Kras Peptide Vaccine to Prevent & Treat Cancer

Key Advantages

- Composition of matter claims to Kras-specific peptides from immunogenic “Hot Regions”
- Multi-valent vaccine targets multiple forms of Kras-driven cancers, including 30% of lung cancer, > 90% of pancreatic cancer, mucinomas, colorectal cancer
- Binding affinity to MHC class II elicits robust Th1 immune response & effectively blocks development of Kras-driven tumors in animal models (1) alone & (2) enhanced protection when combined with immune checkpoint inhibitors (antibodies to PD-L1, VISTA, TIM3, CTLA-4), peptides (PD-1 & PD-L1) or RXR agonists (bexarotene, UAB30, retinoic acid)
- Customizable & multipurpose: specific peptide vaccines for different Kras mutations
- Safe, minimal allergic/ autoimmune responses
- Affordable, large-scale production; stable in storage: desiccate & freeze

Mechanism of Action: We have designed an MHCII-restricted Kras multi-peptide vaccine that consists of four peptides derived from immunogenic “Hot Regions” of K-ras sequence based on a multi-scoring system. Our study has confirmed its >80% anti-cancer efficacy in a doxycycline-inducible KrasG12D model of lung cancer. This Kras multi-peptide vaccine efficiently expanded Kras-specific CD4+ and CD8+ T cells in the lung draining lymph nodes, and elicited a potent anti-tumor immune response. Importantly, K-ras-reactive T cells from vaccinated mice recognized endogenously presented Kras expressed by tumor cells. Cytokines secreted by splenocytes were measured: the most abundant individual cytokine detected in response to the Kras peptide pool was IFN-γ, suggesting that the immune responses of Th1 but not Th2, were predominantly elicited by our novel KRAS-specific peptide vaccine.

Meeting a Market Need: KRAS—mutant cancers (majority in codon 12) are among the most difficult to treat, with poor survival & resistance to chemotherapy. No specific targeted therapies are on the market, partly due to the lack of druggable pockets/cavities on the RAS surface. Peptide vaccination against tumor-associated antigen to treat cancer patients or prevent the development of tumors in high-risk individuals (e.g., former or current smokers) is an area of intense research. We have used longer peptides with predicted binding affinity to MHC class II to develop a multi-peptide, multivalent vaccine which elicits a robust Th1 immune responses and effectively blocks the development of Kras-driven tumors. Our vaccine addresses an unmet medical need for targeted prevention & treatment of Ras-driven cancers.