

PROSTATE CANCER

Targeting SSX cancer–testis antigens for immunotherapy

SSX family proteins are differentially expressed in prostate tumor tissues, and could provide potential targets for cancer treatment using immune therapies, according to a study published in *Cancer Research*.

Sipuleucel-T was the first cancer vaccine to be approved by the FDA for patients with castration-resistant prostate cancer, and has been shown to improve overall survival. Although this approach holds promise for future therapies, development



© Giedrius Zaleckas | Dreamstime.com

has been limited by concerns that many of the prostate cancer antigens investigated thus far are also expressed in normal tissue. However, cancer–testis antigens might hold the key. “The cancer–testis antigens are normally only expressed in MHC class I deficient germ cells, but can become aberrantly expressed in malignant tissues,” explains Doug McNeel, who led the study. “Their expression in MHC class I-expressing tumors makes them essentially tumor-specific targets for T-cell directed therapies.”

Having previously shown that the cancer–testis antigen SSX-2 was expressed in prostate cancer cell lines, McNeel’s team used PCR to investigate whether other SSX family members were present, finding that three SSX-family proteins were either frequently expressed in prostate cancer cell lines or could be induced by treatment with epigenetic modifying agents. They went on to test patient tumor samples, and found that SSX proteins were present in samples of

metastatic human prostate cancers, but not in the primary tumors, suggesting these genes are specifically associated with metastatic disease. Finally, the team investigated how the various SSX proteins could be targeted therapeutically, showing that SSX-2-specific T cells (specific for a dominant HLA-A2-restricted epitope) were able to distinguish between the highly homologous SSX proteins expressed in the prostate, suggesting that they could potentially be simultaneously targeted by SSX-directed immunization.

In a field where immunological therapy could prove to be pivotal in managing advanced disease, these data are promising. The team are now conducting studies to evaluate how best to target these SSX family members using DNA vaccines.

Annette Fenner

Original article Smith, H. A. *et al.* Expression and therapeutic targeting of the SSX family of cancer–testis antigens in prostate cancer. *Cancer Res.* 71, 6785–6795 (2011)