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DNA vaccines for human use: Use of APC specifical promoter will improve long term memory cells, recall immune response

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Statement of the problem:

Interactions of TCR, co-stimulator antigens are essential for development of T-cell-dependent effector functions. Lack of this interaction results in greatly reduced activation of CD4 cells-"Anergy" and inappropriate or prolonged T-cell activation including autoimmune response. All available DNA plasmids use CMV promoter allowing express inserted antigen even in non-APC cells. To target DNA plasmid to APC, CMV promoter was replaced by APC specific macrosialin promoter in vector pacgfp1-Nl. Expression of GFP transcripts was 22 times higher and protein expression was 3 times higher in Raw267.7 in comparison with L929. Further, these plasmids vector were inserted by prm-E gene from Japanese encephalitis virus (JEV). Immunizing mice with these with promoters resulted in N'Ab response, cytokines. Despite of lower expression in macrosialin promoter, protection from lethal 10LD50 dose of JEV was 87.5% in both. Cytokine response generated demonstrated that CMV promoter developed Th2 response vs Th1 in macrosialin plasmid.

Conclusion & Significance:

To develop DNA vaccine for human use, with long term memory response, APC specific promoter plasmid can be developed. Adding T cell epitopes and encapsulating these in current approved nanoparticles will further improve vaccine for human use.

Publications

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Biography

Milind M Gore, (Former) Scientist G, National Institute of Virology, Pune, India. Currently, no affiliation. 40 years' experience in Flaviviruses. For phd, worked on CMI of GBS ATM. Worked at Wistar Institute on Rabies immune response. Further, I developed diagnostics, chimeric Th-B cell peptide, DNA vaccines against Japanese encephalitis virus along with innate and protective immune response. I established NIV Gorakhpur Unit, in Eastern Uttar Pradesh to work on encephalitis patients, vaccine efficacy of attenuated JE vaccine. I collaborated with PATH, Pasteur Institute.

Guided of seven phd students with 70 publications. I am combining all this in terms of vaccine development to keep in mind clinical side effects, morbidity and autoimmunity. I am interested in improving DNA vaccine plasmid by APC specific promoter and encapsulating in nanoparticles. This DNA vaccine vector is useful against influenza, Covid and West Nile virus vaccine. Free to contribute as visiting scientist.

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