PROSTATE CANCER

The androgen receptor—a novel target for vaccines

The androgen receptor is a potential target for prostate cancer vaccines, according to a research group from Wisconsin, USA. Olson *et al.* used several rodent models to demonstrate the efficacy of a DNA vaccine (pTVG-AR) that targets the androgen receptor ligand-binding domain, which demonstrates high levels of intraspecies and interspecies sequence homology.

The researchers found that pTVG-AR immunization of HHDII-DR1 mice—which express human histocompatibility leukocyte antigen (HLA)-A2 and HLA-DR1—augmented *in vivo* cytotoxic HLA-A2-restricted immune responses. Splenocytes from immunized mice were able to lyse syngeneic human prostate cancer cells; an effect that was absent from controls. Encouragingly, this immune response was accompanied by decreased tumour burden and increased overall survival.

To confirm these findings, Olson and colleagues used a novel prostate tumour model—transgenic heterozygous A2/TRAMP mice that express human HLA-A2 and develop prostate tumours naturally with age. Immunization of these mice with pTVG-AR resulted in a significant decrease in the prevalence of well and moderately differentiated tumours compared with controls. A higher frequency of infiltrating CD8⁺ T cells was also reported in the immunized animals.

In addition to this new model for preclinical vaccine evaluation, the investigators also reported a novel computer-assisted methodology for objectively evaluating prostate tumour histology. The Vectra™ imaging system and inForm software (Caliper Life Sciences, Hopkinton, MA, USA) were used to develop an analysis programme trained to distinguish between histological grades of disease based on morphological patterns.

Although several prostate-cancer-specific antigens have been identified as

Courtesy of Brian Olson

immunotherapeutic agents, this is the first report of a vaccine that targets a protein involved in tumour cell oncogenicity. “We expect this vaccine to prevent the development of viable tumour escape variants, as decreased expression of the androgen receptor should result in decreased oncogenicity,” comments Douglas McNeel, who led the research.

In the near future, the authors hope to enter this vaccine into phase I clinical trials. “We are currently evaluating how immune responses to the androgen receptor are affected by tumour progression” divulges McNeel. “We also wish to determine whether there is a synergistic effect of combining immunization with other traditional therapies.”

Thus far, the research group has focused on therapeutic vaccination; however, androgen-receptor-targeted prophylactic immunization has not been ruled out. “One caveat is that the androgen receptor is made by other normal cells. Hence, we would need to evaluate the safety of this approach in patients with disease prior to a pure prophylactic setting.”

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Original article Olson, B. M. *et al.* The androgen receptor: a biologically relevant vaccine target for the treatment of prostate cancer. *Cancer Immunol. Immunother.* doi:10.1007/s00262-012-1363-9