The DNA platform allows clinical manufacturing of personalized neoantigen vaccines in 6-8 weeks targeting up to 40 neoantigens per plasmid

Tumor neoantigens are epitopes derived from tumor-specific somatic mutations that are presented on MHC molecules. Neoantigens have emerged as promising targets for personalized cancer immunotherapy due to their frequency in cancer, lack of central tolerance and lack of expression in healthy tissues. There is increasing interest in using personalized vaccines to target tumor neoantigens, however, the complexity involved in the manufacturing process results in long turnaround times and neoantigen payload limitations. Manufacturing of new synthetically designed DNA vaccines can overcome both of these limitations.

Time is a critical factor in personalized cancer vaccine treatment. Typically, only a few months are available for effective treatment before cancer progression or recurrence. Neoantigen vaccines currently available in the clinic have manufacturing times of over 12 weeks. This results in short treatment windows, and in some cases, disease progression before the vaccine is available. Using the DNA platform, we have streamlined a manufacturing chain comprising entirely of third party NGS providers and contract manufacturing organizations that already allows us to shorten turnaround time from tumor biopsy to clinical grade vaccine in 6-8 weeks enabling patient treatment earlier. The manufacturing process will be adopted in our first in human clinical trial (GT-30) targeting patients with advanced hepatocellular carcinoma in combination with standard of care pembrolizumab.

Neoantigens frequently occur as passenger mutations, so it is important to simultaneously target a high number of them in order to prevent immuno-evasion by the tumor. Clinical trials using neoantigen vaccines are targeting 10-20 neoantigens per patient. This limit is due to the difficulty and/or linear increase of cost to manufacture per targeted neoantigen. Using DNA, we have encoded up to 40 neoantigens in a single plasmid. In preclinical models, the inclusion of up to 40 neoantigens in a single plasmid resulted in maintained immunogenicity of the different epitopes, and no evidence of antigen interference was found. Furthermore, immunization using a single relevant epitope exerted similar anti-tumor effect when delivered together with 11, 23, or 59 irrelevant epitopes. This allows for the potential targeting of all identified neoantigens in the majority of cancer patients.

In conclusion, the DNA platform, is uniquely suited to target tumor neoantigens. It has demonstrated strong CD8 T cell priming in the clinic, allows manufacturing of personalized neoantigen vaccines in a shorter turnaround time than other platforms (6-8 weeks with our current outsourced model) and targets a higher number of neoantigens (40+ per plasmid).

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