**Abstract: CHIMERIC PROTEINS AS IMMUNE TARGETS IN PROSTATE CANCER**

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***Background:*** Cancer vaccines aim to elicit antigen-specific T cell responses against tumor antigens. Most prostate cancer vaccines to date target mis-expressed or over-expressed proteins; however, these proteins are often dispensable for the tumor, allowing for antigen escape, or have tolerance mechanisms in place that may curb induction of T cell immunity. Recent studies provide compelling evidence that tumor-specific mutations are a novel source of T cell targetable antigens (neoantigens). Metastatic Castration Resistant Prostate Cancers (mCRPC) contain several recurrently mutated fusion proteins that may serve as viable immune targets. The TMPRSS2:ERG fusion protein is found in a large proportion of mCRPC, is involved in several oncogenic pathways, and predicts poor overall survival; thus, this fusion is likely functionally important for tumor maintenance, progression, and metastasis.

***Hypothesis:*** Gene fusions, such as TMPRSS2:ERG, generate chimeric amino acid sequences that are targetable by T cells.

***Methods and Results*:** With this aim, we pulsed autologous dendritic cells with peptides corresponding to the TMPSS2:ERG type VI fusion site to activate and expand naïve fusion-specific T cells from peripheral blood of healthy donors. After two rounds of stimulation, expanded T cell cultures were assessed by interferon-γ ELISPOT for recognition of fusion peptides. T cell responses to two epitopes spanning the TMPRSS2:ERG fusion were confirmed in an HLA-A*02:01 healthy donor. These two peptides were predicted to bind HLA-A*02:01, which was confirmed by MHC stabilization assays. Currently, we are assessing whether these minimal peptides are naturally processed as well as whether antigen-specific T cell clones can lyse tumor cells that express the TMPRSS2:ERG type VI fusion protein.

***Conclusions and Future Directions*:** Future studies will assess TMPRSS2:ERG positive mCRPC patients for the presence of pre-existing T cell responses to this fusion. Our findings to date have implications for the use of fusions as T cell targetable epitopes for therapeutic vaccination against fusion oncogenes in prostate cancer.