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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. HOW TO CURE DISEASES BEFORE THEY HAVE EVEN EVOLVED: *“What if, Goldblatt wondered, some host proteins are essential for viral replication but not for the survival of the host? If so, disabling these proteins should block viral replication without killing healthy cells.”*

2. STRETCHING FOR REVERSIBLE ENZYME ACTIVATION: *“The material could prove useful for biosensors, tissue engineering, and externally controlled drug delivery, the team suggests.”*

3. MULTIPLEXED DETECTION OF BACTERIA AND TOXINS USING A MICROFLOW CYTOMETER: *“The respective limits of detection for bacteria (Escherichia coli, Listeria, and Salmonella) were found to be 10(3), 10(5), and 10(4) cfu/mL for the microflow cytometer and 10(3), 10(6), and 10(5) cfu/mL for the commercial system. limits of detection for the toxins (cholera toxin, staphylococcal enterotoxin B, and ricin) were 1.6, 0.064, and 1.6 ng/mL for the microflow cytometer and 1.6, 0.064, and 8.0 ng/mL for the commercial system..”*

4. STUDIES ON CuTAPC-NANOTUBE-MODIFIED ELECTRODES AS CHEMICAL SENSORS FOR NO: *“Their high surface area and simple preparation protocol made them potential candidates as the modification layer of electrodes for sensor application.”*

5. ETS2 REGULATING NEURODEGENERATIVE SIGNALING PATHWAY OF HUMAN NEURONAL (SH-SY5Y) CELLS EXPOSED TO SINGLE AND REPEATED LOW-DOSE SARIN (GB): *“The overall data delineate an in vitro experimental model suitable for studying the neuropathology of cells and may provide novel insights into therapeutic interventions..”*

CB Daily Report

HOW TO CURE DISEASES BEFORE THEY HAVE EVEN EVOLVED

By Bob Holmes
New Scientist
August 10, 2009

"If you look at the viruses that are the biggest threats of modern times, most of them were unknown through human history: HIV, SARS, Ebola. You don't know where the next one is coming from. How do you develop therapeutics for the unknown and unknowable, given that you won't have time to develop a vaccine for a new agent after it appears?" he asks.

Goldblatt and a few other researchers think they have the answer. They are working on an entirely new class of antiviral drugs that should do something seemingly impossible: work against a wide range of existing viruses and also be effective against viruses that have not even evolved yet. What's more, it should be extremely difficult for any virus to become resistant to these drugs.

This might sound too good to be true, but the first trials of these drugs are already producing encouraging early results. If just a few of them live up to their promise in full-scale human trials - no sure thing - they will be a medical breakthrough on a par with the discovery of penicillin. At last, doctors will be able to treat viral diseases as ably as they do bacterial ones.

The conventional strategy for developing antivirals is "one bug, one drug" - finding a drug that blocks viral replication by binding to part of a viral protein. The trouble is, any minor mutation that slightly changes the shape of the protein can render these drugs useless, as is happening with Tamiflu. The hundreds of millions of dollars governments worldwide have spent stockpiling this drug could well turn out to be futile.

A few existing antiviral drugs, such as interferons, do work against a wide range of viruses. However, these drugs merely rev up the body's immune system, which makes them less effective than doctors would like.

Back in the late 1990s, when Goldblatt was at DARPA, he began to wonder whether there was another strategy, one that exploits the key weakness of all viruses: their utter dependence on their hosts. By themselves, viruses are more helpless than newborn babies. They can replicate only by tricking their host cells into making more copies of them, a process that can involve hundreds of host proteins.

What if, Goldblatt wondered, some host proteins are essential for viral replication but not for the survival of the host? If so, disabling these proteins should block viral replication without killing healthy cells."

The full article can be found at: <http://www.newscientist.com/article/mg20327200.100-how-to-cure-diseases-before-they-have-even-evolved.html?page=1>

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STRETCHING FOR REVERSIBLE ENZYME ACTIVATION

By James Urquhart

Chemistry World

August 10, 2009

“A new kind of biologically inspired nanomaterial that can be chemically turned on and off by mechanical stretching has been devised by French researchers. The material could prove useful for biosensors, tissue engineering, and externally controlled drug delivery, the team suggests.

In nature, cells have the ability to turn mechanical forces into chemical activity by so-called 'mechanotransductive' processes. Key to these processes are particular proteins called cryptic site proteins. These proteins are usually inactive because their recognition sites are hidden, but under mechanical stretching, the sites become exposed and the biochemical signalling pathways are activated.

Now, Philippe Lavallo and colleagues based at a number of institutes in Strasbourg, France, have mimicked this phenomenon by creating a new type of mechanically responsive material using enzymes and polyelectrolyte multi-layered films. 'Our work presents the first example of a synthetic "cryptic-like" system that behaves in a similar way to mechanotransductive processes,' says Lavallo.

Although scientists have created similar systems that trigger chemical reactions under force in the past, Lavallo points out that this is 'the first example of a system where such an induction takes place in a reversible manner.'

The material comprises two film layers. The first layer acts as a micro-container and is loaded with enzymes. This is capped by a second, chemically different layer which works as a mechanically sensitive nanobarrier that 'masks' the enzymes from a substrate, thereby preventing biocatalysis. However, when this nanobarrier is mechanically stretched, the enzymes are exposed, which kick-starts biocatalytic activity. Returning the nanobarrier film to its unstretched state masks the enzymes once again.”

The full article can be found at: <http://www.rsc.org/chemistryworld/News/2009/August/10080901.asp>

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MULTIPLEXED DETECTION OF BACTERIA AND TOXINS USING A MICROFLOW CYTOMETER

Chemical & Chemistry

August 21, 2009

"A microfabricated flow cytometer was used to demonstrate multiplexed detection of bacteria and toxins using fluorescent coded microspheres. Antibody-coated microspheres bound biothreat targets in a sandwich immunoassay format."

"The microfluidic cytometer focused the microspheres in three dimensions within the laser interrogation region using passive groove structures to surround the sample stream with sheath fluid. Optical analysis at four different wavelengths identified the coded microspheres and quantified target bound by the presence of phycoerythrin tracer. The multiplexed assays in the microflow cytometer had performance approaching that of a commercial benchtop flow cytometer."

"The respective limits of detection for bacteria (*Escherichia coli*, *Listeria*, and *Salmonella*) were found to be 10^3 , 10^5 , and 10^4 cfu/mL for the microflow cytometer and 10^3 , 10^6 , and 10^5 cfu/mL for the commercial system. limits of detection for the toxins (cholera toxin, staphylococcal enterotoxin B, and ricin) were 1.6, 0.064, and 1.6 ng/mL for the microflow cytometer and 1.6, 0.064, and 8.0 ng/mL for the commercial system.."

The full article can be found at: (J.S. Kim, et. al., "Multiplexed Detection of Bacteria and Toxins Using a Microflow Cytometer". *Analytical Chemistry*, 2009;81(13):5426-5432). Link not available.

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STUDIES ON CUTAPC-NANOTUBE-MODIFIED ELECTRODES AS CHEMICAL SENSORS FOR NO

Nanotechnology Weekly
August 10, 2009

"Poly-copper tetraaminophthalocyanine (CuTAPc) nanotubes were successfully fabricated on porous alumina templates by electropolymerization."

"Their high surface area and simple preparation protocol made them potential candidates as the modification layer of electrodes for sensor application. High sensitivities and improved linear ranges were obtained through different measurements such as differential pulse voltammetry (DPV), differential potential amperometric (DPA) and electrochemical impedance spectroscopy (EIS)."

"Detection limits as low as 10 nM were demonstrated in common voltammetric analysis with ultra-high response current in the μ A range."

The full article can be found at: (F. Gu, et. al., "Studies on CuTAPc-nanotube-modified electrodes as chemical sensors for NO". *Nanotechnology*, 2009;20(30):5501). Link not available.

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HUMAN NEURONAL (SH-SY5Y) CELLS EXPOSED TO SINGLE AND REPEATED LOW-DOSE SARIN (GB)

Ecology, Environment & Conservation

August 21, 2009

"The mechanistic understanding of low-level sarin-induced neurotoxicity after single or repeated doses has yet to be explored at a cellular level. Using the microarray (Affymetrix-GeneChips) transcription profiling approach, the present study examined gene expression in human SH-SY5Y cells exposed to, single Q and 24 h) or repeated (2 x 24 h) doses of sarin (5 mu g/mL) to delineate the possible mechanism."

"Two hundred twenty-four genes whose expression was significantly ($P < 0.01$) altered by at least 3-fold were selected by GeneSpringGX analysis. The comparative gene expression data confirmed the transcriptional changes to be related to close and exposure time of sarin. The effect of a single noncytotoxic sarin dose on gene transcription was variable, whereas repeated doses over 48 h persistently down-regulated genes linked to neurodegenerative mechanisms. Thirty persistently altered genes were validated using real-time quantitative reverse transcription-polymerase chain reaction (qRT-PCR). Similar qRT-PCR profiles obtained in sarin-treated SH-SY5Y and HCN-1A cells confirmed the cell-independent alterations in expression levels. Genes (ETS2, APOE, PSEN1, DDC, and CD9) implicated mainly in the regulation of sarin-induced neuropathogenesis were further confirmed by Western blot and double-immunofluorescence assays. The regulome pathway suggests a new feasible mechanism by which sarin increases ETS2 expression and takes control over other genes involved in the neurodegenerative pathway."

"The overall data delineate an in vitro experimental model suitable for studying the neuropathology of cells and may provide novel insights into therapeutic interventions.."

The full article can be found at: (A. Pachiappan, et. al., "ETS2 Regulating Neurodegenerative Signaling Pathway of Human Neuronal (SH-SY5Y) Cells Exposed to Single and Repeated Low-Dose Sarin (GB)". *Chemical Research in Toxicology*, 2009; 22(6): 990-996). Link not available.

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