contaminated cans reached 1600-3200 Dlm in 1 ml for type A toxin and 320-640 Dlm in 1 ml for type B toxin. A conclusion concerning the presence of toxin may be made in 12-24 hours and concerning the degree of activity in 3-4 days. By using the indirect hemagglutination reaction in these tests it was possible to expose 1/6-1/64 Dlm of toxin in 1 ml in 1-11/2 hours after setting up the experiment. The method was considerably more sensitive and made it possible to obtain the results faster than by the biological test.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
AD0443673
Corporate Author:
ARMY BIOLOGICAL LABS FREDERICK MD
Unclassified Title:
(U) BOTULINUM TOXOIDS
Personal Author(s):
Cardella, Matteo A
Report Date:
Jun 1964
Media Count:
30 Page(s)
Report Number(s):
TECHNICAL MANUSCRIPT-141
XA-ABL/MD
Monitor Series:
ABL/MD
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
23 - AVAILABILITY: DOCUMENT PARTIALLY ILLEGIBLE
Distribution Statement:
Availability: Document partially illegible.
Abstract:
(U) Procedures were developed for preparing purified aluminum-phosphate-absorbed, univalent, bivalent, and pentavalent botulinum toxoids to immunize man. All preparations were well tolerated and elicited satisfactory antitoxin responses in man, whether administered as a single antigen or in combination. Four separate pentavalent Type ABCDE toxoids produced immune responses to each antigen in a considerable proportion of individuals following an initial series of three injections. A booster injection administered one year after the initial injection markedly increased the antitoxin titers, and measurable antitoxin titers were found in 86 to 100% of the individuals immunized. The toxoids were antigenic for mice, guinea pigs, and rabbits. In guinea pigs the toxoids afforded a high level of resistance to challenge with toxins administered by various routes.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
AD0612552
Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/612552.pdf
Size: 1 MB

Handle / proxy Url: http://handle.dtic.mil/100.2/AD612552
Corporate Author:
OXFORD UNIV (UNITED KINGDOM)
Unclassified Title:
(U) EXOTOXINS
Personal Author(s):
Van Heyningen, W E
Arseculeratne, S N
Report Date:
Jan 1964
Media Count:
22 Page(s)
Report Number(s):
X5-DRIC*
Monitor Series:
DRIC*
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
Distribution Statement:
Approved for public release; distribution is unlimited.
Abstract:
(U) Contents: Diphtheria toxin The physiology of diphtheria toxin production The nature of diphtheria toxin The mode of action of diphtheria toxin Staphylococcal toxins Staphylococcal alpha toxin Staphylococcal leucocidin Staphylococcal enterotoxin Neurotoxins Dysentery toxin Botulinum toxin Tetanus toxin.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
AD0424666
Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/424666.pdf
Size: 546 KB
Handle / proxy Url: http://handle.dtic.mil/100.2/AD424666
Corporate Author:
ARMY BIOLOGICAL LABS FREDERICK MD
Unclassified Title:
(U) EFFECT OF GUANDINIUM SALTS ON THE TOXICITY OF BOTULINUM TOXIN
Personal Author(s):
Stefanye, David
Iwamasa, Robert T
Schantz, Edward J
Sepro, Leonard

Report Date:
Oct 1963
Media Count:
13 Page(s)
Report Number(s):
TM-108
XA-ABL/MD
Monitor Series:
ABL/MD
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
23 - AVAILABILITY: DOCUMENT PARTIALLY ILLEGIBLE
Distribution Statement:
Approved for public release; distribution is unlimited. Document partially illegible.
Abstract:
(U) The effect of guanidinium salts on the stability of botulinum toxin and the mechanisms through which denaturation by these salts occurs is described. Some salts are effective in reducing toxicity at low concentrations; in others, toxicity is retainedeven in saturated solution. The nature of the interaction is complex, involving more than a change in folding or conformation. The hypothesis that salt solutions with higb thermodynamic water activity labilize the hydrogen-bonded structure of the protein is shown to be invalid. Also shown to be inapplicable is the hypothesis that a direct effect of the anion on the quanidinium cation leads to a reduction of its thermodynamic activity and ability to break hydrogen bonds. The protective mechanism appears to operate via binding of anions across clusters of cationic sites on the charged protein to preserve spatial configurations and charge distributions.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
AD0404870
Corporate Author:
ARMY BIOLOGICAL LABS FREDERICK MD
Unclassified Title:
(U) RESISTANCE OF GUINEA PIGS IMMUNIZED WITH BOTULINUM TOXOIDS TO AEROGENIC CHALLENGE WITH TOXIN
Descriptive Note:
Technical manuscript
Personal Author(s):
Cardella, Matteo A
Jemski, Joseph V
Tonik, Ellis J
Fiock, Mary A
Report Date:
May 1963

Media Count:
9 Page(s)
Report Number(s):
TM-66
XA-ABL/MD
Monitor Series:
ABL/MD
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
23 - AVAILABILITY: DOCUMENT PARTIALLY ILLEGIBLE
Distribution Statement:
Availability: Document partially illegible.
Abstract:
(U) Data are presented showing that active immunization of guinea pigs with botulinum toxoids afforded a high level of protection to challenge with botulinum toxins by the respiratory route. Resistance to challenge by this route was similar to resistance afforded to challenge by the parenteral and oral routes. The high survival percentages obtained in these studies made it impossible to establish any relationship between serum antitoxin titer and resistance to challenge. This report presents results of some studies to determine resistance afforded actively immunized guinea pigs to challenge with botulinum toxins by the respiratory route. Expression of LD50 estimates in guinea pig intraperitoneal LD50 suggests that normal guinea pigs show essentially similar susceptially to the five toxins administered by the respiratory route. The respiratory susceptibility is more closely related to their oral susceptibility than to their intraperitoneal susceptibility with at least four of the five types.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
AD0404553
Corporate Author:
ARMY BIOLOGICAL LABS FREDERICK MD
Unclassified Title:
(U) THE ROLE OF WATER IN THE ETIOLOGY OF ANIMAL BOTULISM METHOD OF DETECTION OF BOTULISMUS TOXIN C IN WATER,
Personal Author(s):
Pigoury, L
Michel, C
Chabassol, AND C
Report Date:
Mar 1963
Media Count:
2 Page(s)
Report Number(s):
Trans-751

Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
AD0286060
Corporate Author:
ARMY RESEARCH OFFICE WASHINGTON DC
Unclassified Title:
(U) PROBLEMS AND PROGRESS IN THE STUDY OF ORAL TOXICITY OF BACTERIAL TOXINS
Personal Author(s):
LAMANNA, CARL
Report Date:
Dec 1962
Media Count:
21 Page(s)
Report Number(s):
XA-ARO/DC
Monitor Series:
ARO/DC
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
23 - AVAILABILITY: DOCUMENT PARTIALLY ILLEGIBLE
Distribution Statement:
Availability: Document partially illegible.
Abstract:
(U) Food poisoning is caused by the consumption of harmful chemical products produced by the growth of bacteria. Absorption from the intestine into the blood stream takes place by way of the lymphatic system draining the intestine. Evidence was presented for the concept that even the normal intestine presents no absolute barrier to systemic absorption of protein by way of the lymphatics. The high potency of bacterial toxins accounts for their oral toxicity. Only fantastically small amounts of toxins need escape digestion and be absorbed in order for them to still remain poisonous upon consumption and exposure to digestive juices. A hypothesis was presented that relates food poisoning by bacterial toxins to accidental circumstances of contact with these poisons rather than any unusual chemical properties that permit them to escape the vicissitudes normal to proteins in the gut.
Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
AD0285026
Corporate Author:
ARMY BIOLOGICAL LABS FREDERICK MD
Unclassified Title:
(U) MODERN TREATMENT OF RESPIRATORY FAILURE IN BOTULISM
Personal Author(s):
RULNJEVIC, JURAJ
SVARA, VESNA
Report Date:
11 Sep 1962
Media Count:
1 Page(s)
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
AD0291036
Corporate Author:
ARMY BIOLOGICAL LABS FREDERICK MD
Unclassified Title:
(U) RESULTS OF COMPARATIVE EXPERIMENTAL INVESTIGATIONS INTO THE THERAPEUTIC EFFECTIVE OF ANTITOXIN, FORMOL TOXOID, AND THE COMBINATION OF THE TWO ON THE INTOXICATION INDUCED BY CL. BOTULINI (D)*-TOXIN
Personal Author(s):
KATIC, R V
Report Date:
Sep 1962
Media Count:
1 Page(s)
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:

AD0636854

Corporate Author:
ARMY BIOLOGICAL LABS FREDERICK MD

Unclassified Title:
(U) STUDIES OF IMMUNITY TO TOXINS OF CLOSTRIDIUM BOTULINUM. VIII. IMMUNOLOGICAL RESPONSE OF MAN TO PURIFIED BIVALENT AB BOTULINUM TOXOID

Personal Author(s):
Fiock, Mary A
Devine, Leonard F
Gearinger, Naomi F
Duff, James T
Wright, George G

Report Date:
20 May 1961

Media Count:
8 Page(s)

Report Number(s):
XA-ABL/MD

Monitor Series:
ABL/MD

Report Classification:
Unclassified

Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY
23 - AVAILABILITY: DOCUMENT PARTIALLY ILLEGIBLE

Distribution Statement:
Approved for public release; distribution is unlimited., Availability: Available only to DTIC users. U.S. Government or Federal Purpose Rights License., Availability: Document partially illegible.

Abstract:
(U) The response of man to immunization with a purified, bivalent, AB botulinum toxoid was investigated. The toxoid was well tolerated; only occasional mild local reactions were encountered. Four schedules of immunization were studied; 0.5-ml injections were given at 0, 2, 4 and 6 weeks, at 0 and 8 weeks, at 0, 2 and 10 weeks and at 0 and 10 weeks; serum antitoxin titers were determined at intervals thereafter. Titers of 0.02 unit of type A and 0.005 unit of type B antitoxin were considered satisfactory, since guinea pigs with these antitoxin levels survived intraperitoneal i.p. challenge with approximately 106 mouse i.p. LD50 of homologous toxin. The 0-2-10 week immunization schedule produced the highest proportion of satisfactory titers and the highest mean titers. Booster inoculations of 0.5 ml were given 1 year after the initial injection, except for one group in which boosters were given after 6 months. Marked increases in antitoxin titers were observed following the 1-year boosters, the mean titers reaching a value at least 500 times the satisfactory level and remaining well above this level for at least 2 years. Six-month boosters were considerably less effective, both with respect to the magnitude and to the duration of the secondary response. Prior immunization with univalent type A toxoid depressed the response to the type B component of the bivalent preparation. After storage for 3 1/4 years at 4C the toxoid appeared to have deteriorated slightly, although considerable antigenicity remained.

Abstract Classification:
Unclassified

Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
AD0253253
Corporate Author:
CALIFORNIA UNIV OAKLAND NAVAL BIOLOGICAL LAB
Unclassified Title:
(U) ORAL POISONING BY BACTERIAL EXOTOXINS EXEMPLIFIED IN BOTULISM
Personal Author(s):
LAMANNA, CARL
Report Date:
30 Sep 1960
Media Count:
8 Page(s)
Report Number(s):
XB-ONR
XB-BUMED
Contract Number:
NONR-22273
Monitor Series:
ONR
BUMED
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
20 - JOURNAL ARTICLES; DTIC USERS ONLY
23 - AVAILABILITY: DOCUMENT PARTIALLY ILLEGIBLE
Distribution Statement:
Availability: Pub. in Annals of the New York Academy of Sciences, v90 p1109-1114, 11 Nov 1960. Available only to DTIC users. No copies furnished by NTIS., Availability: Document partially illegible.
Abstract:
(U) No evidence has been developed for pinpointing the chemical basis for toxicity, both parenteral and oral, in botulism. Oral toxicity for botulinal toxin can hardly be considered as unusual property because diphtheria and tetanus toxins, bacterial exotoxins not ordinarily thought of as oral poisons, will cause toxemia when ingested. Perhaps in diphtheria this fact has some role to play in the natural infection since the organisms growing in the nasopharyngeal area are producing toxin that must in part be ingested as an inevitable consequence of the swallowing reflex. Thought should be given to the possibility that some cases of cryptogenic tetanus may arise from oral or intestinal posioning. Oral toxicity of botulinal toxin would appear to be affected by any factor that can influence the length of residence of active toxin in the small intestine and the permeability of the small intestine to whole protein. Our knowledge of these problems is still at the stage of development of fundamental descriptive data. In the immediate future we will require knowledge of the anatomical and physiological bases for these data as they are acquired before we can proceed to the ultimate biochemical understanding of toxicity at the molecular level.

Abstract Classification:
Unclassified

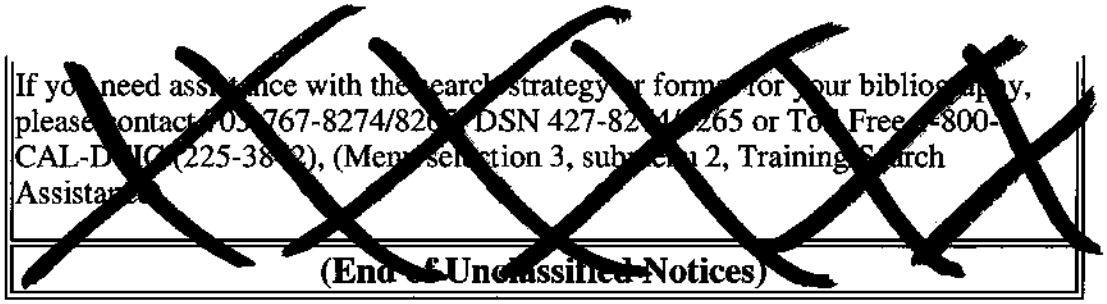
Technical Reports Collection

Citation Format: FOIA(U2)

Accession Number:
AD0240949
Full Text (pdf) Availability:
View Full Text (pdf)
File: /U2/240949.pdf
Size: 665 KB
Handle / proxy Url: http://handle.dtic.mil/100.2/AD240949
Corporate Author:
CALIFORNIA UNIV OAKLAND NAVAL BIOLOGICAL LAB
Unclassified Title:
(U) ON THE SIZE OF THE TOXIC PARTICLE PASSING THE INTESTINAL BARRIER IN BOTULISM
Personal Author(s):
Heckly, Robert J
Hildebrand, G J
Lamanna, Carl
Report Date:
26 Jan 1960
Media Count:
17 Page(s)
Report Number(s):
XB-BUMED
Contract Number:
NONR-22273
Monitor Series:
BUMED
Report Classification:
Unclassified
Distribution Limitation(s):
01 - APPROVED FOR PUBLIC RELEASE
23 - AVAILABILITY: DOCUMENT PARTIALLY ILLEGIBLE
Distribution Statement:
Approved for public release; distribution is unlimited. Document partially illegible.

Highest Classification: UNCLASSIFIED

Encl 2



Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
ADB321585
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/b321585.pdf
Size: 15 MB
Corporate Author:
CREATV MICROTECH INC POTOMAC MD
Unclassified Title:
(U) Rapid Detection of Active versus Inactive Botulinum Toxin
Descriptive Note:
Final rept. 8 Nov 2005-31 Jul 2006
Personal Autbor(s):
Tang, Cha-Mei
Hang, Jun
Zhu, Peixuan
Lee, Jia-Hai
Li, Shuhong
Amstutz, Pete
Report Date:
31 Jul 2006
Media Count:
22 Page(s)
Report Number(s):
XA-AMCOM
Contract Number:
W31P4Q-06-C-0087
ARPA ORDER-U051-23
Monitor Series:
AMCOM
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies only; Proprietary Information; JUL 2006. Other requests shall be referred to Defense Advanced Research Projects Agency, Attn: SPO, 3701 N.

Fairfax Dr., Arlington, VA 22203-1714

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
ADB316066
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/b316066.pdf
Size: 422 KB
Corporate Author:
PLANET BIOTECHNOLOGY HAYWARD CA
Unclassified Title:
(U) Botulinum Toxin Plantibodies
Descriptive Note:
Annual rept. 15 Oct 2004-14 Oct 2005
Personal Author(s):
Wycoff, Keith
Report Date:
Nov 2005
Media Count:
13 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-03-C-0103
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies only; Specific Authority; Proprietary Information; NOV 2005. Other requests shall be referred to U.S. Army Medical Research and Materiel Command, 504 Scott St., Ft. Detrick, MD 21702-5012.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
ADB316432
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/b316432.pdf
Size: 353 KB

Corporate Author:
MAYO FOUNDATION ROCHESTER MN
Unclassified Title:
(U) Development of Small-Molecular Countermeasures for Botulinum Neurotoxins
Descriptive Note:
Annual rept. 15 Oct 2003-14 Oct 2004
Personal Author(s):
Pang, Yuan-Ping
Report Date:
Nov 2005
Media Count:
9 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
W81XWH-04-2-0001
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies only; Proprietary Information; NOV 2005. Other requests shall be referred to U.S. Army Medical Research and Materiel Comd., 504 Scott St., Fort Detrick, MD 21702-5012.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
ADB311690
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/b311690.pdf
Size: 2 MB
Corporate Author:
PENNSYLVANIA STATE UNIV HERSHEY
Unclassified Title:
(U) Effective of Ganglioside Derivatives as Potential Ligands for Botulinum Neurotoxin Serotype A
Descriptive Note:
Final rept. 28 Jun 2002-27 Jun 2005
Personal Author(s):
Schengrund, Cara-Lynne
Yowler, Brian C
Petro, Kimberly
Report Date:
Jul 2005

Media Count:
27 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-02-1-0676
Monitor Series:
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Citation Format: FOIA(UL)

Accession Number:
ADB316433
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File: /UL/b316433.pdf
Size: 5 MB
Corporate Author:
MAYO CLINIC ROCHESTER MN
Unclassified Title:
(U) Development of Small-Molecular Countermeasures for Botulinum Neurotoxins
Descriptive Note:
Annual rept. 15 Oct 2004-14 Oct 2005
Personal Author(s):
Pang, Yuan-Ping
Report Date:
Nov 2004
Media Count:
78 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
W81XWH-04-2-0001
Monitor Series:
USAMRMC
Report Classification:
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Distribution Limitation(s):
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Distribution Statement:

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Accession Number:
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Full Text (pdf) Availability:
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File: /UL/b305395.pdf
Size: 12 MB
Corporate Author:
WEST DESERT TEST CENTER DUGWAY PROVINGGROUND UTAH
Unclassified Title:
(U) Abbreviated Test Report for Technology Readiness Assessment 04-1
Descriptive Note:
Abbreviated test rept. Jun-Sep 2004
Personal Author(s):
Hogan, Jeffery N
Harper, Bruce G
Report Date:
Sep 2004
Media Count:
65 Page(s)
Report Number(s):
WDTC-TR-04-083
XA-ADTC/APG
Contract Number:
8-ES-685-TRE-002
Monitor Series:
ADTC/APG
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
26 - NOT AVAILABLE IN MICROFICHE
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies only; Test and Evaluation; Sep 2004. Other requests shall be referred to U.S. Army Research Development and Engineering Command, Technology Readiness Assessment Office, Attn: AMSRD-ECE-RT-DE, Bldg. 3326, 5183 Blackhawk Rd., Aberdeen Proving Ground, MD 21010., Availability: This document is not available from DTIC in microfiche.

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Accession Number:
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File: /UL/b302526.pdf
Size: 2 MB
Corporate Author:
PENNSYLVANIA STATE UNIV HERSHEY
Unclassified Title:
(U) Effectiveness of Ganglioside Derivatives as Potential Ligands for Botulinum Neurotoxin Serotype A
Descriptive Note:
Annual rept. 28 Jun 2003-27 Jun 2004
Personal Author(s):
Schengrund, Cara-Lynne
Yowler, Brian C
Petro, Kimerly
Report Date:
Jul 2004
Media Count:
43 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-02-1-0676
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
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Accession Number:
ADB296829
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/b296829.pdf
Size: 567 KB
Corporate Author:
PLANET BIOTECHNOLOGY HAYWARD CA
Unclassified Title:
(U) Botulinum Toxin Plantibodies

Descriptive Note:
Final rept. 1 Aug 2003-31 Jan 2004
Personal Author(s):
Wycoff, Keith
Report Date:
Feb 2004
Media Count:
13 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-03-C-0103
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies only; Proprietary Info., Specific Authority; Feb 2004. Other requests shall be referred to U.S. Army Medical Research and Materiel Command, 504 Scott St., Ft. Detrick, MD 21702-5012.

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Citation Format: FOIA(UL)

Accession Number:
ADB309462
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/b309462.pdf
Size: 8 MB
Corporate Author:
MASSACHUSETTS UNIV NORTH DARTMOUTH
Unclassified Title:
(U) Protein Receptor(s) of Botulinum Neurotoxin
Descriptive Note:
Annual rept. 19 Dec 2002-18 Dec 2003
Personal Author(s):
Singh, Bal R
Report Date:
Jan 2004
Media Count:
139 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-02-C-0001
Monitor Series:

USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
Distribution Statement:
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Citation Format: FOIA(UL)

Accession Number:
ADB295166
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/b295166.pdf
Size: 906 KB
Corporate Author:
SCRIPPS RESEARCH INST LA JOLLA CA
Unclassified Title:
(U) Three-Dimensional Structure Determination of Botulinum Toxin
Descriptive Note:
Annual rept. 1 Oct 2002-30 Sep 2003
Personal Author(s):
Stevens, Raymond C
Report Date:
Oct 2003
Media Count:
13 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-00-C-0040
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies only; Proprietary Information; Oct 2003. Other requests shall be referred to US Army Medical Research and Materiel Command, 504 Scott Street, Ft. Detrick, MD 21702-5012

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Citation Format: FOIA(UL)

Accession Number:
ADB290578
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/b290578.pdf
Size: 711 KB
Corporate Author:
PENNSYLVANIA STATE UNIV HERSHEY
Unclassified Title:
(U) Effectiveness of Ganglioside Derivatives as Potential Lignands for Botulinum Neurotoxin Serotype A
Descriptive Note:
Annual rept. 28 Jun 2002-27 Jun 2003
Personal Author(s):
Schengrund, Cara-Lynne
Yowler, Brian C
Report Date:
Jul 2003
Media Count:
14 Page(s)
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XA-USAMRMC
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DAMD17-02-1-0676
Monitor Series:
USAMRMC
Report Classification:
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Distribution Statement:
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Citation Format: FOIA(UL)

Accession Number:
ADB288393
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/b288393.pdf
Size: 1 MB
Corporate Author:
ANALYTICAL BIOLOGICAL SERVICES INC WILMINGTON DE
Unclassified Title:

(U) Fluorescent Liposomes for Detection for Detection of Biowarfare Agent Toxins in Water

Descriptive Note:
Final rept. 1 Oct 2002-31 Mar 2003

Personal Author(s):
Reppy, Mary A

Report Date:
29 Apr 2003

Media Count:
18 Page(s)

Report Number(s):
ARO-73-FINAL
ARO-44187.1-CH-ST1
XA-ARO

Contract Number:
DAAD19-02-C-0072

Monitor Series:
44187.1-CH-ST1
ARO

Report Classification:
Unclassified

Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED

Distribution Statement:
Distribution authorized to U.S. Gov't. agencies only; Proprietary Info.; Apr 2003. Other requests shall be referred to US Army Reseach Ofc., PO Box 12211, Research Triangle Park, NC 27709-2211.

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Citation Format: FOIA(UL)

Accession Number:
ADB288545

Full Text (pdf) Availability:
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File: /UL/b288545.pdf
Size: 8 MB

Corporate Author:
SOUTHEASTERN MASSACHUSETTS UNIV NORTH DARTMOUTH

Unclassified Title:
(U) Protein Receptor(s) of Botulinum Neurotoxin

Descriptive Note:
Annual rept. 19 Dec 2001-18 Dec 2002

Personal Author(s):
Singh, Bal R

Report Date:
Jan 2003

Media Count:
131 Page(s)

Report Number(s):

XA-USAMRMC
Contract Number:
DAMD17-02-C-0001
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies only; Proprietary Info.; Jan 03. Other requests shall be referred to U.S. Army Medical Research and Materiel Command, 504 Scott St., Ft. Detrick, MD 21702-5012.

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Citation Format: FOIA(UL)

Accession Number:
ADB286724
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/b286724.pdf
Size: 3 MB
Corporate Author:
SCRIPPS RESEARCH INST LA JOLLA CA
Unclassified Title:
(U) Structural Understanding of Botulinum Neurotoxin for Mechanistic Understanding, Vaccine Development and Inhibitor Design
Descriptive Note:
Annual rept. 1 Oct 2001-30 Sep 2002
Personal Author(s):
Stevens, Raymond C
Report Date:
Oct 2002
Media Count:
47 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-00-C-0040
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies only; Proprietary Info.; Oct 2002. Other requests shall be referred to U.S. Army Medical Research and Materiel Command, 504 Scott St., Ft.

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Citation Format: FOIA(UL)

Accession Number:
ADB283879
Full Text (pdf) Availability:
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File: /UL/b283879.pdf
Size: 1 MB
Corporate Author:
HAWAII BIOTECHNOLOGY GROUP INC AIEA
Unclassified Title:
(U) Combinatorial Discovery and Optimization of Botulinum Toxin Inhibitors
Descriptive Note:
Annual rept. 1 Sep 2001-31 Aug 2002
Personal Author(s):
O'Malley, Sean
Report Date:
Sep 2002
Media Count:
28 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-00-C-0032
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies only; Proprietary Info.; Sep 2002. Other requests shall be referred to U.S. Army Medical Research and Materiel Command, 504 Scott St., Ft. Detrick, MD 21702-5012.

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Accession Number:
ADB282190
Full Text (pdf) Availability:
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File: /UL/b282190.pdf
Size: 4 MB

Corporate Author:
METABIOLOGICS INC MADISON WI
Unclassified Title:
(U) Development of Delivery Vehicle Targeting Cholinergic Neurons
Descriptive Note:
Final rept. 12 Jun 2000-11 Jun 2002, Phase 2
Personal Author(s):
Goodnough, Michael C
Report Date:
Jul 2002
Media Count:
59 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-99-C-9098
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
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Distribution Statement:
Distribution authorized to U.S. Gov't. agencies only; Proprietary Information; Jul 2002. Other requests shall be referred to US Army Medical Research and Materiel Command, 504 Scott Street, Fort Detrick, MD 21702

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Accession Number:
ADB322073
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File: /UL/b322073.pdf
Size: 987 KB
Corporate Author:
ARMY MEDICAL RESEARCH INST OF CHEMICAL DEFENSE ABERDEEN PROVING GROUND MD
Unclassified Title:
(U) Botulism in Casablanca (11 Cases)
Descriptive Note:
Journal article
Personal Author(s):
Ouagari, Z
Chakib, A
Sodqi, M
Marih, L
Filali, K M

Benslama, A
Idrissi, L
Moutawakkil, S
Himmich, H

Report Date:
Jan 2002

Media Count:
15 Page(s)

Report Number(s):
XA-USAMRICD

Monitor Series:
USAMRICD

Report Classification:
Unclassified

Distribution Limitation(s):
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Distribution Statement:
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Size: 1 MB

Corporate Author:
SCRIPPS RESEARCH INST LA JOLLA CA

Unclassified Title:
(U) Three-Dimensional Structure Determination of Botulinum Toxin

Descriptive Note:
Annual rept. 1 Oct 2000-30 Sep 2001

Personal Author(s):
Stevens, Raymond C

Report Date:
Oct 2001

Media Count:
25 Page(s)

Report Number(s):
XA-USAMRMC

Contract Number:
DAMD17-00-C-0040

Monitor Series:
USAMRMC

Report Classification:
Unclassified
Distribution Limitation(s):
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Distribution Statement:
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Accession Number:
ADB278857
Full Text (pdf) Availability:
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File: /UL/b278857.pdf
Size: 2 MB
Corporate Author:
HAWAII BIOTECHNOLOGY GROUP INC AIEA
Unclassified Title:
(U) Combinatorial Discovery and Optimization of Botulinum Toxin Inhibitors
Descriptive Note:
Annual rept. 1 Sep 2000-31 Aug 2001
Personal Author(s):
Grothaus, Paul G
Report Date:
Sep 2001
Media Count:
39 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-00-C-0032
Monitor Series:
USAMRMC
Report Classification:
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Distribution Limitation(s):
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Distribution Statement:
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Accession Number:
ADB277933
Full Text (pdf) Availability:
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File: /UL/b277933.pdf
Size: 1 MB
Corporate Author:
SOLUS BIODEFENSE WASHINGTON DC
Unclassified Title:
(U) Synthesis of Combinatorial Libraries Containing Potential Inhibitors of Botulinum Neurotoxin Protease Activity
Descriptive Note:
Final rept. 8 Jan-7 Jun 2001, Phase 1
Personal Author(s):
VON Hanwehr, Roger
Lewis, David E
Report Date:
Aug 2001
Media Count:
31 Page(s)
Report Numher(s):
XA-USAMRMC
Contract Number:
DAMD17-01-C-0014
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
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Distribution Statement:
Distribution authorized to U.S. Gov't. agencies only; Specific Authority, Proprietary Info.; Aug 2001. Other requests shall be referred to U.S. Army Medical Research and Materiel Command, 504 Scott St., Ft. Detrick, MD 21702-5012.

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Citation Format: FOIA(UL)

Accession Number:
ADC066644
Corporate Author:
DYNAMICS TECHNOLOGY INC TORRANCE CA
Unclassified Title:
(U) Waterborne BW-Related Effluents
Descriptive Note:
Final rept. 8 Jun 2000-30 Jun 2001
Personal Author(s):
Borchardt, S R
Randolph, C R

Platte, R D

Report Date:
30 Jun 2001

Media Count:
74 Page(s)

Report Number(s):
DTIE-01-0040
XD-DARPA

Contract Number:
MDA972-00-C-0048
ARPA ORDER J994/05

Monitor Series:
DARPA

Report Classification:
SECRET

Distribution Limitation(s):
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Distribution Statement:
Distribution authorized to U.S. Gov't. agencies only; Proprietary Info.; Jun 2001. Other requests shall be referred to Defense Advanced Research Projects Agcy., 3701 N. Fairfax Dr., Arlington, VA 22203-1714.

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Accession Number:
ADA386484

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File: /UL/a386484.pdf
Size: 1 MB

Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD

Unclassified Title:
(U) Light Chain of Botulinum A Neurotoxin Expressed as an Inclusion Body from a Synthetic Gene is Catalytically and Functionally Active

Personal Author(s):
Ahmed, S A
Smith, Leonard A

Report Date:
02 Feb 2001

Media Count:
14 Page(s)

Report Number(s):
XA-USAMRIID

Monitor Series:
USAMRIID

Report Classification:
Unclassified

Distribution Limitation(s):
12 - U.S. GOVT. AND THEIR CONTRACTORS
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Distribution Statement:
Distribution: DTIC Users Only., Availability: Pub. in Journal of Protein Chemistry, v19 n6 p475-487, 2000. Available only to DTI

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ADA385319
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/a385319.pdf
Size: 3 MB
Corporate Author:
BATTELLE MEDICAL RESEARCH AND EVALUATION FACILITY COLUMBUS OH
Unclassified Title:
(U) A Medical Research and Evaluation Facility (MREF) and Studies Supporting the Medical Chemical Defense Program
Descriptive Note:
Final rept. 31 Jan 1989-31 Dec 2000
Personal Author(s):
Olson, Carl T
Report Date:
Dec 2000
Media Count:
51 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-89-C-9050
Monitor Series:
USAMRMC
Report Classification:
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Distribution Limitation(s):
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Accession Number:
ADA382472

Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/a382472.pdf
Size: 14 MB

Corporate Author:
BATTELLE MEMORIAL INST COLUMBUS OH

Unclassified Title:
(U) Neurophysiologic and Neuropathologic Effects in Monkeys of Low Level Exposures to Sarin, Pryidostigmine, Pesticides, and Botulinum Toxoid

Descriptive Note:
Final rept. 30 Sep 1997-30 Jun 2000

Personal Author(s):
Olson, Carl T
Podell, Michael
Sahenk, Zarife
Lordo, Robert
Kinney, Pamela

Report Date:
Jul 2000

Media Count:
272 Page(s)

Report Number(s):
XA-USAMRMC

Contract Number:
DAMD17-97-C-7065

Monitor Series:
USAMRMC

Report Classification:
Unclassified

Distribution Limitation(s):
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Citation Format: FOIA(UL)

Accession Number:
ADA375184

Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/a375184.pdf
Size: 10 MB

Corporate Author:
BATTELLE MEMORIAL INST COLUMBUS OH

Unclassified Title:
(U) Effect of Increasing Toxin Levels on Guineau Pigs Passively Immunized With Human Botulinum Immune Globulin

Descriptive Note:

Final rept. Task 97-52
Personal Author(s):
Olson, Carl T
Report Date:
Jan 2000
Media Count:
265 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-89-C-9050
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
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Citation Format: FOIA(UL)

Accession Number:
ADA395548
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/a395548.pdf
Size: 275 KB
Corporate Author:
FOOD AND DRUG ADMINISTRATION ROCKVILLE MD
Unclassified Title:
(U) Vaccines, Pharmaceutical Products, and Bioterrorism: Challenges for the U.S. Food and Drug Administration
Personal Author(s):
Zoon, Kathryn C
Report Date:
Aug 1999
Media Count:
4 Page(s)
Report Number(s):
XD-OSD
Monitor Series:
OSD
Report Classification:
Unclassified
Distribution Limitation(s):
12 - U.S. GOVT. AND THEIR CONTRACTORS
20 - JOURNAL ARTICLES; DTIC USERS ONLY

Distribution Statement:
Distribution: DTIC Users Only., Availability: Pub. in Emerging Infectious Diseases v 5 n4 p534-537, Jul-Aug 1999. Available only

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Citation Format: FOIA(UL)

Accession Number:
ADA395481
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/a395481.pdf
Size: 445 KB
Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD
Unclassified Title:
(U) Potential Biological Weapons Threats
Personal Author(s):
Kortepeter, Mark G
Parker, Gerald W
Report Date:
Aug 1999
Media Count:
6 Page(s)
Report Number(s):
XD-OSD
Monitor Series:
OSD
Report Classification:
Unclassified
Distribution Limitation(s):
12 - U.S. GOVT. AND THEIR CONTRACTORS
20 - JOURNAL ARTICLES; DTIC USERS ONLY
Distribution Statement:
Distribution: DTIC Users Only., Availability: Pub. in Emerging Infectious Diseases v5 n4 p523-527, Jul-Aug 1999. Available only

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Citation Format: FOIA(UL)

Accession Number:
ADB247025
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/b247025.pdf
Size: 4 MB
Corporate Author:

PROMEGA MADISON WI

Unclassified Title:
(U) The Design and Synthesis of Orally Active Inhibitors of Botulinum Toxin Metalloproteases

Descriptive Note:
Annual rept. 2 Mar 98-1 Mar 99

Personal Author(s):
Zdanovsky, Alexey G

Report Date:
Apr 1999

Media Count:
78 Page(s)

Report Number(s):
XA-USAMRMC

Contract Number:
DAMD17-97-C-7026

Monitor Series:
USAMRMC

Report Classification:
Unclassified

Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED

Distribution Statement:
Distribution authorized to U.S. Gov't. agencies only; Specific Authority; Apr 99. Other requests shall be referred to U.S. Army Medical Research and Materiel Command, 504 Scott St, Fort Detrick, MD 21702-5012.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
ADA361498

Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/a361498.pdf
Size: 5 MB

Corporate Author:
BATTELLE MEMORIAL INST COLUMBUS OH

Unclassified Title:
(U) A Medical Research and Evaluation Facility (MREF) and Studies Supporting the Medical Chemical Defense Program.

Descriptive Note:
Final rept. Task 97-51

Personal Author(s):
Olson, Carl T
Gelzleichter, Thomas R
Myers, Melissa A
Menton, Ronald G
Niemuth, Nancy A

Report Date:

Mar 1999
Media Count:
176 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-89-C-9050
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
12 - U.S. GOVT. AND THEIR CONTRACTORS
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Distribution: DTIC Users Only.

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Accession Number:
ADA361299
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/a361299.pdf
Size: 12 MB
Corporate Author:
BATTELLE MEDICAL RESEARCH AND EVALUATION FACILITY WEST JEFFERSON OH
Unclassified Title:
(U) Evaluation of the Passive Protection Against Five Serotypes of Botulinum Toxin Provided by Botulinum Human Immune Globulin in an Animal Model
Descriptive Note:
Final rept.
Personal Author(s):
Gelzleichter, Thomas R
Myers, Melissa A
Menton, Ronald G
Niemuth, nancy A
Matthews, M C
Report Date:
May 1998
Media Count:
344 Page(s)
Report Number(s):
TASK-96-45
XA-USAMRMC
Contract Number:
DAMD17-89-C-9050
Monitor Series:

USAMRMC
Report Classification:
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Accession Number:
ADB238755
Full Text (pdf) Availability:
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File: /UL/b238755.pdf
Size: 1 MB
Corporate Author:
PROMEGA MADISON WI
Unclassified Title:
(U) The Design and Construction of Botulinum Toxin Drug Delivery Vehicles
Descriptive Note:
Final rept. 14 Nov 97-13 May 98
Personal Author(s):
Zdanovsky, Alexey G
Report Date:
May 1998
Media Count:
25 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-98-C-8015
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies only; Specific Authority; Oct 98 Other requests shall be referred to Army Medical Research and Materiel Command, Fort Detrick, MD 21702-5012

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Citation Format: FOIA(UL)

Accession Number:
ADB236084
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/b236084.pdf
Size: 3 MB
Corporate Author:
OPHIDIAN PHARMACEUTICALS INC MADISON WI
Unclassified Title:
(U) Quantitative Detection of Toxins Using Novel Compounds that Bind to Carbohydrate Binding Sites.
Descriptive Note:
Final rept. Pbase I-14 Nov 97-13 May 98
Personal Author(s):
Firca, Joseph R
Report Date:
May 1998
Media Count:
68 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-98-C-8007
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies only; Specific Authority; Jun 98. Other requests shall be referred to U.S. Army Medical Research and Materiel Command, 504 Scott Street, Fort Detrick, MD 21702-5012.

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Citation Format: FOIA(UL)

Accession Number:
ADA364139
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/a364139.pdf
Size: 6 MB
Corporate Author:
RAND NATIONAL DEFENSE RESEARCH INST SANTA MONICA CA
Unclassified Title:
(U) Military Use of Drugs Not Yet Approved by the FDA for CW/BW Defense. Lessons from the Gulf War
Personal Author(s):

Rettig, Richard A
Report Date:
Feb 1998
Media Count:
118 Page(s)
Report Number(s):
RAND-MR-1018/9-OSD
XD-OSD
Contract Number:
DASW01-95-C-0059
Monitor Series:
OSD
Report Classification:
Unclassified
Distribution Limitation(s):
12 - U.S. GOVT. AND THEIR CONTRACTORS
Distribution Statement:
Distribution: DTIC Users Only.

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Citation Format: FOIA(UL)

Accession Number:
ADB233079
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/b233079.pdf
Size: 1 MB
Corporate Author:
HBR TECHNOLOGIES INC HODGE LA
Unclassified Title:
(U) Development of Decontamination Compounds for Therapeutic Use on Chemical Threat Agent Wounds.
Descriptive Note:
Final rept 1 Jan -31 Dec 97
Personal Author(s):
Dankert, John R
Report Date:
Dec 1997
Media Count:
29 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-97-C-7031
Monitor Series:
USAMRMC
Report Classification:
Unclassified

Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies only; Proprietary Information; Nov 97. Other requests shall be referred to U.S. Army Medical Research and Materiel Command, 504 Scott St., Fort Detrick, MD 21702-5012.

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Citation Format: FOIA(UL)

Accession Number:
ADB234008
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/b234008.pdf
Size: 1 MB
Corporate Author:
HAWAII BIOTECHNOLOGY GROUP INC AIEA
Unclassified Title:
(U) Combinatorial Transition State Analog Inhibitor Library for Botulinum Toxin
Descriptive Note:
Final rept. Phase I 8 Nov 96-24 Jul 97
Personal Author(s):
Grothaus, Paul G
Report Date:
Jul 1997
Media Count:
30 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-97-C-7021
Monitor Series:
USAMRMC
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies only; Specific Authority; Mar 98. Other requests shall be referred to US Army Medical Research and Materiel Comd., ATTN: MCMR-RMI-S. Fort Detrick, Frederick, MD 21702-5012.

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Citation Format: FOIA(UL)

Accession Number:

ADB228576
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View Full Text (pdf)
File: /UL/b228576.pdf
Size: 18 MB
Corporate Author:
ARMY CONCEPTS ANALYSIS AGENCY BETHESDA MD
Unclassified Title:
(U) Biological Casualty Assessment Study (BIOCAS)
Descriptive Note:
Final rept. Jan-Jul 97
Personal Author(s):
Launstein, Robert J
Report Date:
Jul 1997
Media Count:
174 Page(s)
Report Number(s):
CAA-MR-97-34
XA-TAPC
Monitor Series:
TAPC
Report Classification:
Unclassified
Distribution Limitation(s):
02 - U.S. GOVT. AND THEIR CONTRACTORS
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies and their contractors; Specific Authority 17 Feb 1998. Other requests shall be referred to Army Personnel Command., 200 Stovall Street, Alexandria, Va 22332-0400.

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ADB227739
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File: /UL/b227739.pdf
Size: 1 MB
Corporate Author:
EDGEWOOD RESEARCH DEVELOPMENT AND ENGINEERING CENTER ABERDEEN PROVING GROUNDMD
Unclassified Title:
(U) Process Description for the Manufacture of Genetically Engineered Anti-Botulinum Toxin B

Monoclonal Antibodies.
Descriptive Note:
Final rept. Mar 91-May 96,
Personal Author(s):
Olsen, Gilbert G , II
Myers, Mark
Wohnlich, Lisa
Kracke, Suzanne
Phan, Kim
Report Date:
Jun 1997
Media Count:
38 Page(s)
Report Number(s):
ERDEC-SP-051
XA-AMC
Monitor Series:
AMC
Report Classification:
Unclassified
Distribution Limitation(s):
02 - U.S. GOVT. AND THEIR CONTRACTORS
57 - EXPORT CONTROL
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies and their contractors; Critical Technology; Jun 97. Other requests shall be referred to Dir., ERDEC, Attn: SCBRD-RT, Aberdeen Proving Ground, MD 21010-5423., This document contains export-controlled technical data.

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ADA395362
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File: /UL/a395362.pdf
Size: 1 MB
Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD
Unclassified Title:
(U) Clinical Recognition and Management of Patients Exposed to Biological Warfare Agents
Personal Author(s):
Franz, David R
Jahrling, Peter B
Friedlander, Arthur M

McClain, David J
Hoover, David L
Report Date:
Jan 1997
Media Count:
14 Page(s)
Report Number(s):
XD-OASD/PA
Monitor Series:
OASD/PA
Report Classification:
Unclassified
Distribution Limitation(s):
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ADA312774
Full Text (pdf) Availability:
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File: /UL/a312774.pdf
Size: 2 MB
Corporate Author:
NEBRASKA UNIV LINCOLN
Unclassified Title:
(U) Fermentation, Recovery, and Purification of the Hc Fragment of the Botulinum Neurotoxin from Pichia Pastoris.
Descriptive Note:
Annual rept.,
Personal Author(s):
Meagher, Michael M
Report Date:
Apr 1996
Media Count:
37 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-95-C-5003
Monitor Series:
USAMRMC
Report Classification:
Unclassified

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Distribution: DTIC Users Only.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
ADB259869
Corporate Author:
HAWAII BIOTECHNOLOGY GROUP INC AIEA
Unclassified Title:
(U) A94-073 Recombinant Antibodies for Chemical/Biological Warfare (CBW) Detection
Descriptive Note:
Final progress rept., Phase I, 15 Mar-15 Sep 1995
Personal Author(s):
Nakano, Eileen T
Bignami, Gary
Report Date:
Nov 1995
Media Count:
26 Page(s)
Report Number(s):
XA-ERDEC
Contract Number:
DAAM01-95-C-0027
Monitor Series:
ERDEC
Report Classification:
Unclassified
Distribution Limitation(s):
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ADB205628
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/b205628.pdf
Size: 1 MB

Corporate Author:
EAI CORP ABINGDON MD
Unclassified Title:
(U) Simplified Downwind Hazard Prediction for Biological Agents (SDWHPBA). Volume 1. Development of SDWHPBA Calculator.
Descriptive Note:
Technical rept.,
Personal Author(s):
Metz, Dennis
Lewis, Mark E
Report Date:
Jun 1995
Media Count:
40 Page(s)
Report Number(s):
DPG/JCP-95/013A
DPG/JCP-95/013A
XA- DPG/JCP
Contract Number:
DAAD09-93-D-0003
Monitor Series:
95/013A
DPG/JCP
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
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Accession Number:
ADA294284
Full Text (pdf) Availability:
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File: /UL/a294284.pdf
Size: 16 MB
Corporate Author:
IMPERIAL COLL OF SCIENCE AND TECHNOLOGY LONDON (UNITED KINGDOM) DEPT OF BIOCH EMISTRY
Unclassified Title:
(U) Exploitation of Botulinum Neurotoxins for Research and Clinical Purposes.
Descriptive Note:
Final rept. Nov 91-Feb 95,
Personal Author(s):

Dolly, James O
Report Date:
28 Feb 1995
Media Count:
254 Page(s)
Report Number(s):
XA-USAMRMC
Contract Number:
DAMD17-91-Z-1035
Monitor Series:
USAMRMC
Report Classification:
Unclassified
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Accession Number:
ADA301280
Full Text (pdf) Availability:
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File: /UL/a301280.pdf
Size: 733 KB
Corporate Author:
ARMY MEDICAL RESEARCH INST OF CHEMICAL DEFENSE ABERDEEN PROVING GROUND MD
Unclassified Title:
(U) Interactions between Heavy Metal Chelators and Botulinum Neurotoxins at the Mouse Neuromuscular Junction,
Personal Author(s):
Sheridan, Robert E
Deshpande, Sharad S
Report Date:
Jan 1995
Media Count:
13 Page(s)
Report Number(s):
USAMRICD-P93-031
XA-USAMRICD
Monitor Series:
USAMRICD
Report Classification:
Unclassified
Distribution Limitation(s):
12 - U.S. GOVT. AND THEIR CONTRACTORS

20 - JOURNAL ARTICLES; DTIC USERS ONLY

Distribution Statement:

Distribution: DTIC Users Only., Availability: Pub. in Toxicon, v33 n4 p539-549, 1995. Available only to DTIC users.No copies fur

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ADA279867

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View Full Text (pdf)

File: /UL/a279867.pdf

Size: 338 KB

Corporate Author:

VETERANS ADMINISTRATION MEDICAL CENTER PITTSBURGH PA

Unclassified Title:

(U) X-Ray Crystallography of Botulinum Neurotoxins

Descriptive Note:

Midterm rept. 1 May 1993-30 Apr 1994

Personal Author(s):

Sax, Martin

Pletcher, J

Report Date:

14 Apr 1994

Media Count:

8 Page(s)

Report Number(s):

XA-USAMRDALC

Contract Number:

MIPR-93MM3357

Monitor Series:

USAMRDALC

Report Classification:

Unclassified

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Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:

ADA275958

Corporate Author:

ARMY BIOMEDICAL RESEARCH AND DEVELOPMENT LAB FORT DETRICK MD

Unclassified Title:
(U) Treatment for Removal of Biotoxins from Drinking Water
Descriptive Note:
Technical rept. Oct 1989-Sep 1991
Personal Author(s):
Wannemacher, Robert W , Jr
Dinterman, Richard E
Thompson, William L
Schmidt, Mark O
Burrows, W D
Report Date:
Sep 1993
Media Count:
45 Page(s)
Report Number(s):
USABRDL-TR-9120
XA-USAMRDC
Monitor Series:
USAMRDC
Report Classification:
Unclassified
Distribution Limitation(s):
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Citation Format: FOIA(UL)

Accession Number:
ADC960230
Corporate Author:
JAYCOR BEAVERCREEK OH
Unclassified Title:
(U) Standards for Chemical and Biological Warfare Hazard Modeling. Volume 2. Characteristics of Biological Agents
Descriptive Note:
Final rept. May 1992-May 1993
Personal Author(s):
Wells, Charles H
Patrick, William C , III
Hawley, H B
Wells, William A
Replogle, Clyde R
Report Date:
Jul 1993
Media Count:
72 Page(s)
Report Number(s):

AL/CF-TR-1993-0117-VOL-2
XC-AL/CF

Contract Number:
F33615-89-C-0533

Monitor Series:
TR-1993-0117-VOL-2
AL/CF

Report Classification:
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Citation Format: FOIA(UL)

Accession Number:
ADA267039

Corporate Author:
WALTER REED ARMY INST OF RESEARCH WASHINGTON DC DIV OF EXPERIMENTAL THERAPEUTICS

Unclassified Title:
(U) Botulinum Toxin Inhibits Arachidonic Acid Release Associated with Acetylcholine Release from PC12 Cells

Descriptive Note:
Journal article

Personal Author(s):
Ray, Prabhati
Berman, Jonathan D
Middleton, Wilbert
Brendle, Jeams

Report Date:
25 May 1993

Media Count:
9 Page(s)

Report Number(s):
XA-USAMRDC

Monitor Series:
USAMRDC

Report Classification:
Unclassified

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12 - U.S. GOVT. AND THEIR CONTRACTORS
20 - JOURNAL ARTICLES; DTIC USERS ONLY

Distribution Statement:
Distribution: DTIC Users Only., Availability: Pub. in Jnl. of Biological Chemistry, v268 n15

p11, 057-11,064, 25 May 93. Availab

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Citation Format: FOIA(UL)

Accession Number:
ADP008894
Corporate Author:
ARMY MEDICAL RESEARCH INST OF CHEMICAL DEFENSE ABERDEEN PROVING GROUND MD
Unclassified Title:
(U) Antagonism of Botulinum Toxin-Induced Muscle Weakness by Aminopyridines in Rat Phrenic Nerve-Hemidiaphragm Preparations
Personal Author(s):
Adler, Michael
Scovill, John
Deshpande, Sharad S
Report Date:
13 May 1993
Media Count:
8 Page(s)
Report Number(s):
XA-USAMRICD
Monitor Series:
USAMRICD
Report Classification:
Unclassified
Distribution Limitation(s):
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Accession Number:
ADA266973
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/a266973.pdf
Size: 779 KB
Corporate Author:
SCIENCE AND TECHNOLOGY CORP HAMPTON VA
Unclassified Title:
(U) Evaluation of Cocktailed Antibodies for Toxin and Pathogen Assays on the Light Addressable Potentiometric Sensor
Descriptive Note:

Final rept. Aug 1990-Jul 1992
Personal Author(s):
Menking, Deborah G
Johnson, Clifton R
Eure, Samuel L
Report Date:
May 1993
Media Count:
27 Page(s)
Report Number(s):
STC-TR-2630
ERDEC-CR-036
XA-ERDEC
Contract Number:
DAAA15-89-D-0007
Monitor Series:
CR-036
ERDEC
Report Classification:
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Citation Format: FOIA(UL)

Accession Number:
ADA269617
Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD
Unclassified Title:
(U) Efficacy of Prophylactic and Therapeutic Administration of Antitoxin for Inhalation Botulism
Personal Author(s):
Franz, David R
Pitt, Louise M
Clayton, Michael A
Hanes, Martha A
Rose, Kenneth J
Report Date:
Jan 1993
Media Count:
4 Page(s)
Report Number(s):
XA-USAMRIID
Monitor Series:
USAMRIID

Report Classification:
Unclassified
Distribution Limitation(s):
12 - U.S. GOVT. AND THEIR CONTRACTORS
20 - JOURNAL ARTICLES; DTIC USERS ONLY
Distribution Statement:
Distribution: DTIC Users Only., Availability: Pub. in Botulinum and Tetanus Neurotoxins, p473-476, 1993. Available to DTIC users

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Citation Format: FOIA(UL)

Accession Number:
ADB172818
Corporate Author:
DEFENCE RESEARCH ESTABLISHMENT SUFFIELD RALSTON (ALBERTA)
Unclassified Title:
(U) Toxic Polypeptide Fragments: Potential BW Threats?
Personal Author(s):
Bader, D E
Nagata, L P
Report Date:
Jan 1993
Media Count:
38 Page(s)
Report Number(s):
DRES-SR-568
X5-XD
Monitor Series:
XD
Report Classification:
Unclassified
Distribution Limitation(s):
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Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
ADA245627
Corporate Author:
IMPERIAL COLL OF SCIENCE AND TECHNOLOGYLONDON (UNITED KINGDOM)
Unclassified Title:
(U) Multiple Domains of Botulinum Neurotoxin Contribute to Its Inhibition of Transmitter

Release in Aplysia Neurons
Personal Author(s):
Poulain, Bernard
Wadsworth, Jonathan D
Shone, Clifford C
Mochida, Sumiko
Lande, Simon
Report Date:
25 Dec 1989
Media Count:
8 Page(s)
Report Number(s):
XA-USAMRDC
Contract Number:
DAMD17-88-C-8008
Monitor Series:
USAMRDC
Report Classification:
Unclassified
Distribution Limitation(s):
12 - U.S. GOVT. AND THEIR CONTRACTORS
20 - JOURNAL ARTICLES; DTIC USERS ONLY
Distribution Statement:
Distribution: DTIC Users Only., Availability: Pub. in Jnl. of Biological Chemistry, v264 n36 p21928-21933, 25 Dec 1989. Availabl

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Citation Format: FOIA(UL)

Accession Number:
ADB136745
Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD
Unclassified Title:
(U) More on the Destructive Power of Free Active Chlorine on Type A Botulinic Toxin.
Report Date:
Jan 1989
Media Count:
10 Page(s)
Report Number(s):
USAMRIID-MUL-762
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies only; Proprietary Info.; 4 Oct 89. Other requests shall he referred to USAMRIID, Bldg 1425, Ft. Detrick, Frederick, MD 21701-5011.

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Citation Format: FOIA(UL)

Accession Number:
ADB123565
Corporate Author:
ARMED FORCES MEDICAL INTELLIGENCE CENTER FORT DETRICK FREDERICK MD
Unclassified Title:
(U) Serotherapy for Botulism Patients,
Personal Author(s):
Nikiforov, V N
Glukhikh, O A
Nikiforov, V V
Rezepov, F F
Akhizov, T Y
Report Date:
01 Jun 1988
Media Count:
6 Page(s)
Report Number(s):
AFMIC-HT-075-88
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
Distribution Statement:
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Citation Format: FOIA(UL)

Accession Number:
ADB123437
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/b123437.pdf
Size: 764 KB
Corporate Author:
ARMED FORCES MEDICAL INTELLIGENCE CENTER FORT DETRICK FEDERICK MD
Unclassified Title:
(U) Specific Antitoxic Therapy for Botulism
Personal Author(s):
Nikiforov, V N
Nikiforov, V V
Glukhikh, O A
Tashpulatov, Sh A

Report Date:
24 May 1988
Media Count:
11 Page(s)
Report Number(s):
AFMIC-HT-062-88
XA-AFMIC
Monitor Series:
AFMIC
Report Classification:
Unclassified
Distribution Limitation(s):
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23 - AVAILABILITY: DOCUMENT PARTIALLY ILLEGIBLE
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies only; Proprietary Information; 24 MAY 1988. Other requests shall be referred to Armed Forces Medical Intelligence Center, Attn: IS, Fort Detrick, Frederick, MD 21701-5004. Document partially illegible.

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Citation Format: FOIA(UL)

Accession Number:
ADB118345
Corporate Author:
ARMED FORCES MEDICAL INTELLIGENCE CENTER FORT DETRICK FREDERICK MD
Unclassified Title:
(U) Injuries Caused by Biological Warfare Agents (Schadigung Durch Biologische Kampfmittel),
Personal Author(s):
Werner, G
Report Date:
12 Feb 1988
Media Count:
6 Page(s)
Report Number(s):
AFMIC-HT-211-87
Report Classification:
Unclassified
Distribution Limitation(s):
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Citation Format: FOIA(UL)

Accession Number:
ADB140512
Corporate Author:
ARMY MEDICAL RESEARCH INST OF CHEMICAL DEFENSE ABERDEEN PROVING GROUND MD
Unclassified Title:
(U) Medical Defense Against Weapons of Mass Destruction: Bacteriological (Biological) Weapons
Personal Author(s):
Imangulov, R J
Report Date:
Jan 1988
Media Count:
14 Page(s)
Report Number(s):
XA-USAMRICD
Monitor Series:
USAMRICD
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
Distribution Statement:
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Citation Format: FOIA(UL)

Accession Number:
ADB136601
Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD
Unclassified Title:
(U) Recurrent Cases of Botulism,
Personal Author(s):
Shneyder, V P
Report Date:
14 Oct 1987
Media Count:
4 Page(s)
Report Number(s):
USAMRIID-MUL-763
Report Classification:
Unclassified
Distribution Limitation(s):

03 - U.S. GOVT. ONLY; DOD CONTROLLED

Distribution Statement:

Distribution authorized to U.S. Gov't. agencies only; Proprietary Info.; 22 Sep 89. Other requests shall be referred to USAMRIID/Library, Fort Detrick, Frederick, MD 21701-5011.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:

ADB111310

Corporate Author:

FOREIGN TECHNOLOGY DIV WRIGHT-PATTERSON AFB OH

Unclassified Title:

(U) Journal of Military Medicine (Selected Articles).

Report Date:

11 Mar 1987

Media Count:

153 Page(s)

Report Number(s):

FTD-ID(RS)T-0265-86

Report Classification:

Unclassified

Distribution Limitation(s):

02 - U.S. GOVT. AND THEIR CONTRACTORS

Distribution Statement:

Distribution limited to U.S. Gov't. agencies and their contractors; Copyright, Specific Authority; 11 Mar 87. Other requests must be referred to FTD/STINFO, Wright-Patterson AFB, OH 45433.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:

ADB118062

Corporate Author:

ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD

Unclassified Title:

(U) Early Diagnosis of Botulism,

Personal Author(s):

Nikiforov, V N
Fokin, M A
Vil'fand, N A
Vartanyan, K Z
Akhizarova, T Ya

Report Date:

Jan 1987

Media Count:

7 Page(s)

Report Number(s):
USAMRIID-MUL-727
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
Distribution Statement:
Distribution limited to U.S. Gov't. agencies only; Proprietary Info.; 5 Jan 87. Other requests must be referred to US Army Medical Research Inst. of Infectious Diseases, Fort Detrick, MD 21701.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
ADB101718
Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD
Unclassified Title:
(U) Effect of 4-Aminopyridine on the Development of Experimental Botulinic Intoxication (Vliyaniye 4-Aminopiridina na Razvitiye Eksperimental'noy Botulinicheskoy Intoksikatsii),
Personal Author(s):
Morrison,V V
Kryzhanovskiy,G N
Report Date:
Jan 1986
Media Count:
7 Page(s)
Report Number(s):
USAMRIID-MUL-0693
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
Distribution Statement:
Distribution limited to U.S. Gov't. agencies only; Proprietary Info.; 15 May 86. Other requests must be referred to Library, U.S. Army Medical Research Institute of Infectious Diseases, Fort Detrick, MD 21701.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
ADB101806
Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD
Unclassified Title:
(U) Induction and Modulation of Humoral Immunity in Mice By Local Nasal Administration of

Botulinus B Toxoid,

Personal Author(s):

Hoermeyer,Ewa
Schultz,A
Sailer,J
Opitz,G
Stuenkel,K

Report Date:

Jan 1985

Media Count:

14 Page(s)

Report Number(s):

USAMRIID-MUL-691

Report Classification:

Unclassified

Distribution Limitation(s):

03 - U.S. GOVT. ONLY; DOD CONTROLLED

Distribution Statement:

Distribution limited to U.S. Gov't. agencies only; Proprietary Info.; 15 May 86. Other requests must be referred to US Army Medical Research Institute of Infectious Diseases, Fort Detrick, Frederick, MD 21701.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:

ADB050791

Corporate Author:

ARMY MEDICAL INTELLIGENCE AND INFORMATION AGENCY FORT DETRICK MD

Unclassified Title:

(U) Hygienic Problems in Removing Toxic Substances from Water Using Chlorine Compounds (Gigienicheskie Voprosy Ochistki Vody ot Toksicheskikh Veshchestv s Pomosh'iu Khlorsoder Khlorsoderzhashchikh Preparatov),

Personal Author(s):

Shtannikov,Ye V
Morozov,Ya M

Report Date:

Aug 1980

Media Count:

11 Page(s)

Report Number(s):

USAMIIA-HT-067-80

Report Classification:

Unclassified

Distribution Limitation(s):

03 - U.S. GOVT. ONLY; DOD CONTROLLED

Distribution Statement:

Distribution limited to U.S. Gov't. agencies only; Copyright, Proprietary Info.; 4 Aug 80. Other requests for this document must be referred to Director, Army Medical Intelligence and

Information Agency, Attn; SGMI-IS. Fort Detrick, Frederick, MD 21701.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
ADB050785
Corporate Author:
ARMY MEDICAL INTELLIGENCE AND INFORMATION AGENCY FORT DETRICK MD
Unclassified Title:
(U) Contemporary Views on the Molecular Structure of the Botulin Toxin (Wspotczesne Poglady na Strkture Molekularna Toksyny Botulinowej),
Personal Author(s):
Cygan,Z
Report Date:
Jul 1980
Media Count:
20 Page(s)
Report Number(s):
USAMIIA-HT-051-80
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
Distribution Statement:
Distribution limited to U.S. Gov't. agencies only; Copyright, Proprietary Info.; 4 Aug 80. Other requests for this document must be referred to Director, Army Medical Intelligence and Information Agency, Attn: SGMI-IS. Fort Detrick, Frederick, MD 21701.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
ADB047697
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/b047697.pdf
Size: 451 KB
Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD
Unclassified Title:
(U) The Preparation of Purified Type F Sorbed Botulin Toxin. Report II. Activity of Crude Toxins and Antitoxins
Personal Author(s):
Tsarapkin, V P
Report Date:
28 Nov 1978

Media Count:
8 Page(s)
Report Number(s):
USAMRIID-MUL-0571
XA-USAMRIID
Monitor Series:
USAMRIID
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies only; Proprietary Information; 16 JUN 1980. Other requests shall be referred to Commander, Army Medical Research and Development Command, Attn: USAMRIID. Fort Detrick, Frederick, MD 21701.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
ADB047696
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/b047696.pdf
Size: 1 MB
Corporate Author:
ARMY MEDICAL RESEARCH INST OF INFECTIOUS DISEASES FORT DETRICK MD
Unclassified Title:
(U) Toxin Formation by the Type F Cl. botulinum on Nonmeat Nutrient Media
Personal Author(s):
Perova, Ye V
Bulatova, T I
Lukina, L S
Report Date:
28 Nov 1978
Media Count:
13 Page(s)
Report Number(s):
USAMRIID-MUL-0569
XA-USAMRIID
Monitor Series:
USAMRIID
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies only; Proprietary Information; 16 JUN 1980. Other requests shall be referred to Army Medical Research Inst. of Infectious Diseases, Fort

Detrick, MD 21701.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
ADB001970
Corporate Author:
ARMY FOREIGN SCIENCE AND TECHNOLOGY CENTER CHARLOTTESVILLE VA
Unclassified Title:
(U) Evaluation of Sera against Clostridium Botulinum A, B, E and F for Diagnostic Purpose,
Personal Author(s):
Mierzejewski,Jerzy
Report Date:
22 Nov 1974
Media Count:
3 Page(s)
Report Number(s):
FSTC-HT-23-1447-71
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
Distribution Statement:
Distribution limited to U.S. Gov't. agencies only; Proprietary Info.; 1 Oct 72. Other requests for this document must be referred to Commander, Army Foreign Science and Technology Center, Charlottesville, Va. 22901.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0922032
Corporate Author:
ARMY FOREIGN SCIENCE AND TECHNOLOGY CENTER CHARLOTTESVILLE VA
Unclassified Title:
(U) Combined Effects of Botulin Toxin and Isopropyl Methylphosphonofluoridate
Personal Author(s):
Mierzejewski, T
Kujawski, J
Report Date:
18 Mar 1974
Media Count:
13 Page(s)
Report Number(s):
FSTC-HT-23-1790-73
XA-FSTC

Monitor Series:
FSTC
Report Classification:
Unclassified
Distribution Limitation(s):
02 - U.S. GOVT. AND THEIR CONTRACTORS
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies and their contractors; Specific Authority; 17 May 1984. Other requests shall be referred to Commander, Army Foreign Science and Technology Center, Charlottesville, VA 22901.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0518986
Corporate Author:
NAVAL WEAPONS LAB DAHLGREN VA
Unclassified Title:
(U) Preliminary Ranking OF Navy Needs for BC Detection.
Descriptive Note:
Technical rept.,
Personal Author(s):
Plost, C I
Crocker, G R
Freiling, E C
Report Date:
Sep 1971
Media Count:
19 Page(s)
Report Number(s):
NWL-TR-2637
Report Classification:
Unclassified
Distribution Limitation(s):
03 - U.S. GOVT. ONLY; DOD CONTROLLED
Distribution Statement:
Distribution limited to U.S. Gov't. agencies only; Test and Evaluation; Sep 85. Other requests must be referred to Commander, Naval Weapons Lab., Dahlgren, Va. 22448.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0869349
Corporate Author:
FLORIDA STATE UNIV TALLAHASSEE

Unclassified Title:
(U) The Documentation of Avian Resistance to Botulism.
Descriptive Note:
Final rept. 1 Jul 68-30 Jun 69,
Personal Author(s):
Pates,Anne L
Cohen,Glenn M
Report Date:
15 Mar 1970
Media Count:
29 Page(s)
Contract Number:
DADA17-68-C-8165
Report Classification:
Unclassified
Distribution Limitation(s):
04 - DOD ONLY; DOD CONTROLLED
Distribution Statement:
Distribution: DoD only: others to Commanding General, Army Medical Research and Development Command, Attn: MEDDH-SI. Washington, D. C. 20314.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0880954
Corporate Author:
ALBANY MEDICAL COLL N Y INST OF EXPERIMENTAL PATHOLOGY AND TOXICOLOGY
Unclassified Title:
(U) Experimental Studies of Toxic Effects.
Descriptive Note:
Final rept. 23 Mar 64-15 Jun 68,
Personal Author(s):
Coulston,Frederick
Report Date:
22 Jul 1968
Media Count:
18 Page(s)
Contract Number:
DA-18-035-AMC-124(A)
Report Classification:
Unclassified
Distribution Limitation(s):
05 - CONTROLLED; DOD CONTROLLED
Distribution Statement:
Distribution: Controlled: all requests to Commanding Officer, Army Edgewood Arsenal, Attn: SMUEA-TSTI-T. Edgewood Arsenal, Md. 21010.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0497829
Corporate Author:
FORT DETRICK FREDERICK MD APPLIED AEROBIOLOGY DIV
Unclassified Title:
(U) Effects of Radiation Environments. V. Dry Agent Response to 14 Mev Neutrons,
Personal Author(s):
Scherff,Roger A
Report Date:
28 Sep 1967
Media Count:
16 Page(s)
Report Nnmber(s):
Test-A-2239
Report Classification:
Unclassified
Distribution Limitation(s):
05 - CONTROLLED; DOD CONTROLLED
Distribution Statement:
Distribution: Controlled: all requests to Commanding Officer, Fort Detrick, Attn: Technical Information Div. Frederick, Md. 21701.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0498362
Corporate Author:
FORT DETRICK FREDERICK MD APPLIED AEROBIOLOGY DIV
Unclassified Title:
(U) The Aerosol Properties of Two Preparations of Dried Type A Botulinum Toxin,
Personal Author(s):
Jemski, Joseph V
Report Date:
16 Dec 1965
Media Count:
11 Page(s)
Report Number(s):
TEST-A-1733
XA-DA
Monitor Series:
DA
Report Classification:
Unclassified
Distribution Limitation(s):

04 - DOD ONLY; DOD CONTROLLED
23 - AVAILABILITY: DOCUMENT PARTIALLY ILLEGIBLE

Distribution Statement:
Distribution authorized to DoD only; Specific Authority; 7 Sep 2004. Other requests shall be referred to U.S. Army Medical Research and Materiel Command, Attn: MCMR-RMI-S, 504 Scott Street, Fort Detrick, MD 21702-5012., Availability: Document partially illegible.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0466832
Corporate Author:
PENNSYLVANIA HOSPITAL PHILADELPHIA
Unclassified Title:
(U) BIOCHEMISTRY AND MECHANISM OF ACTION OF TOXIC PROTEINS.
Descriptive Note:
Annual progress rept., 1 Jul 64-30 Jun 65,
Personal Author(s):
Zacks,Sumner I
Sheff,Michael F
Report Date:
30 Jun 1965
Media Count:
1 Page(s)
Contract Number:
DA18 035AMC43A
Report Classification:
Unclassified
Distribution Limitation(s):
02 - U.S. GOVT. AND THEIR CONTRACTORS

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0460135
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/460135.pdf
Size: 455 KB
Corporate Author:
ARMY FOREIGN SCIENCE AND TECHNOLOGY CENTER CHARLOTTESVILLE VA
Unclassified Title:
(U) THE BOTULINUS TOXIN--A BIOLOGICAL WARFARE AGENT
Personal Author(s):
Vierling, R

Report Date:
Jan 1965
Media Count:
11 Page(s)
Report Number(s):
FSTC-381-T64-92
XA-FSTC
Monitor Series:
FSTC
Report Classification:
Unclassified
Distribution Limitation(s):
02 - U.S. GOVT. AND THEIR CONTRACTORS
23 - AVAILABILITY: DOCUMENT PARTIALLY ILLEGIBLE
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies and their contractors; Foreign Government Information; JAN 1965. Other requests shall be referred to Army Foreign Science and Technology Center, Washington, DC. Document partially illegible.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0450987
Corporate Author:
CHEMICAL RESEARCH AND DEVELOPMENT LABS EDGEWOOD ARSENAL MD
Unclassified Title:
(U) EXPERIMENTAL BOTULISM IN MONKEYS - A CLINICAL PATHOLOGICAL STUDY
Personal Author(s):
Herrero, Brunildo A
Ecklund, Allen E
Streett, C S
Ford, Duane F
King, John K
Report Date:
Nov 1964
Media Count:
35 Page(s)
Report Number(s):
CRDL-3235
XA-CRDL
Monitor Series:
CRDL
Report Classification:
Unclassified
Distribution Limitation(s):
02 - U.S. GOVT. AND THEIR CONTRACTORS
Distribution Statement:

Distribution authorized to U.S. Gov't. agencies and their contractors; Administrative/Operational Use; Nov 1964. Other requests shall be referred to Chemical Research and Development Laboratories, Edgewood Arsenal, MD. 21010.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0441550
Corporate Author:
CHEMICAL RESEARCH AND DEVELOPMENT LABS EDGEWOOD ARSENAL MD
Unclassified Title:
(U) THE BIOLOGICAL INTERACTION OF CURARE AND BOTULINUM TOXIN IN MICE
Descriptive Note:
Rept. for Nov 1962-Feb 1963
Personal Author(s):
Thomas, William U
McNamara, Bernard P
Report Date:
Apr 1964
Media Count:
20 Page(s)
Report Number(s):
CRDL-TM-24-76
XA-CRDL
Monitor Series:
CRDL
Report Classification:
Unclassified
Distribution Limitation(s):
02 - U.S. GOVT. AND THEIR CONTRACTORS
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies and their contractors; Administrative/Operational Use; Apr 1964. Other requests shall be referred to Chemical Research and Development Labs. Edgewood Arsenal, MD.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0452275
Corporate Author:
LUND UNIV (SWEDEN)
Unclassified Title:
(U) RESTORATION OF FUNCTION IN BOTULINUM PARALYSIS BY EXPERIMENTAL NERVE REGENERATION
Personal Author(s):

Thesleff, S
Zelena, J
Hofmann, W W

Report Date:
18 Feb 1964

Media Count:
4 Page(s)

Report Number(s):
AFOSR-64-2160
XC-AFOSR

Contract Number:
AF-EOAR-63-12

Monitor Series:
64-2160
AFOSR

Report Classification:
Unclassified

Distribution Limitation(s):
02 - U.S. GOVT. AND THEIR CONTRACTORS

Distribution Statement:
Distribution authorized to U.S. Gov't. agencies and their contractors; Administrative/Operational Use; Feb 1964. Other requests shall be referred to Air Force Office of Scientific Research, Bolling AFB, Washington, DC 20332.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0428519

Corporate Author:
ARMY BIOLOGICAL LABS FREDERICK MD

Unclassified Title:
(U) SPECIFICATIONS FOR MANUFACTURE OF BOTULISM TOXOID, ADSORBED, PENTAVALENT, TYPES ABCDE

Personal Author(s):
Cardella, Matteo A
Wright, George G

Report Date:
Jan 1964

Media Count:
13 Page(s)

Report Number(s):
TECHNICAL
STUDY-46
XA-ABL/MD

Monitor Series:
ABL/MD

Report Classification:
Unclassified

Distribution Limitation(s):
02 - U.S. GOVT. AND THEIR CONTRACTORS
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies and their contractors; Administrative/Operational use; Jan 1964. Other requests shall be referred to Army Biological Labs, Frederick MD.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0336302
Corporate Author:
ARMY BIOLOGICAL LABS FREDERICK MD
Unclassified Title:
(U) RESPONSE OF VARIOUS ANIMAL SPECIES TO BOTULINUM TOXIN ADMINISTERED BY DIFFERENT ROUTES
Personal Author(s):
Demchak,Peter
Miller,William S
Tonik,Ellis J
Report Date:
Apr 1963
Media Count:
26 Page(s)
Report Number(s):
TM-29
Report Classification:
CONFIDENTIAL
Distribution Limitation(s):
05 - CONTROLLED; DOD CONTROLLED
Distribution Statement:
Further dissemination only as directed by Director, U.S. Army Biological Labs., Fredrick, MD.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0498180
Corporate Author:
FORT DETRICK FREDERICK MD APPLIED AEROBIOLOBY DIV
Unclassified Title:
(U) Aerosol Evaluation of Stored Botulinum Toxin
Personal Author(s):
Miller, William S
Report Date:
12 Mar 1963
Media Count:

18 Page(s)
Report Number(s):
TEST-A-1672
XA-SMUFD
Monitor Series:
SMUFD
Report Classification:
Unclassified
Distribution Limitation(s):
05 - CONTROLLED; DOD CONTROLLED
23 - AVAILABILITY: DOCUMENT PARTIALLY ILLEGIBLE
Distribution Statement:
Distribution: Further dissemination only as directed by Commander, U.S. Army Dugway Proving Ground, CSTE-DTC-DP-WD-JC-P, Attn: JCP Program Manager, Dugway UT 84022, 12 MAR 1963, or higher DoD authority. Document partially illegible.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0490591
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/490591.pdf
Size: 2 MB
Corporate Author:
ARMOUR RESEARCH FOUNDATION CHICAGO IL
Unclassified Title:
(U) BIOCHEMISTRY OF TOXIC PROTEINS (Dissociation of Clostridium Botulinum Type A Toxin in Dextran Gel)
Descriptive Note:
Formal rept. 15 Sep 1960-31 Oct 1962
Personal Autbor(s):
Riesen, W H
Hawrylewicz, E J
Report Date:
31 Dec 1962
Media Count:
81 Page(s)
Report Number(s):
XA-ABL/MD
Contract Number:
DA-18-108-405-CML-928
Monitor Series:
ABL/MD
Report Classification:
Unclassified
Distribution Limitation(s):
02 - U.S. GOVT. AND THEIR CONTRACTORS

23 - AVAILABILITY: DOCUMENT PARTIALLY ILLEGIBLE

Distribution Statement:

Distribution authorized to U.S. Gov't. agencies and their contractors; Administrative/Operational Use; 31 DEC 1962. Other requests shall be referred to Army Biological Chemical Research and Development Labs., Frederick, MDCenter. Document partially illegible.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0274491
Corporate Autbor:
ARMY BIOLOGICAL LABS FREDERICK MD
Unclassified Title:
(U) STUDIES ON THE ENZYMATIC DIGESTION OF BOTULINUM TOXIN
Personal Author(s):
SPERO,LEONARD
SCHANTZ,EDWARD J
Report Date:
Apr 1962
Media Count:
1 Page(s)
Report Classification:
Unclassified
Distribution Limitation(s):
02 - U.S. GOVT. AND THEIR CONTRACTORS

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0350594
Corporate Author:
BOOZ-ALLEN APPLIED RESEARCH BETHESDA MD
Unclassified Title:
(U) A STUDY OF BIOLOGICAL AND CHEMICAL WARFARE TARGET EFFECTS VOLUME 1. CHARACTERISTICS OF BIOLOGICAL AND CHEMICAL WARFARE
Report Date:
22 Jan 1962
Media Count:
165 Page(s)
Report Number(s):
XB-NWL
Contract Number:
N178-7919
Monitor Series:
NWL

Report Classification:
Unclassified
Distribution Limitation(s):
02 - U.S. GOVT. AND THEIR CONTRACTORS
23 - AVAILABILITY: DOCUMENT PARTIALLY ILLEGIBLE
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies and their contractors; Administrative/Operational Use; Jan 1962. Other requests shall be referred to Naval Weapons Lab., Dahlgren, VA., Availability: Document partially illegible.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
ADB252369
Corporate Author:
QUARTERMASTER FOOD AND CONTAINER INST FOR THE ARMED FORCES CHICAGO IL
Unclassified Title:
(U) Canned Subsistence Eritrea. (Food)
Report Date:
12 Jan 1962
Media Count:
5 Page(s)
Report Number(s):
QMFCIAF-NR-197-62(ERI)
XA-QMFCIAF
Monitor Series:
QMFCIAF
Report Classification:
Unclassified
Distribution Limitation(s):
05 - CONTROLLED; DOD CONTROLLED
Distribution Statement:
Distribution: Further dissemination only as directed by Dept. of the Army, Washington, DC 20310 (Jan 62) or higher DoD authority.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0497653
Corporate Author:
FORT DETRICK FREDERICK MD APPLIED AEROBIOLOGY DIV
Unclassified Title:
(U) Aerosol Challenge of Three Groups of Guinea Pigs, Parenterally Immunized with Three Production Lots of Pentavalent Botulinum Toxoid, with Type A Botulinum Toxin Disseminated

by the Hartman Fixture at 75 F and 50 Per Cent Relative Humidity,

Personal Author(s):
Jemski,Joseph V

Report Date:
04 Dec 1961

Media Count:
26 Page(s)

Report Number(s):
Test-A-1474

Report Classification:
Unclassified

Distribution Limitation(s):
05 - CONTROLLED; DOD CONTROLLED

Distribution Statement:
Distribution: Controlled: all requests to Commanding Officer, Fort Detrick, Attn: Technical Information Div. Frederick, Md. 21701.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0497670

Corporate Author:
FORT DETRICK FREDERICK MD APPLIED AEROBIOLOBY DIV

Unclassified Title:
(U) Final Evaluation of Dried Botulinum Toxin

Personal Author(s):
Wadley, F M

Report Date:
22 Sep 1961

Media Count:
11 Page(s)

Report Number(s):
TEST-A-1507
XA-SMUFD

Monitor Series:
SMUFD

Report Classification:
Unclassified

Distribution Limitation(s):
05 - CONTROLLED; DOD CONTROLLED
23 - AVAILABILITY: DOCUMENT PARTIALLY ILLEGIBLE

Distribution Statement:
Distribution: Further dissemination only as directed by Commander, U.S. Army Dugway Proving Ground, CSTE-DTC-DP-WD-JC-P, Attn: JCP Program Manager, Dugway UT 84022, 22 SEP 1961, or higher DoD authority. Document partially illegible.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0497563
Corporate Author:
FORT DETRICK FREDERICK MD APPLIED AEROBIOLOGY DIV
Unclassified Title:
(U) Cballenge of Parenterally Immunized Guinea Pigs with Aerosols of Botulinum Toxins Disseminated by the Hartman Fixture at 75 F and 50 Per Cent Relative Humidity,
Personal Author(s):
Jemski,Joseph V
Report Date:
02 Aug 1961
Media Count:
19 Page(s)
Report Number(s):
Test-A-1323
Report Classification:
Unclassified
Distribution Limitation(s):
05 - CONTROLLED; DOD CONTROLLED
Distribution Statement:
Distribution: Controlled: all requests to Commanding Officer, Fort Detrick, Attn: Technical Information Div. Frederick, Md. 21701.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0267067
Corporate Author:
ARMY CHEMICAL CORPS ENGINEERING COMMANDARMY CHEMICAL CENTER MD
Unclassified Title:
(U) PLANT DESIGN FOR LARGE-SCALE PRODUCTION OF PENTAVALENT BOTULINUM TOXOID
Personal Author(s):
ABELOW, IRA
Report Date:
Jun 1961
Media Count:
180 Page(s)
Report Number(s):
ENCR-50
XA-CHEMCOR
Monitor Series:
CHEMCOR
Report Classification:
Unclassified
Distribution Limitation(s):

02 - U.S. GOVT. AND THEIR CONTRACTORS

Distribution Statement:

Distribution authorized to U.S. Gov't. agencies and their contractors; Administrative/Operational Use; Jun 1961. Other requests shall be referred to Commanding Officer, Chemical Corps, Army Chemical Center, MD.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:

AD0594388

Corporate Author:

FORT DETRICK FREDERICK MD APPLIED AEROBIOLOGY DIV

Unclassified Title:

(U) Evaluation of a Dried Preparation of Botulinum Toxin

Personal Author(s):

Demchak, Peter
Leopold, Sidney

Report Date:

19 Oct 1960

Media Count:

16 Page(s)

Report Number(s):

TEST-A-1334
XA-DPG

Monitor Series:

DPG

Report Classification:

Unclassified

Distribution Limitation(s):

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Distribution Statement:

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Citation Format: FOIA(UL)

Accession Number:

AD0262293

Corporate Author:

LUND UNIV (SWEDEN)

Unclassified Title:

(U) ELECTROMYOGRAPHIC FINDINGS IN EXPERIMENTAL BOTULINUM INTOXICATION

Personal Author(s):

Josefsson, J O
Thesleff, S
Report Date:
22 Sep 1960
Media Count:
8 Page(s)
Report Number(s):
AFOSR-1284
XC-AFOSR
Contract Number:
AF 61(052)-106
Monitor Series:
1284
AFOSR
Report Classification:
Unclassified
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Distribution Statement:
Distribution authorized to U.S. Gov't. agencies and their contractors; Administrative/Operational Use; 22 SEP 1960. Other requests shall be referred to Air Force Office of Scientific Research, Bolling AFB, Washington, DC.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0260151
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/260151.pdf
Size: 127 KB
Corporate Author:
NAVAL MEDICAL RESEARCH UNIT NO 1 BERKELEY CA
Unclassified Title:
(U) PHAGOCYTOSIS OF STAPHYLOCOCCI BY MOUSE LEUKOCYTES IN THE PRESENCE OF BOTULINUM TOXIN
Descriptive Note:
Journal article
Personal Author(s):
Freeman, Noel L
Report Date:
01 Aug 1960
Media Count:
5 Page(s)
Report Number(s):
XB-NMRC
Monitor Series:

NMRC
Report Classification:
Unclassified
Distribution Limitation(s):
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23 - AVAILABILITY: DOCUMENT PARTIALLY ILLEGIBLE
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Citation Format: FOIA(UL)

Accession Numher:
AD0246885
Corporate Author:
LUND UNIV (SWEDEN)
Unclassified Title:
(U) SUPERSENSITIVITY OF SKELETAL MUSCLE PRODUCED BY BOTULINUM TOXIN
Personal Author(s):
THESLEFF,S
Report Date:
03 Feb 1960
Media Count:
1 Page(s)
Report Number(s):
TN-4
AFOSR-TN-60-1422
Contract Number:
DA-11-022-ORD-1998
DA-20-018-ORD-147
Monitor Series:
TN-60-1422
Report Classification:
Unclassified
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Citation Format: FOIA(UL)

Accession Number:
AD0497593
Corporate Author:
FORT DETRICK FREDERICK MD APPLIED AEROBIOLOGY DIV

Unclassified Title:
(U) Recoveries and Guinea Pig LD50s of Aerosols of Botulinum Toxins Disseminated by the Hartman Fixture at 75 F and 50 Per Cent Relative Humidity,
Personal Author(s):
Jemski,Joseph V
Report Date:
Jan 1960
Media Count:
21 Page(s)
Report Number(s):
Test-A-1274
Report Classification:
Unclassified
Distribution Limitation(s):
05 - CONTROLLED; DOD CONTROLLED
Distribution Statement:
Distribution: Controlled: all requests to Commanding Officer, Fort Detrick, Attn: Technical Information Div. Frederick, Md. 21701.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Numher:
AD0238954
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/238954.pdf
Size: 237 KB
Corporate Author:
CALIFORNIA UNIV OAKLAND NAVAL BIOLOGICAL LAB
Unclassified Title:
(U) INFLUENCE OF INGESTED FOODS ON THE ORAL TOXICITY IN MICE OF CRYSTALLINE BOTULINAL TYPE A TOXIN
Personal Author(s):
Lamanna, Carl
Meyers, Charles E
Report Date:
03 Aug 1959
Media Count:
5 Page(s)
Report Number(s):
XB-NAVEXOS
Monitor Series:
NAVEXOS
Report Classification:
Unclassified
Distribution Limitation(s):
02 - U.S. GOVT. AND THEIR CONTRACTORS
Distribution Statement:

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Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0221929
Corporate Author:
ARMY BIOLOGICAL LABS FREDERICK MD
Unclassified Title:
(U) DEVELOPMENT OF A BIVALENT TYPE AB BOTULINUM TOXOID
Personal Author(s):
CARDELLA,MATTEO A
Report Date:
May 1958
Media Count:
1 Page(s)
Report Classification:
Unclassified
Distribution Limitation(s):
02 - U.S. GOVT. AND THEIR CONTRACTORS
25 - NOT AVAILABLE IN HARD COPY
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Distribution: No Forn, Availability: Microfiche copies only.

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Citation Format: FOIA(UL)

Accession Number:
AD0107519
Corporate Author:
DIRECTORATE OF SCIENTIFIC INTELLIGENCE (CANADA)
Unclassified Title:
(U) DETECTION OF BOTULINUM TOXIN, ARTIFICIALLY INTRODUCED INTO FOOD PRODUCTS BY MEANS OF THE PHAGOCYTIC INDEX DETERMINATION
Personal Author(s):
SAVIN,V R
Report Date:
Feb 1956
Media Count:
1 Page(s)
Report Number(s):
T14
Report Classification:
Unclassified

Distribution Limitation(s):
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Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0074744
Corporate Author:
DIRECTORATE OF SCIENTIFIC INTELLIGENCE (CANADA)
Unclassified Title:
(U) OBSERVATIONS ON THE "SENSITIZING" ACTION MECHANISM OF THE BOTULINUM TOXIN
Personal Author(s):
MINERVIN,S M
ZLAK,S P
CHERVYAKOVA,K I
Report Date:
Aug 1955
Media Count:
1 Page(s)
Report Number(s):
T2
Report Classification:
Unclassified
Distribution Limitation(s):
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Citation Format: FOIA(UL)

Accession Number:
AD0026883
Corporate Author:
JOHNS HOPKINS UNIV BALTIMORE MD
Unclassified Title:
(U) QUARTERLY REPT NO. 9 (FINAL) TO 1 SEPTEMBER 1954 (TYPE C BOTULINAL TOXOIDS)
Report Date:
01 Sep 1954
Media Count:
1 Page(s)
Contract Number:
DA18 064CML470
Report Classification:
Unclassified
Distribution Limitation(s):

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Citation Format: FOIA(UL)

Accession Number:
AD0042078
Corporate Author:
PARKE DAVIS AND CO DETROIT MICH
Unclassified Title:
(U) CLOSTRIDIUM BOTULINUM
Personal Author(s):
DEVLIN,H B
Report Date:
31 Mar 1954
Media Count:
1 Page(s)
Report Classification:
Unclassified
Distribution Limitation(s):
02 - U.S. GOVT. AND THEIR CONTRACTORS

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Citation Format: FOIA(UL)

Accession Number:
AD0049733
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/049733.pdf
Size: 647 KB
Corporate Author:
DEFENCE RESEARCH KINGSTON LAB KINGSTON(ONTARIO)
Unclassified Title:
(U) CLOSTRIDIUM BOTULINUM TYPE E TOXIN AND TOXOID
Personal Author(s):
Barron, A L
Reed, G B
Report Date:
Jan 1954
Media Count:
26 Page(s)
Report Number(s):
DRB-42
X5-DRB
Monitor Series:
DRB

Report Classification:
Unclassified
Distribution Limitation(s):
02 - U.S. GOVT. AND THEIR CONTRACTORS
23 - AVAILABILITY: DOCUMENT PARTIALLY ILLEGIBLE
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies and their contractors; Foreign Government Information; OCT 1954. Other requests shall be referred to Canadian Embassy, 501 Pennsylvania Avenue, NW, Washington, DC 20008. Document partially illegible.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0025980
Full Text (pdf) Availability:
View Full Text (pdf)
File: /UL/025980.pdf
Size: 700 KB
Corporate Author:
PENNSYLVANIA UNIV PHILADELPHIA
Unclassified Title:
(U) FEASIBILITY OF INCLUDING BW AND CW ANTI-PERSONNEL AGENTS IN WOUND PRODUCING WEAPONS
Personal Author(s):
Bennett, Ralph E
Gieryn, H T
Kime, F D
Van Meter, C T
Miller, Jr, P H
Report Date:
14 Dec 1953
Media Count:
16 Page(s)
Report Number(s):
R-13-02
XA-ABL/MD
Monitor Series:
ABL/MD
Report Classification:
Unclassified
Distribution Limitation(s):
02 - U.S. GOVT. AND THEIR CONTRACTORS
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies and their contractors; Administrative/Operational Use; 14 DEC 1953. Other requests shall be referred to Army Ballistic Lab., Aberdeen Proving Ground, MD 21010.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0222754
Corporate Author:
ARMY BIOLOGICAL LABS FREDERICK MD
Unclassified Title:
(U) BOTULINUM TOXIN AND THE MOTOR END PLATE
Descriptive Note:
Interim rept. no. 42
Personal Author(s):
STOVER JR , J H
FINGERMAN, M
FORESTER, R H
Report Date:
Jul 1953
Media Count:
13 Page(s)
Report Number(s):
XA-ABL/MD
Monitor Series:
ABL/MD
Report Classification:
Unclassified
Distribution Limitation(s):
02 - U.S. GOVT. AND THEIR CONTRACTORS
Distribution Statement:
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Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0006953
Corporate Author:
JOHNS HOPKINS UNIV BALTIMORE MD
Unclassified Title:
(U) SEVENTH QUARTERLY REPORT OF RESEARCH-OCT 2, 1952 TO JAN 2, 1953 (BOTULINAL TOXIN)
Report Date:
02 Jan 1953
Media Count:
1 Page(s)
Contract Number:
DA18 064CML470

Report Classification:
Unclassified
Distribution Limitation(s):
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Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
AD0000136
Corporate Author:
DIRECTOR SCIENTIFIC INFORMATION SERVICES OTTAWA (ONTARIO)
Unclassified Title:
(U) EFFECT OF LACTIC ACID BACTERIA ON B. BOTULINUS ON TOXIGENESIS IN LACTIC ACID SOY FOOD PRODUCTS
Personal Author(s):
Glotova, Ye V
Chebotareva, S V
Hope, E R
Report Date:
24 Nov 1952
Media Count:
14 Page(s)
Report Number(s):
T70R
X5-DSIS
Monitor Series:
DSIS
Report Classification:
Unclassified
Distribution Limitation(s):
02 - U.S. GOVT. AND THEIR CONTRACTORS
Distribution Statement:
Distribution authorized to U.S. Gov't. agencies and their contractors; Foreign Gov't. Info.; 24 Nov 1952. Other requests sball be referred to the Canadian Embassy, 501 Pennsylvania Ave., NW, Washington, DC 20001.

Technical Reports Collection

Citation Format: FOIA(UL)

Accession Number:
ADB959386
Corporate Author:
TEXAS UNIV AT AUSTIN
Unclassified Title:
(U) Spore Formation and Spore Germination of Anaerobic Food Spoilage Organisms, Especially Clostridium Botulinum.

Descriptive Note:
Rept. no. 4(II), 15 Dec 46-15 Apr 47,
Personal Author(s):
Wynne,E S
Foster,Jackson W
Report Date:
01 Jul 1946
Media Count:
8 Page(s)
Contract Number:
W-11-009-qm-70190
Report Classification:
Unclassified
Distribution Limitation(s):
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Citation Format: FOIA(UL)

Accession Number:
ADB959441
Corporate Author:
TEXAS UNIV AT AUSTIN DEPT OF BACTERIOLOGY
Unclassified Title:
(U) Spore Formation and Spore Germination of Anaerobic Food Spoilage Organisms, Especially Clostridium Botulinum.
Descriptive Note:
Rept. no. 2, 1 Feb-31 Mar 47,
Personal Author(s):
Wynne,E S
Foster,Jackson W
Report Date:
01 Jul 1946
Media Count:
3 Page(s)
Contract Number:
W-11-009-qm-70190
Report Classification:
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Accession Number:
ADB959530
Corporate Author:
TEXAS UNIV AT AUSTIN DEPT OF BACTERIOLOGY
Unclassified Title:
(U) Spore Formation and Spore Germination of Anaerobic Food Spoilage Organisms, Especially Clostridium Botulinum.
Descriptive Note:
Rept. no. 4(IV), Aug 46-Apr 47,
Personal Author(s):
Foster,J W
Report Date:
01 Jul 1946
Media Count:
14 Page(s)
Contract Number:
W11-009-qm-70190
Report Classification:
Unclassified
Distribution Limitation(s):
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Citation Format: FOIA(UL)

Accession Number:
ADB959449
Corporate Autbor:
TEXAS UNIV AT AUSTIN DEPT OF BACTERIOLOGY
Unclassified Title:
(U) Spore Formation and Spore Germination of Anaerobic Food Spoilage Organisms, Especially Clostridium Botulinum.
Descriptive Note:
Rept. no. 3, 1 Apr-31 May 47,
Personal Author(s):
Foster,J W
Wynne,E S
Report Date:
01 Jul 1946
Media Count:
3 Page(s)
Contract Number:
W-11-009-qm-70190
Report Classification:
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Accession Number:
ADB959440
Corporate Author:
TEXAS UNIV AT AUSTIN DEPT OF BACTERIOLOGY
Unclassified Title:
(U) Spore Formation and Spore Germination of Anaerobic Food Spoilage Organisms, Especially Clostridium Botulinum.
Descriptive Note:
Rept. no. 6, 1 Jul-31 Dec 47,
Personal Author(s):
Wynne,E S
Foster,Jackson W
Report Date:
01 Jul 1946
Media Count:
8 Page(s)
Contract Number:
W-11-009-qm-70190
Report Classification:
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Accession Number:
ADB959433
Corporate Author:
TEXAS UNIV AT AUSTIN DEPT OF BACTERIOLOGY
Unclassified Title:
(U) Spore Formation and Spore Germination of Anaerobic Food Spoilage Organisms, Especially Clostridium botulinum
Descriptive Note:
Rept. no. 1, 1 Aug 1946-1 Feb 1947
Personal Author(s):
Foster, J W

Report Date:
01 Jul 1946
Media Count:
4 Page(s)
Report Number(s):
XA-QMFCIAF
Contract Number:
W-11-009-QM-70190
Monitor Series:
QMFCIAF
Report Classification:
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Distribution Limitation(s):
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Citation Format: FOIA(UL)

Accession Number:
ADB800209
Corporate Author:
DEFENCE RESEARCH BOARD OTTAWA (ONTARIO)
Unclassified Title:
(U) The Nature of the Toxin of Bacillus Botulinus,
Personal Author(s):
Rodopulo, A K
Report Date:
Jan 1941
Media Count:
6 Page(s)
Report Number(s):
X5-XD
Monitor Series:
XD
Report Classification:
Unclassified
Distribution Limitation(s):
04 - DOD ONLY; DOD CONTROLLED
Distribution Statement:
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