The pig as a model for therapeutic human anti-cancer vaccine development, elucidating the T-cell reactivity against IDO and RhoC

Overgaard, Nana Haahr; Frøsig, Thomas Mørch; Welner, Simon; Rasmussen, Michael; Ilsøe, Mette; Sørensen, Maria Rathmann; Andersen, Mads Hald; Buus, Søren; Jungersen, Gregers

Publication date:
2015

Document Version
Peer reviewed version

The pig as a model for therapeutic human anti-cancer vaccine development, elucidating the T-cell reactivity against IDO and RhoC

Nana Haahr Overgaard[1], Thomas Mørch Frøsig[1], Simon Welner[1], Michael Rasmussen[2], Mette Ilsøe[1], Maria Rathmann Sørensen[1], Mads Hald Andersen[3], Søren Buus[2] and Gregers Jungersen[1]

[1]National Veterinary Institute, Technical University of Denmark, Copenhagen, Denmark. [2]Department of International Health, Immunology and Microbiology, University of Copenhagen, Copenhagen N, Denmark. [3]Center for Cancer Immune Therapy, Department of Hematology, Copenhagen University Hospital, Herlev, Denmark.

Immunotherapy against cancer has shown increased overall survival of metastatic cancer patients and is a promising new vaccine target. For this to succeed, appropriate tailoring of vaccine formulations to mount *in vivo* cytotoxic T cell (CTL) responses towards co-delivered cancer antigens is important. Previous development of therapeutic cancer vaccines has largely been based on studies in mice and the majority of these candidate vaccines failed to establish therapeutic responses in subsequent human clinical trials. Since the porcine immunome is more closely related to the human counterpart, we here introduce pigs as a superior large animal model for human cancer vaccine development via the use of our unique technology for swine leukocyte antigen (SLA) production. IDO and RhoC, both known to be important in human cancer development and progression, were used as vaccine targets. Pigs were immunized with overlapping 20-mer peptides spanning the entire porcine IDO and RhoC sequences formulated in a panel of CTL-inducing adjuvants. 198 candidate IDO- and RhoC-derived 9-11mer peptides potentially binding to SLA-1*04:01, -1*07:02, -2*04:01, -2*05:02 and/or -3*04:01 were identified *in silico*, and peptide-SLA complex stability measurements revealed 89 stable ($t_{½} \geq 0.5$ hour) complexes. Vaccine-induced peptide-specific CTL responses were monitored using IFN-γ release as a read out. We found responses to IDO- and RhoC-derived peptides across all groups; surprisingly non-stably binding peptides also induced responses. None of the adjuvants was found to be superior as they were all capable of generating CTL responses to IDO and RhoC hence supporting the further use of pigs as a large animal model for vaccine development against human cancer.