INVESTIGATING EPIGENETIC REGULATION OF T CELL EXHAUSTION

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T cell exhaustion occurs during persistent viral infections and in many cancers and is characterized by an enduring disability of cytotoxic T cells to kill infected or malignant cells. Being the target of many emerging cancer immunotherapies, the accurate identification of exhausted T cells in cancers is of high importance. The current approach is based on cell surface marker expression but cannot provide the required accuracy, since many markers on exhausted T cells are shared with well-functioning effector T cells. We are currently performing a whole-genome DNA methylation screening to identify epigenetic marks that are unique to exhausted T cells. This epigenetic "exhausted T cell signature" will be used to develop a highly sensitive technique to accurately determine the frequency of exhausted T cells in unseparated tumor specimens from ovarian cancer patients. Moreover, in-depth analyses on the regulation and function of novel genes that display a distinct epigenetic profile in exhausted T cells will be performed to further our current understanding on the establishment and imprinting of exhaustion.