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## The pig as a large preclinical model for therapeutic human anti-cancer vaccine development

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Development of therapeutic cancer vaccines has largely been based on rodent models and the majority failed to establish therapeutic responses in clinical trials. Since the porcine immunome is closely related to the human counterpart, using pigs as a large animal model for human cancer vaccine development has great potential. We administered peptides derived from porcine IDO, a cancer antigen important in human disease, formulated in Th<sub>1</sub>-inducing adjuvants to outbred pigs. By *in silico* prediction 136 candidate IDO-derived peptides were identified and peptide-SLA class I complex stability measurements revealed 89 stable ( $t_{1/2} \geq 0.5$  hour) complexes with expressed SLA alleles. We showed that using our immunization strategy it was possible to break the peripheral tolerance and induce a cell-mediated response to an endogenous antigen. Mounting a proper Th<sub>1</sub> response is highly dependent on peptide dose; we therefore designed a dose titration study with 15 Göttingen minipigs receiving intraperitoneal injections of either 1 µg, 10 µg or 100 µg of 30-31mer peptides covering the majority of IDO-derived potential cytotoxic T lymphocyte (CTL) epitopes. Peptides were formulated in CAF09, an adjuvant comprised of cationic DDA liposomes decorated with poly (I:C) and MMG as immune modulators. Interestingly, the 1 µg group was the only one showing responses to all immunization peptides following seven injections as determined by IFN-γ ELISpot. These data show that a reduction in dose can result in a highly specific Th<sub>1</sub>-biased response. To test the CTL functionality we designed an *in vivo* cytotoxicity assay, where purified PBMCs fluorescently labelled and pulsed with IDO-derived target peptides were administered intravenously back into each donor and killing capacity was measured by flow cytometry. In some animals we observed indications of *in vivo* specific killing of peptide-pulsed target cells as compared to control cells also fluorescently labelled with a different dye.