MEDICAL COLLEGE OF WISCONSIN
Office of TECHNOLOGY DEVELOPMENT

Patents to Patients®

Kras Peptide Vaccine to Prevent & Treat Cancer

MCW C1922 & C2012

Stage of Development:
Tested in animals

PCT/US2018/016890
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US Provisional 62/804,322
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Publication
Immunoprevention of KRAS Lung Cancer by Multipeptide Vaccine Oncotarget 2017

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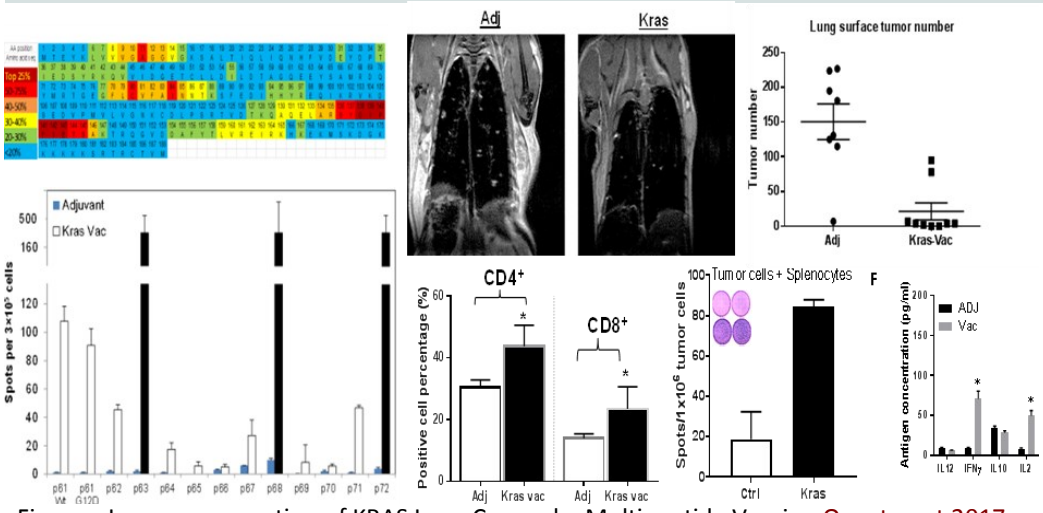
Key Advantages

- 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, mucinous adenoma, 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



Figures: Immunoprevention of KRAS Lung Cancer by Multipeptide Vaccine Oncotarget 2017

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.