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Elucidating the T-cell reactivity against porcine IDO and RhoC to establish the pig as an animal model for vaccine development against human cancer

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Immune therapy of cancer has recently experienced a great breakthrough with prolonged overall survival in patients with metastatic disease following the use of checkpoint inhibitors and T cell therapy with *ex vivo* expanded CD8+ cytotoxic T cells (CTLs). In the further development of immune therapies against cancer, vaccine formulations tailored to mount *in vivo* CTL responses towards co-delivered cancer antigens will be an important hallmark. Recognition of antigen-derived peptides presented in the context of major histocompatibility complex (MHC) class I molecules on cancer cells is a requirement for activation of CTLs. Previously, the development of therapeutic anti-cancer vaccines have largely been based on rodent models, in particular mice; however the majority of these fail to establish a therapeutic response once put into clinical trials. Pigs have the potential of serving as a model superior to rodents as they are more closely related to humans in terms of immunology and physiology. Here, we introduce pigs as a supplementary large animal model for human cancer vaccine development via the use of our unique technology for swine leukocyte antigen (SLA) production. IDO and RhoC, two tumor antigens previously identified as important players in human cancer development and progression, were used as vaccine targets. Using peptide-MHC-I binding predictors we identified IDO-derived and RhoC-derived candidate peptides potentially binding to five different broadly distributed SLA molecules. We measured the peptide-SLA complex stability of these and found a total of 89 stable ($t_{½} \geq 0.5$ hours) peptide-MHC complexes with SLA-1*04:01, -1*07:02, -2*04:01, -2*05:02 and/or -3*04:01. For a pilot study, 12 pigs were immunized with overlapping 20-mer peptides spanning the entire IDO and RhoC sequences formulated in a panel of CTL-inducing adjuvants. Vaccine and adjuvant efficacy will be evaluated through immunological assays among others including *ex vivo* stimulation of whole blood with identified stable SLA-binding peptides and quantification of peptide-specific CTLs. Hence, these data elucidate the potential in using pigs as a large animal model for human anti-cancer vaccine development.