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Self-adjuvanting promiscuous peptide of *Mycobacterium tuberculosis* augments polyfunctional Th17 cells and evokes better memory T cell response than BCG

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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 Guerin (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 PhD in 1986 from Agra University, Agra, India. In 1989 he joined as a faculty member at the CSIR-Institute of Microbial Technology, Chandigarh, India. He has done pioneer work in the field of Immunology of Infectious Diseases with particular interest in Vaccines. He is a recipient of the highest award in science in India "Shanti Swarup Bhatnagar Award" and is a member of Indian Academy of Sciences. He has been a visiting scientist at the Hammersmith Hospital, London and Trudeau Institute, NY, USA. He has published 67 manuscripts in the high impact journals.

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