Joint (USU & HJF)
Office of Technology Transfer

Platform Vaccine Development Strategy (HJF 165-07)

Preserving the Immunogenicity of Lethally Irradiated Microorganism Vaccine Epitopes

Issued and Pending Patents

Invention: A novel method to produce vaccines.

This technology provides a strategy for rapid development of safe and effective new vaccines. It is based upon the discovery that certain Mn^{2+}-peptide compositions selectively protect proteins, but not nucleic acids, from ionizing radiation. Thus, supralethal radiation exposure can be used to destroy a microorganism's genome, while pre-addition of the compositions preserves the microorganism's outer structure and native epitopes. The resultant sterilized microorganism "shell" is highly immunogenic. Proof of principle has been shown in animal models for both bacteria (MRSA) and virus (VEEV), with functional protective immune response demonstrated for MRSA.

- Safe – Replication incompetent and non-infectious.
- Effective – Presents numerous natural epitopes to host.
- Broad – Applicable to any microorganism, including emerging pathogens and those for which current vaccines are not effective.
- Reduced development time and risk – No need to identify or isolate epitopes; Critical protective experiments in animal can be done immediately.
- Inexpensive – Mn^{2+}-peptide compositions composed of simple laboratory reagents and short peptides.
- Patent Protected – Issued patents in Australia and Japan, two allowed U.S. applications.

Background: *Deinococcus radiodurans* is an extremophile that can withstand 3,000 times the radiation levels that would kill a human being. How the bacteria can survive such conditions, and how its survival mechanisms can be utilized to benefit the public, have been a research focus at the Uniformed Services University of the Health Sciences (USU) for over two decades. In the late 1990s, whole gene sequencing gave USU scientists and DOE collaborators sufficient control of *D. radiodurans* to engineer a bacterium for radioactive bioremediation. Protection was transferrable, as ultrafiltrates of *D. radiodurans* proved sufficient to keep proteins in other radiation-challenged bacteria intact. By the early 2000s, understanding of *D. radiodurans'* survival mechanism had progressed to the point that critical factors, such as accumulated intracellular Mn^{2+}, had been identified. In 2010, particular radio-protective Mn^{2+}-peptide complexes, which can be wholly chemically synthesized, were reported. Today, it is recognized that the Mn^{2+}-containing compositions may facilitate an alternative to standard vaccine development that must carefully balance epitope integrity against infectivity. In a technically simple method of de-coupling protein and nucleic acid damage, these compositions make it possible to develop "ideal" vaccines with both the safety of recombinant formulations and the efficacy of attenuated pathogen-based product.

Patent Status: This invention is protected by two patent families, based on PCT nos. US2008/073479 and US2011/034484, with national filings in Australia, Brazil, Canada, China, Europe, India, and Japan. The portfolio includes issued patents in Australia and Japan and two allowed applications in the U.S. One allowed U.S. application is directed toward a

continued

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method of producing a bacterial ultrafiltrate composition that preserves microorganism protein function after radiation exposure. The second allowed application is directed toward a method of producing a replication-deficient microorganism. In order to continue prosecution and allow further commercially-focused prosecution, HJF has additionally filed continuation applications.

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Sample Publications:

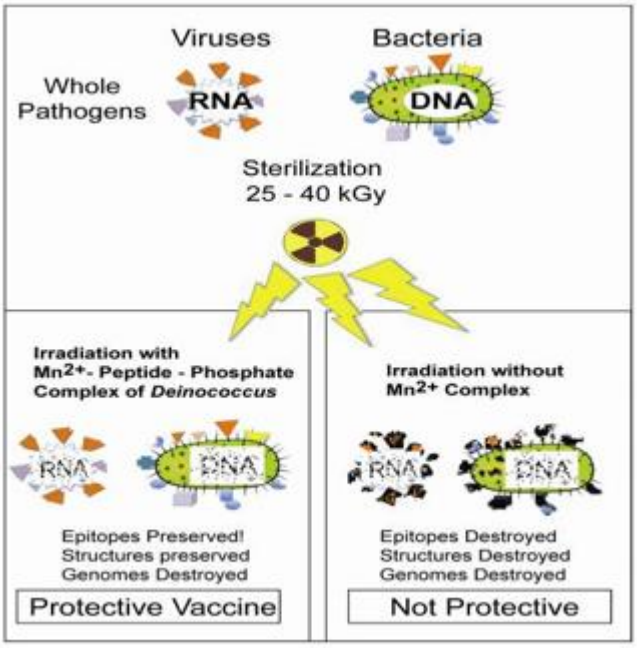
See https://www.usuhs.edu/pat/deinococcus-lab-publications

E.K. Gaidamakova, I.A. Myles, D.P. McDaniel, C.J. Fowler, P.A. Valdez, S. Naik, M. Gayen, P. Gupta, A. Sharma, P.J. Glass, R.K. Maheshwari, S.K. Datta, M.J. Daly (2012) Preserving Immunogenicity of Lethally Irradiated Viral and Bacterial Vaccine Epitopes Using a Radio-Protective Mn($^{2+}$)-Peptide Complex from Deinococcus. Cell Host Microbe, 12(1), 117-124.

M.J. Daly, E.K. Gaidamakova, V.Y. Matrosova, J.G. Kiang, R. Fukumoto, D.Y. Lee, N.B. Wehr, G.A. Viteri, B.S. Berlett, R.L. Levine (2010) Small-molecule antioxidant proteome-shields in Deinococcus radiodurans. PLoS ONE, 5(9), e12570.

M.J. Daly, E.K. Gaidamakova, V.Y. Matrosova, A. Vasilenko, Min Zhai, R.D. Leapman, B. Lai, B. Ravel, Shu-Mei W. Li, K.M. Kemner, J.K. Fredrickson (2007) Protein oxidation implicated as the primary determinant of bacterial radioresistance. PLoS Biology, 5(4), e92.

M.J. Daly, E.K. Gaidamakova, V.Y. Matrosova, A. Vasilenko, M. Zhai, A. Venkateswaran, M. Hess, M.V. Omelchenko, H.M. Kostandarithes, K.S. Makarova, L.P. Wackett, J.K. Fredrickson, D. Ghosal (2004) Accumulation of Mn(II) in Deinococcus radiodurans Facilitates Gamma-Radiation Resistance. Science 306, 1025-1028.



A vaccine made by the above strategy protected mice against infection by methicillin resistant Staphylococcus aureus (MRSA)

The HJF Office of Technology Transfer & Commercialization is seeking partners to further develop and commercialize this technology.

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