Establishing the pig as a large animal model for vaccine development against human cancer - DTU Orbit (03/12/2018)

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Immunotherapy has increased overall survival of metastatic cancer patients, and cancer antigens are promising vaccine targets. To fulfill the promise, appropriate tailoring of the vaccine formulations to mount in vivo cytotoxic T cell (CTL) responses toward co-delivered cancer antigens is essential. Previous development of therapeutic cancer vaccines has largely been based on studies in mice, and the majority of these candidate vaccines failed to induce therapeutic responses in the subsequent human clinical trials. Given that antigen dose and vaccine volume in pigs are translatable to humans and the porcine immunome is closer related to the human counterpart, we here introduce pigs as a supplementary large animal model for human cancer vaccine development. IDO and RhoC, both important in human cancer development and progression, were used as vaccine targets and 12 pigs were immunized with overlapping 20mer peptides spanning the entire porcine IDO and RhoC sequences formulated in CTL-inducing adjuvants: CAF09, CASAC, Montanide ISA 51 VG, or PBS. Taking advantage of recombinant swine MHC class I molecules (SLAs), the peptide-SLA complex stability was measured for 198 IDO- or RhoC-derived 9-11mer peptides predicted to bind to SLA-1*04:01, −1*07:02, −2*04:01, −2*05:02, and/or −3*04:01. This identified 89 stable (t½ ≥ 0.5 h) peptide-SLA complexes. By IFN-γ release in PBMC cultures we monitored the vaccine-induced peptide-specific CTL responses, and found responses to both IDO- and RhoC-derived peptides across all groups with no adjuvant being superior. These findings support the further use of pigs as a large animal model for vaccine development against human cancer.