Javed N Agrewala et al., Madridge J Vaccines. 2017
http://dx.doi.org/10.18689/2638-1966.a1.004

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International Conference on Vaccines

February 20-22, 2017 Baltimore, USA

A novel vaccine construct comprising of lipidated peptide protects against Mycobacterium tuberculosis by bolstering enduring memory T cell response

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Background: Vaccines have been successful in worldwide eradication of dreaded diseases like smallpox, diphtheria, tetanus, yellow fever, whooping cough, polio, and measles. Unfortunately, such triumph has not been achieved in controlling tuberculosis (TB) globally. Bacillus Calmette Guérin (BCG) is the only available vaccine against TB. Paradoxically, BCG has deciphered successful results in the Western population but has failed in TB-endemic areas. Hence, it is quite crucial to understand the immunity responsible for controlling Mycobacterium tuberculosis infection and factors responsible for the failure of BCG in TB-endemic countries. Consequently, introducing radical changes in the vaccines that would impart protection in the populations where BCG has failed. One of the main reasons considered for BCG failure in TB-endemic areas is impediment by environmental mycobacteria in its processing by antigen presenting cells and generation of memory T-cell response.

Methods: The peripheral blood mononuclear cells of sputum positive pulmonary TB patients and their house-hold contacts were separated by ficoll-hypaque gradient method. The cells were cultured with L91 and proliferation was monitored by CFSE-dye dilution assay and phenotypic markers by flowcytometry using fluorochrome tagged appropriate antibodies and their isotype-matched controls.

Results: Keeping in view the shortcomings of BCG, we developed a unique lipopeptide (L91) by linking the promiscuous peptide (sequence 91-110) of 16 kDa antigen of Mycobacterium tuberculosis to Toll-Like Receptor-2 agonist Pam2Cys. L91 does not require extensive antigen processing and targets and activate dendritic cells. This is evidenced by the fact that L91 significantly improved the activation and proliferation of polyfunctional Th1 and Th17 cells of the TB patients and their house-hold contacts. Furthermore, L91 surmounts the barrier of major histocompatibility complex polymorphism. Importantly, this peptide has self-adjuvanting property and induces enduring memory T cell response, which is significantly better than BCG.

Conclusion: L91 can be a potent future vaccine candidate against tuberculosis in TB-endemic and non-endemic zones.

Biography:

Javed N Agrewala did his BSc, MSc and PhD from Agra University, Agra. In 1989, he joined as a Scientist at the CSIR-Institute of Microbial Technology, Chandigarh. He was a Visiting Scientist at the Royal Postgraduate Medical School, Hammersmith Hospital, London, UK [1994-1996] and Trudeau Institute, Saranac Lake, USA [2001-2002]. Currently, he is working as a Chief Scientist at the CSIR-Institute of Microbial Technology, Chandigarh. He received the Shanti Swaroop Bhatnagar award, National Bioscience award for career development and new idea research talent award. He received a fellowship from Medical Research Council (MRC), UK