

11 March 2010

This supplement has been prepared to present scientific and technical news items that may be of more interest to technical personnel at RDT&E activities and the labs, or the medics rather than the broader readership of the basic CB Daily. Due to the nature of the material, the articles, if available online, are usually only available through subscription services thus making specific links generally unavailable. Thus, usually only the bibliographic citation is available for use by an activity's technical library.

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Chem-Bio News - S&T Edition

- 1. ATP CONFORMATIONS AND ION BINDING MODES IN THE ACTIVE SITE OF ANTHRAX EDEMA FACTOR: A COMPUTATIONAL ANALYSIS:** *"Additionally, the two-cation binding mode restrains the mobility of the reaction products, and thus their tendency to dissociate."*
- 2. NEW MULTISPECIFIC ARRAY AS A TOOL FOR ELECTROCHEMICAL IMPEDANCE SPECTROSCOPY-BASED BIOSENSING:** *"Examples of array use for label-free genetic sensing of 2.7 kb-long target Yersinia pestis DNA and for protein sensing of Ricin Toxin Chain A (RTA) are presented....."*
- 3. IMMUNE REQUIREMENTS OF POST-EXPOSURE IMMUNIZATION WITH MODIFIED VACCINIA ANKARA OF LETHALLY INFECTED MICE:** *"By using various gene-targeted and transgenic mouse strains we show that NK cells, CD4 T cells, CD8 T cells and antibodies are essential for the clearance of ECTV after post-exposure immunization."*
- 4. POPULAR NANOPARTICLE CAUSES TOXICITY IN FISH, STUDY SHOWS:** *"Silver has been used in the past as an antimicrobial agent. It's a known toxicant to microorganisms," he said. "Nanosilver is being considered by the EPA for environmental exposure profiling, much like a pesticide."*
- 5. PREDICTING DRUG-TARGET INTERACTION NETWORKS BASED ON FUNCTIONAL GROUPS AND BIOLOGICAL FEATURES:** *"Study of drug-target interaction networks is an important topic for drug development. It is both time-consuming and costly to determine compound-protein interactions or potential drug-target interactions by experiments alone. As a complement, the in silico prediction methods can provide us with very useful information in a timely manner."*

CB Daily Report

ATP CONFORMATIONS AND ION BINDING MODES IN THE ACTIVE SITE OF ANTHRAX EDEMA FACTOR: A COMPUTATIONAL ANALYSIS

Pharma Investments, Ventures & Law Weekly
February 21, 2010

"The Edema Factor (EF), one of the virulence factors of anthrax, is an adenylyl cyclase that promotes the overproduction of cyclic-AMP (cAMP) from ATP, and therefore perturbs cell signaling. Crystallographic structures of EF bound to ATP analogs and reaction products, cyclic-AMP, and Pyrophosphate (PPi), revealed different substrate conformations and catalytic-cation binding modes, one or two cations being observed in the active site."

"To shed light into the biological significance of these crystallographic structures, the energetics, geometry, and dynamics of the active site are analyzed using molecular dynamics simulations. The ATP conformation observed in the one-metal-ion structure allows stronger interactions with the catalytic ion, and ATP is more restrained than in the structure containing two Mg(2+) ions. Therefore, we propose that the conformation observed in the one-ion crystal structure is a more probable starting point for the reaction. The simulations also suggest that a C3'-endo sugar pucker facilitates nucleophilic attack."

"Additionally, the two-cation binding mode restrains the mobility of the reaction products, and thus their tendency to dissociate."

The full article can be found at: (L. Martinez, et. al., "ATP conformations and ion binding modes in the active site of anthrax edema factor: a computational analysis". Proteins, 2009;77(4):971-83). Link not available.

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NEW MULTISPECIFIC ARRAY AS A TOOL FOR ELECTROCHEMICAL IMPEDANCE SPECTROSCOPY-BASED BIOSENSING

Medical Imaging Week
February 27, 2010

"Using electrochemical impedance spectroscopy (EIS) for biosensing applications typically requires repetitive experiments. To address this need, we have designed a multispecific electrochemical array with eight individually addressable 2mm-diameter gold working electrodes for rapid biosensing data accumulation by EIS in the presence of redox agent."

"The array allows to incorporate multiple negative controls in the course of a single binding experiment, as well as to perform parallel identical experiments to improve reliability of detection. The array is fit with attached electrochemical cell with Ag/AgCl mini reference electrode and can be used to process macro samples of 0.5-1 ml or micro samples of 5 microl in a drop-wise fashion. Eight individual EIS measurements are completed in 15 min. The reported array is disposable, economical and is easy to use. Examples of array use for

label-free genetic sensing of 2.7 kb-long target *Yersinia pestis* DNA and for protein sensing of Ricin Toxin Chain A (RTA) are presented."

The full article can be found at: (E. Komarova, et. al., "New multispecific array as a tool for electrochemical impedance spectroscopy-based biosensing". *Biosensors & Bioelectronics*, 2010; 25(6): 1389-94). Link not available.

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IMMUNE REQUIREMENTS OF POST-EXPOSURE IMMUNIZATION WITH MODIFIED VACCINIA ANKARA OF LETHALLY INFECTED MICE

By Henning Lauterbach, Ronny Kassub, Juliane Pätzold, Jana Körner, Michael Brückel, Admar Verschoor, Paul Chaplin, Mark Suter, Hubertus Hochrein

PLoS One

March 10, 2010

"Abstract

Current prophylactic vaccines work via the induction of B and T cell mediated memory that effectively control further replication of the pathogen after entry. In the case of therapeutic or post-exposure vaccinations the situation is far more complex, because the pathogen has time to establish itself in the host, start producing immune-inhibitory molecules and spread into distant organs. So far it is unclear which immune parameters have to be activated in order to thwart an existing lethal infection. Using the mousepox model, we investigated the immunological mechanisms responsible for a successful post-exposure immunization with modified vaccinia Ankara (MVA). In contrast to intranasal application of MVA, we found that intravenous immunization fully protected mice infected with ectromelia virus (ECTV) when applied three days after infection. Intravenous MVA immunization induced strong innate and adaptive immune responses in lethally infected mice. By using various gene-targeted and transgenic mouse strains we show that NK cells, CD4 T cells, CD8 T cells and antibodies are essential for the clearance of ECTV after post-exposure immunization. Post-exposure immunization with MVA is an effective measure in a murine model of human smallpox. MVA activates innate and adaptive immune parameters and only a combination thereof is able to purge ECTV from its host. These data not only provide a basis for therapeutic vaccinations in the case of the deliberate release of pathogenic poxviruses but possibly also for the treatment of chronic infections and cancer."

The full article can be found at: http://www.plosone.org/article/info:doi%2F10.1371%2Fjournal.pone.0009659?utm_source=feedburner&utm_medium=feed&utm_campaign=Feed%3A+plosone%2FPLoSONE+%28PLoS+ONE+Alerts%3A+New+Articles%29

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POPULAR NANOPARTICLE CAUSES TOXICITY IN FISH, STUDY SHOWS

Nano Techwire

March 07, 2010

"A nanoparticle growing in popularity as a bactericidal agent has been shown to be toxic to fish, according to a Purdue University study.

Tested on fathead minnows – an organism often used to test the effects of toxicity on aquatic life -- nanosilver suspended in solution proved toxic and even lethal to the minnows. When the nanosilver was allowed to settle, the solution became several times less toxic but still caused malformations in the minnows."

.....

"Turco also indicated there has been little work done to estimate the current level of nanosilver being released into the environment.

"Silver has been used in the past as an antimicrobial agent. It's a known toxicant to microorganisms," he said. "Nanosilver is being considered by the EPA for environmental exposure profiling, much like a pesticide."

The full article can be found at: <http://nanotechwire.com/news.asp?nid=9511>

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PREDICTING DRUG-TARGET INTERACTION NETWORKS BASED ON FUNCTIONAL GROUPS AND BIOLOGICAL FEATURES

By Zhisong He, Jian Zhang, Xiao-He Shi, Le-Le Hu, Xiangyin Kong, Yu-Dong Cai¹, Kuo-Chen Chou

PLoS One

March 11, 2010

"Abstract

Background

Study of drug-target interaction networks is an important topic for drug development. It is both time-consuming and costly to determine compound-protein interactions or potential drug-target interactions by experiments alone. As a complement, the in silico prediction methods can provide us with very useful information in a timely manner.

Methods/Principal Findings

To realize this, drug compounds are encoded with functional groups and proteins encoded by biological features including biochemical and physicochemical properties. The optimal feature selection procedures are adopted by means of the mRMR (Maximum Relevance Minimum Redundancy) method. Instead of classifying the proteins as a whole family, target proteins are divided into four groups: enzymes, ion channels, G-protein-coupled receptors and nuclear receptors. Thus, four independent predictors are established using the Nearest Neighbor algorithm as their operation engine, with each to predict the interactions between

drugs and one of the four protein groups. As a result, the overall success rates by the jackknife cross-validation tests achieved with the four predictors are 85.48%, 80.78%, 78.49%, and 85.66%, respectively.

Conclusion/Significance

Our results indicate that the network prediction system thus established is quite promising and encouraging.”

The full article can be found at: <http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0009603;jsessionid=227B5874EC75F262AD451410CC3F6E6D>

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