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## **Chem-Bio News - S&T Edition**

**1. FIVE TYROSINES AND TWO SERINES IN HUMAN ALBUMIN ARE LABELED BY THE ORGANOPHOSPHORUS AGENT FP-BIOTIN:** *"These results will be useful in the development of specific antibodies to detect OP exposure and to engineer albumin for use as an OP scavenger."*

**2. ENGINEERED RECOMBINANT HUMAN PARAOXONASE 1 (RHUPON1) PURIFIED FROM ESCHERICHIA COLI PROTECTS AGAINST ORGANOPHOSPHATE POISONING:** *"The injected rHuPON1 is nontoxic, persists in serum for at least 2 days after injection, and provides protection against DZO exposures of at least three times the median lethal dose value."*

**3. A NASAL INTERLEUKIN-12 DNA VACCINE COEXPRESSING YERSINIA PESTIS F1-V FUSION PROTEIN CONFERS PROTECTION AGAINST PNEUMONIC PLAGUE:** *"These results show that IL-12 can be used as a molecular adjuvant to enhance protective immunity against pneumonic plague, but in a dose-dependent fashion."*

**4. CADMIUM(II) COMPLEXES OF THE GLYCEROPHOSPHODIESTER-DEGRADING ENZYME GPDQ AND A BIOMIMETIC N,O LIGAND:** *"The glycerophosphodiester-degrading enzyme GpdQ from Enterobacter aerogenes is a promising bioremediator owing to its ability to degrade some organophosphate pesticides and diester products originating from the hydrolysis of nerve agents such as VX."*

**5. EFFECT OF FOOD MATRICES ON THE BIOLOGICAL ACTIVITY OF RICIN:** *"This study demonstrates that the cell-free translation assay is a rapid and sensitive method for detection of biologically active ricin toxin in ground beef, low-fat milk, and liquid chicken egg and that food matrices can greatly affect the thermal stability of ricin."*

# **CB Daily Report**

**Chem-Bio News**

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## **FIVE TYROSINES AND TWO SERINES IN HUMAN ALBUMIN ARE LABELED BY THE ORGANOPHOSPHORUS AGENT FP-BIOTIN**

Energy & Ecology Business

November 28, 20

"Tyrosine 411 of human albumin is an established site for covalent attachment of 10-fluoroethoxyphosphinyl-N-biotinamidopentyldecanamide (FP-biotin), diisopropylfluorophosphate, chlorpyrifos oxon, soman, sarin, and dichlorvos. This work investigated the hypothesis that other residues in albumin could be modified by organophosphorus agents (OP)."

"Human plasma was aggressively treated with FP-biotin; plasma proteins were separated into high and low abundant portions using a proteome partitioning antibody kit, and the proteins were digested with trypsin. The FP-biotinylated tryptic peptides were isolated by binding to monomeric avidin beads. The major sites of covalent attachment identified by mass spectrometry were Y138, Y148, Y401, Y411, Y452, S232, and S287 of human albumin. Prolonged treatment of pure human albumin with chlorpyrifos oxon labeled Y138, Y150, Y161, Y401, Y411, and Y452. To identify the most reactive residue, albumin was treated for 2 h with DFP, FP-biotin, chlorpyrifos oxon, or soman, digested with trypsin or pepsin, and analyzed by mass spectrometry. The most reactive residue was always Tyr 411. Diethoxyphosphate-labeled Tyr 411 was stable for months at pH 7.4."

"These results will be useful in the development of specific antibodies to detect OP exposure and to engineer albumin for use as an OP scavenger."

The full article can be found at: (S.J. Ding, et. al., "Five tyrosines and two serines in human albumin are labeled by the organophosphorus agent FP-biotin". *Chemical Research in Toxicology*, 2008; 21(9):1787-1794). Link not available.

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## **ENGINEERED RECOMBINANT HUMAN PARAOXONASE 1 (RHUPON1) PURIFIED FROM ESCHERICHIA COLI PROTECTS AGAINST ORGANOPHOSPHATE POISONING**

Drug Week

December 5, 2008

"The high-density lipoprotein-associated enzyme paraoxonase 1 (PON1) hydrolyzes lactones, aromatic esters, and neurotoxic organophosphorus (OP) compounds, including insecticide metabolites and nerve agents. Experiments with mice lacking PON1 (PON1(-/-) mice) have established that plasma PON1 protects against chlorpyrifos/chlorpyrifos-oxon and diazinon/diazoxon (DZO) exposure but does not protect against parathion/paraoxon or nerve agents."

"The catalytic efficiency of PON1 determines whether or not it will protect against a given OP exposure. Expression of active recombinant human PON1 (rHuPON1) in *Escherichia coli* provides a system in which PON1 can be engineered to achieve a catalytic efficiency sufficient to protect against or treat specific OP exposures. Here, we describe the generation of highly purified engineered rHuPON1(K192) that protects against DZO exposure when

injected into PON1(-/-) mice."

"The injected rHuPON1 is nontoxic, persists in serum for at least 2 days after injection, and provides protection against DZO exposures of at least three times the median lethal dose value."

The full article can be found at: (R.C. Stevens, et. al., "Engineered recombinant human paraoxonase 1 (RHuPON1) purified from Escherichia coli protects against organophosphate poisoning". Proceedings of the National Academy of Sciences of the United States of America, 2008; 105(35):12780-12784). Link not available.

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## **A NASAL INTERLEUKIN-12 DNA VACCINE COEXPRESSING YERSINIA PESTIS F1-V FUSION PROTEIN CONFERS PROTECTION AGAINST PNEUMONIC PLAGUE**

Medical Letter on the CDC & FDA

November 30, 2008

"Two bicistronic plasmids were constructed that encoded the protective plague epitopes, capsular antigen (F1-Ag) and virulence antigen (V-Ag) as a F1-V fusion protein but differed in the amounts of IL-12 produced. When applied nasally, serum IgG and mucosal IgA anti-F1-Ag and anti-V-Ag titers were detectable beginning at week 6 after three weekly doses, and recombinant F1-Ag boosts were required to elevate the F1-Ag-specific antibody (Ab) titers. Following pneumonic challenge, the best efficacy was obtained in mice primed with IL-12(Low)/F1-V vaccine with 80% survival compared to mice immunized with IL-12(Low)/F1, IL-12(Low)/V, or IL-12(Low) vector DNA vaccines. Improved expression of IL-12 resulted in lost efficacy when using the IL-12(High)/F1-V DNA vaccine. Despite differences in the amount of IL-12 produced by the two F1-V DNA vaccines, Ab responses and Th cell responses to F1- and V-Ags were similar."

"These results show that IL-12 can be used as a molecular adjuvant to enhance protective immunity against pneumonic plague, but in a dose-dependent fashion."

The full article can be found at: (H. Yamanaka, et. al., " A nasal interleukin-12 DNA vaccine coexpressing Yersinia pestis F1-V fusion protein confers protection against pneumonic plague". Infection and Immunity, 2008; 76(10):4564-4573). Link not available.

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## **CADMIUM(II) COMPLEXES OF THE GLYCEROPHOSPHODIESTER-DEGRADING ENZYME GPDQ AND A BIOMIMETIC N,O LIGAND**

Biotech Law Weekly

November 28, 2008

"The glycerophosphodiester-degrading enzyme GpdQ from Enterobacter aerogenes is a

promising bioremediator owing to its ability to degrade some organophosphate pesticides and diester products originating from the hydrolysis of nerve agents such as VX. Here, the cadmium derivative of GpdQ was prepared by reconstituting the apoenzyme."

"Catalytic measurements with  $(\text{Cd}^{2+})_2\text{-GpdQ}$  and the phosphodiester substrate bis(4-nitrophenyl)phosphate yield  $k(\text{cat}) = 15 \text{ s}^{-1}$ . The  $\text{pK}(\text{a})$  of 9.4, determined from the pH dependence of the catalytic activity, implicates a hydroxide ligand as the catalytic nucleophile. Also prepared was the cadmium-containing biomimetic  $[\text{Cd}_2((\text{HP})_2\text{B})(\text{OAc})_2(\text{OH}_2)](\text{PF}_6)$  (where  $(\text{HP})_2\text{B}$  is [2,6-bis([(2-pyridylmethyl)(2-hydroxyethyl)amino]methyl)-4-methylphenol]), which mimics the asymmetry of the metal ion coordination in the active site of GpdQ. The phosphoesterase-like activity of  $[\text{Cd}_2((\text{HP})_2\text{B})(\text{OAc})_2(\text{OH}_2)](\text{PF}_6)$  was studied using the substrate bis(2,4-dinitrophenyl)phosphate, yielding a kinetically relevant  $\text{pK}(\text{a})$  of 8.9, with  $k(\text{cat}) = 0.004 \text{ s}^{-1}$ ."

The full article can be found at: (R.E. Mirams, et. al., "Cadmium(II) complexes of the glycerophosphodiester-degrading enzyme GpdQ and a biomimetic N,O ligand". Journal of Biological Inorganic Chemistry, 2008; 13(7):1065-1072). Link not available.

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## **EFFECT OF FOOD MATRICES ON THE BIOLOGICAL ACTIVITY OF RICIN**

Food Business Week

December 11, 2008

"The results indicated that ground beef had very little matrix effect on the assay, whereas low-fat milk and liquid chicken egg showed clear interference on the protein translation. A simple dilution in phosphate-buffered saline (PBS) effectively eliminated the translational inhibition from these foods. The concentrations inhibiting 50% of luciferase translation derived from the current study were 0.01 nM for the pure ricin A chain, 0.02 nM for pure ricin, and 0.087 nM for crude ricin in PBS. In most cases, the half inhibitory concentration values for ricin in food matrices were significantly lower than for those in PBS buffer, suggesting that some components in these food matrices might potentiate the activity of ricin. Thermal stability tests indicated that the ficin A chain was the least stable among the three forms of ficin in all matrices measured. The thermal stability of pure and crude ricins varied depending on the matrices. The specific activities of ricin in PBS buffer were confirmed by a neutralization test with ricin-specific and nonspecific antibodies>"

"This study demonstrates that the cell-free translation assay is a rapid and sensitive method for detection of biologically active ricin toxin in ground beef, low-fat milk, and liquid chicken egg and that food matrices can greatly affect the thermal stability of ricin."

The full article can be found at: (X.H. He, et. al., "Effect of Food Matrices on the Biological Activity of Ricin". Journal of Food Protection, 2008; 71(10):2053-2058). Link not available.

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