

**Subjek : Anthrax
Tahun 2004-2008 (12 judul)**

Nandini Verma, Indrajit Chaudhury, Deepak Kumar, Rakha H. Das, Silencing of TNF-[alpha] receptors coordinately suppresses TNF-[alpha] expression through NF-[kappa]B activation blockade in THP-1 macrophage, FEBS Letters, Volume 583, Issue 17, 3 September 2009, Pages 2968-2974, ISSN 0014-5793, DOI: 10.1016/j.febslet.2009.08.007.

(<http://www.sciencedirect.com/science/article/B6T36-4X0PC3X-4/2/eacb0f28e7d7b5886ecbcc86608f80f4>)

Abstract:

Persistently elevated level of TNF-[alpha] has been implicated in several inflammatory disorders, however, its autocrine production through TNF-[alpha] receptors signaling is poorly understood. Here we report that simultaneous silencing of TNF-receptors, R1 and R2 by DNAzyme or siRNA suppressed TNF-[alpha] expression more efficiently than silencing them individually in lipopolysaccharides (LPS) stimulated THP-1 macrophages. Co-silencing of TNF-receptors also inhibited TNF-[alpha] induced NF-[kappa]B activation to a higher extent. It was further observed that NF-[kappa]B inhibitor but not c-Jun N-terminal kinase inhibitor (SP600125) suppressed TNF-[alpha] expression. All these results suggest that TNF-[alpha] expression is regulated by synergistic signaling of TNF receptors through downstream NF-[kappa]B activation.

Keywords: DNAzyme; siRNA; TNF-[alpha]; TNF-R1; TNF-R2; NF-[kappa]B

Antonio Fasanella, Domenico Galante, Giuliano Garofolo, Martin Hugh Jones, Anthrax undervalued zoonosis, Veterinary Microbiology, In Press, Accepted Manuscript, Available online 18 August 2009, ISSN 0378-1135, DOI: 10.1016/j.vetmic.2009.08.016.

(<http://www.sciencedirect.com/science/article/B6TD6-4X1J73F-2/2/951698b1e7a223b78b2f0c5e91791444>)

Abstract:

Anthrax is a non-contagious disease, known since ancient times but it became a matter of global public interest after the bioterrorist attacks in the U.S.A. during the autumn of 2001. The concern of politicians and civil authorities everywhere towards this emergency necessitated a significant research effort and the prevention of new bioterrorist acts. But anthrax is primarily a disease that affects livestock and wildlife; its distribution is worldwide; and it can represent a danger to humans but especially when it occurs in areas considered to be free and in atypical seasons and climatic conditions. The atypicality of the phenomenon may lead health workers to misdiagnosis and, consequently, an inappropriate management of affected carcasses with a consequent and inevitable increase in the risk of human infection. This paper emphasizes the importance of increasing attention to this zoonosis. The biggest risk is its underestimation.

Keywords: Bacillus anthracis; Animal; Disease; Zoonosis

Yirong Kong, Qiang Guo, Changming Yu, Dayong Dong, Jian Zhao, Chenguang Cai, Lihua Hou, Xiaohong Song, Ling Fu, Junjie Xu, Wei Chen, Fusion protein of [Delta]27LFn and EFn has the potential as a novel anthrax toxin inhibitor, FEBS Letters, Volume 583, Issue 8, 17 April 2009, Pages 1257-1260, ISSN 0014-5793, DOI: 10.1016/j.febslet.2009.03.053.

(<http://www.sciencedirect.com/science/article/B6T36-4VY2CCF-3/2/a7614bc70ec48a389f60782182af994f>)

Abstract:

PA-binding domain of LF (LFn) or PA-binding domain of EF (EFn) is the anthrax protective antigen (PA) binding domain of anthrax lethal factor (LF) or edema factor (EF). Here we show the development of a novel anthrax toxin inhibitor, fusion protein of N-terminal 27 amino acids deletion

of LFn ([Delta]27LFn) and EFn. In a cell model of intoxication, fusion protein of [Delta]27LFn and EFn ([Delta]27LFn-EFn) was a 62-fold more potent toxin inhibitor than LFn or EFn, and this increased activity corresponded to a 39-fold higher PA-binding affinity by Biacore analysis. More importantly, [Delta]27LFn-EFn could protect the highly susceptible Fischer 344 rats from anthrax lethal toxin challenge. This work suggested that [Delta]27LFn-EFn has the potential as a candidate therapeutic agent against anthrax. Structured summary

MINT-7014735, MINT-7014747, MINT-7014761: PA63 (uniprotkb:P13423) and LF (uniprotkb:P15917) bind (MI:0407) by surface plasmon resonance (MI:0107)

Keywords: Anthrax toxin; PA-binding domain of LF; PA-binding domain of EF; Toxin inhibitor; Fusion protein

Xavier Didelot, Margaret Barker, Daniel Falush, Fergus G. Priest, Evolution of pathogenicity in the *Bacillus cereus* group, *Systematic and Applied Microbiology*, Volume 32, Issue 2, April 2009, Pages 81-90, ISSN 0723-2020, DOI: 10.1016/j.syapm.2009.01.001.

(<http://www.sciencedirect.com/science/article/B7GVX-4VJ4FM5-1/2/ad1a66788750f423a086e78685f98cba>)

Abstract:

The *Bacillus cereus* group of bacteria comprises soil-dwelling saprophytes but on occasion these bacteria can cause a wide range of diseases in humans, including food poisoning, systemic infections and highly lethal forms of anthrax. While anthrax is almost invariably caused by strains from a single evolutionary lineage, *Bacillus anthracis*, variation in the virulence properties of strains from other lineages has not been fully addressed. Using multi-locus sequence data from 667 strains, we reconstructed the evolutionary history of the *B. cereus* group in terms of both clonal inheritance and recombination. The strains included 155 clinical isolates representing *B. anthracis*, and isolates from emetic and diarrhoeal food poisoning, septicaemia and related infections, wound, and lung infections. We confirmed the existence of three major clades and found that clinical isolates of *B. cereus* (with the exception of emetic toxin-producing strains) are evenly distributed between and within clades 1 and 2. *B. anthracis* in particular and emetic toxin-producing *B. cereus* show more clonal structure and are restricted to clade 1. Our characterization of the patterns of genetic exchange showed that there exist partial barriers to gene flow between the three clades. The pathogenic strains do not exhibit atypically high or low rates of recombination, consistent with the opportunistic nature of most pathogenic infections. However, there have been a large number of recent imports in clade 1 of strains from external origins, which is indicative of an on-going shift in gene-flow boundaries for this clade.

Keywords: *Bacillus cereus* group; Multi-locus sequence typing; Evolution of pathogenicity; Homologous recombination; Opportunistic pathogen

Gelagay Ayelet, Laekemariam Yigezu, Aschalew Zeleke, Esayas Gelaye, Kassahun Asmare, Validation of immunity induced by inactivated CCPV vaccine with different adjuvants, *Small Ruminant Research*, Volume 73, Issues 1-3, November 2007, Pages 200-205, ISSN 0921-4488, DOI: 10.1016/j.smallrumres.2007.02.004.

(<http://www.sciencedirect.com/science/article/B6TC5-4N9MYVJ-1/2/bba244a9809a34769e1fe47f4abef905>)

Abstract:

The study was conducted in the premises National Veterinary Institute (NVI) to validate the immunity induced by inactivated F38 antigen adjuvated with saponin and Montanide ISA 50 and combined with and without anthrax vaccine.

Post-inoculation reactions; pyrogenic effects, safety and innocuity of the vaccines were assessed. Increased body temperature and local edematous reactions were seen in animals inoculated with saponin adjuvated CCPV vaccine (100%) while 20% of the goats in ISA 50 adjuvated group showed local reaction. Sera collected from day 0 to 10th week were tested to assess the sero-

conversion using monoclonal antibody based B-ELISA technique. Saponin adjuvated groups, in both monovalent CCPP and in the combined CCPP with anthrax vaccine showed a higher mean percentage of inhibition value as compared with ISA 50 adjuvated vaccine.

After 8 months of post vaccination, contact challenge trial was conducted in 66 experimentally vaccinated and 20 negative control goats combined with 15 actively CCPP sick goats. Various clinical signs were recorded daily, autopsy was done on died goats and the live goats were sacrificed after 2 months of contact. The side by side samples from thoracic exudates, lung and mediastinal and bronchial lymph nodes were collected from goats shown to have developed indicative CCPP lesion for isolation and F38 antigen detection.

The present experimental study indicated that application of inactivated and adjuvated CCPP vaccine significantly reduced the morbidity and development of lesions ($P < 0.001$). Among vaccinated groups CCPP + anthrax + saponin showed better protection, with low rate of nasal discharge and cough at 33% and 28.6%, respectively, and protection level of 94.1% from death and 65% from lung lesion development. However, the variation in protection among the vaccinated groups was not significant ($P > 0.05$).

These findings disclosed that inactivated CCPP vaccine adjuvated with saponin and ISA 50 significantly reduce morbidity and mortality of goats due to CCPP and also indicated the importance of utilization of ISA 50 as alternative adjuvant to minimize post-vaccinal reactions encountered in use of saponin as adjuvant.

Keywords: Adjuvant; Ethiopia; CCPP; F38; Goat; NVI; Vaccine

Claire Bedelian, David Nkedianye, Mario Herrero, Maasai perception of the impact and incidence of malignant catarrhal fever (MCF) in southern Kenya, *Preventive Veterinary Medicine*, Volume 78, Issues 3-4, 17 March 2007, Pages 296-316, ISSN 0167-5877, DOI: 10.1016/j.prevetmed.2006.10.012.

(<http://www.sciencedirect.com/science/article/B6TBK-4MD9FYP-1/2/7b70ae3751b9326b3033c5ca3bd5ced6>)

Abstract:

We investigated the perceived impact of malignant catarrhal fever (MCF) to pastoralists in Isinya Division, a wildlife dispersal area of Nairobi National Park, and used a range of participatory epidemiology methodologies. We compared the relative importance, incidence and impact of MCF compared to other locally defined important diseases with a total of 158 respondents in 11 group meetings and 21 household meetings in July 2004. Direct losses due to disease were investigated through lowered prices as a result of the emergency sale of disease-infected animals.

Overall, Maasai in Isinya Division perceived east coast fever (ECF) to be the most important cattle disease and to have the highest incidence. Anthrax was considered to have the largest impact. In areas within or adjacent to the wildebeest calving zone, MCF was perceived to be the most important cattle disease and also to have the largest impact. Outside the calving zone, MCF was considered the fourth-most important disease with the fourth largest impact, and these were areas where wildebeest were less common. MCF was also the fourth-most common disease, and across the Division incidence was estimated at 5% in calves and 10% in adults. However, MCF incidence varied greatly throughout the study area, from 3% to 12%, and the highest incidence risks were found in areas where wildebeest came to calve. The percent drop in sale price per animal infected with MCF was estimated at 50% for MCF for the year 2003-2004.

Forced avoidance movements away from wildebeest calves were reported to decrease livestock production due to loss of access to prime grazing sites. As suggested by pastoralists in this study, the development of compensation schemes or incentives from wildlife would reduce the conflict between livestock keeping and wildlife conservation.

Keywords: Malignant catarrhal fever; Maasai pastoralists; Participatory appraisal; Participatory epidemiology; Disease impact; Disease incidence; Kenya

Nuria Reig, F.Gisou van der Goot, About lipids and toxins, FEBS Letters, Volume 580, Issue 23, Lipidome and Disease, 9 October 2006, Pages 5572-5579, ISSN 0014-5793, DOI: 10.1016/j.febslet.2006.08.033.

(<http://www.sciencedirect.com/science/article/B6T36-4KRY1SD-C/2/eb4de3f603b3df222c339f1c71af033d>)

Abstract:

Many mono or multicellular organisms secrete soluble proteins, referred to as protein toxins, which alter the behavior of foreign, or target cells, possibly leading to their death. These toxins affect either the cell membrane by forming pores or modifying lipids, or some intracellular target. To reach this target, they must cross one of the cellular membranes, generally that of an intracellular organelle. As described in this minireview, lipids play crucial roles in the intoxication process of most if not all toxins, by allowing/promoting binding, endocytosis, trafficking and/or translocation into the cytoplasm.

Keywords: Toxins; Anthrax; Pore-forming; Cholera toxin; Lysenin; Raft

Alina Deshpande, Rebecca J. Hammon, Claire K. Sanders, Steven W. Graves, Quantitative analysis of the effect of cell type and cellular differentiation on protective antigen binding to human target cells, FEBS Letters, Volume 580, Issue 17, 24 July 2006, Pages 4172-4175, ISSN 0014-5793, DOI: 10.1016/j.febslet.2006.06.070.

(<http://www.sciencedirect.com/science/article/B6T36-4K9C3BP-P/2/340962f661554db9af4b836154fa6a1b>)

Abstract:

We quantitatively measured protective antigen (PA) binding to human cells targeted by anthrax lethal toxin (LT). Affinities were less than 50 nM for all cells, but differentiated cells (macrophages and neutrophils) had significantly increased PA binding and endothelial cells demonstrated the most binding. Combined with the function of such cells, this suggests that PA receptors interact with the extracellular matrix and that differentiation increases the number of PA-specific receptors, which supports previously observed differentiation-induced LT susceptibility. Our results quantifiably confirm that the generality of PA binding will complicate its use as a tumor targeting agent.

Keywords: Protective antigen; Lethal toxin; Human cells; Macrophages; Endothelial cells; Receptors

Herbert Tomaso, Carsten Bartling, Sascha Al Dahouk, Ralf M. Hagen, Holger C. Scholz, Wolfgang Beyer, Heinrich Neubauer, Growth characteristics of *Bacillus anthracis* compared to other *Bacillus* spp. on the selective nutrient media Anthrax Blood Agar(R) and Cereus Ident Agar(R), Systematic and Applied Microbiology, Volume 29, Issue 1, 24 January 2006, Pages 24-28, ISSN 0723-2020, DOI: 10.1016/j.syapm.2005.05.008.

(<http://www.sciencedirect.com/science/article/B7GVX-4GHRC1H-1/2/042f8d538bec3a4fe8f7d800d01493d8>)

Abstract:

Anthrax Blood Agar(R) (ABA) and Cereus Ident Agar(R) (CEI) were evaluated as selective growth media for the isolation of *Bacillus anthracis* using 92 *B. anthracis* and 132 other *Bacillus* strains from 30 species. The positive predictive values for the identification of *B. anthracis* on ABA, CEI, and the combination of both were 72%, 71%, and 90%, respectively. Thus, less than 10% of all species were misidentified using both nutrient media. Species which might be misidentified as *B. anthracis* were *B. cereus*, *B. mycoides*, and *B. thuringiensis*. Particularly, 30% of *B. weihenstephanensis* strains were misidentified as *B. anthracis*.

Keywords: *Bacillus anthracis*; *Bacillus cereus*; Selective nutrient media; Growth media

Gabrielle Bloom, Paul W. Sherman, Dairying barriers affect the distribution of lactose malabsorption, *Evolution and Human Behavior*, Volume 26, Issue 4, July 2005, Pages 301-312, ISSN 1090-5138, DOI: 10.1016/j.evolhumbehav.2004.10.002.

(<http://www.sciencedirect.com/science/article/B6T6H-4GHGV3C-1/2/a56eee32408a5c113b85dd263a0e60a7>)

Abstract:

Most mammals stop drinking milk at weaning, which is also the time when they cease producing lactase, the digestive enzyme that hydrolyzes lactose. Cessation of lactase production and milk drinking also characterize most human populations, especially those of African and Asian descent. However, a genetic mutation that maintains the functionality of lactase production into adulthood occurs commonly among populations from northern Europe, where dairying is practiced routinely. Indeed, the ability to absorb lactose is nutritionally beneficial for adults only if milk consistently is available. What determines the distribution of dairying? We hypothesized that specific environmental circumstances affect where milk-producing ungulates can be raised safely and economically, thus influencing the geographical occurrence of dairying and lactase persistence. To evaluate this hypothesis, we compiled data on adult lactose absorption (LA) and malabsorption (LM) frequencies in 270 indigenous African and Eurasian populations (Appendix A). Partial correlation analyses revealed that, as predicted, adult LM is associated with extreme climates (at high and low latitudes) and, more significantly, with the historical (pre-1900) geographical occurrence of nine deadly, communicable diseases of cattle. These results suggest that areas where adult LM predominates are those where it is impossible or dangerous to maintain dairy herds.

Keywords: Lactase persistence; Lactose malabsorption; Cattle diseases; Dairying barriers; Sleeping sickness; Anthrax; Cholera; Malaria; Nomadism

Paul Keim, Matthew N. Van Ert, Talima Pearson, Amy J. Vogler, Lynn Y. Huynh, David M. Wagner, Anthrax molecular epidemiology and forensics: using the appropriate marker for different evolutionary scales, *Infection, Genetics and Evolution*, Volume 4, Issue 3, 6th International Meeting on Microbial Epidemiological Markers, September 2004, Pages 205-213, ISSN 1567-1348, DOI: 10.1016/j.meegid.2004.02.005.

(<http://www.sciencedirect.com/science/article/B6W8B-4CHJ5WH-1/2/3902cdcd617a618d2c9940fba39e4291>)

Abstract:

Precise identification of *Bacillus anthracis* isolates has aided forensic and epidemiological analyses of natural anthrax cases, bioterrorism acts and industrial scale accidents by state-sponsored bioweapons programs. Because there is little molecular variation among *B. anthracis* isolates, identifying and using rare variation is crucial for precise strain identification. We think that mutation is the primary diversifying force in a clonal, recently emerged pathogen, such as *B. anthracis*, since mutation rate is correlated with diversity on a per locus basis. While single nucleotide polymorphisms (SNPs) are rare, their detection is facilitated by whole genome discovery approaches. As highly stable phylogenetic markers, SNPs are useful for identifying long branches or key phylogenetic positions. Selection of single, diagnostic 'Canonical SNPs' (canSNPs) for these phylogenetic positions allows for efficient and defining assays. We have taken a nested hierarchical strategy for subtyping *B. anthracis*, which is consistent with traditional diagnostics and applicable to a wide range of pathogens. Progressive hierarchical resolving assays using nucleic acids (PHRANA) uses a progression of diagnostic genomic loci that are initially highly stable but with low resolution and, ultimately, very unstable but with high resolution. This approach mitigates the need for data weighting and provides both a deeply rooted phylogenetic hypothesis and high resolution discrimination among closely related isolates.

Keywords: Anthrax; *Bacillus anthracis*; Bioterrorism; Canonical SNPs; canSNPs; Microbial forensics; MLVA; PHRANA; SNPs; SNR

Deena Vardhini, Sujai Suneetha, Niyaz Ahmed, D. S. M. Joshi, S. Karuna, X. Magee, D. S. R. Vijayalakshmi, V. Sridhar, K. V. Karunakar, Juan J. Archelos, Lavanya M. Suneetha, Comparative proteomics of the Mycobacterium leprae binding protein myelin P0: its implication in leprosy and other neurodegenerative diseases, Infection, Genetics and Evolution, Volume 4, Issue 1, March 2004, Pages 21-28, ISSN 1567-1348, DOI: 10.1016/j.meegid.2003.11.001.

(<http://www.sciencedirect.com/science/article/B6W8B-4B9D5V8-2/2/2ea7e57d7cbcbddb69cda700f969cae2>)

Abstract:

Mycobacterium leprae, the causative agent of leprosy invades Schwann cells of the peripheral nerves leading to nerve damage and disfigurement, which is the hallmark of the disease. Wet experiments have shown that M. leprae binds to a major peripheral nerve protein, the myelin P zero (P0). This protein is specific to peripheral nerve and may be important in the initial step of M. leprae binding and invasion of Schwann cells which is the feature of leprosy. Though the receptors on Schwann cells, cytokines, chemokines and antibodies to M. leprae have been identified the molecular mechanism of nerve damage and neurodegeneration is not clearly defined. Recently pathogen and host protein/nucleotide sequence similarities (molecular mimicry) have been implicated in neurodegenerative diseases. The approach of the present study is to utilise bioinformatic tools to understand leprosy nerve damage by carrying out sequence and structural similarity searches of myelin P0 with leproma and other genomic database. Since myelin P0 is unique to peripheral nerve, its sequence and structural similarities in other neuropathogens have also been noted.

Comparison of myelin P0 with the M. leprae proteins revealed two characterised proteins, Ferredoxin NADP reductase and a conserved membrane protein, which showed similarity to the query sequence. Comparison with the entire genomic database (www.ncbi.nlm.nih.gov) by basic local alignment search tool for proteins (BLASTP) and fold classification of structure-structure alignment of proteins (FSSP) searches revealed that myelin P0 had sequence/structural similarities to the poliovirus receptor, coxsackie-adenovirus receptor, anthrax protective antigen, diphtheria toxin, herpes simplex virus, HIV gag-1 peptide, and gp120 among others. These proteins are known to be associated directly or indirectly with neurodegeneration. Sequence and structural similarities to the immunoglobulin regions of myelin P0 could have implications in host-pathogen interactions, as it has homophilic adhesive properties. Although these observed similarities are not highly significant in their percentage identity, they could be functionally important in molecular mimicry, receptor binding and cell signaling events involved in neurodegeneration.

Keywords: Leprosy; Mycobacterium leprae binding protein; Proteomics; Bioinformatics; Myelin P0; Polio virus receptor; Herpes virus receptor