Title: Novel Immunodominant Neoepitope in a KPC Mouse Model of Pancreatic Cancer allowing Identification of Tumor-specific T cells

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Abstract:

The 4662 KPC model is one of the most widely used mouse models of pancreatic cancer. It represents an excluded immune phenotype and closely recapitulates the pathophysiology of pancreatic cancer in humans. We set out to identify the endogenous neoepitopes present in 4662 cells. By combining whole-exome and RNA-sequencing and a bioinformatic neoantigen prediction pipeline, we have identified 15 potential candidate neoantigen epitopes. Ten more highly expressed were selected for validation in an in vivo vaccination study with 4662-tumor bearing mice. The Mrps35-derived neoantigen was found to be immunogenic as we have identified endogenous T-cells responding to this neoepitope, and the response was significantly increased upon vaccination with a synthetic peptide and upon PD1-IL2v therapy. Dextramers based on this peptide were validated and can be used to monitor endogenous tumor-specific CD8+ T-cells in response to immunotherapy. This will support the development of novel therapies for this highly unmet medical need indication.

Biography:

Dr. Ines G. Matos is a Principal Scientist at the Roche Innovation Center Zurich and specializes in early drug discovery for oncology. In her role, she leads multiple interdisciplinary project teams. Her expertise spans various modalities, including targeted cytokines, immune- stimulating antibody conjugates, Antibody-drug Conjugates (ADCs), and macrocyclic peptide conjugates.