Merkel Cell Carcinoma (MCC)

- Rare but aggressive form of skin cancer
- MCC typically presents as a painless, red or purple, rapidly growing nodule
- Risk factors: long-term sun exposure, Caucasian ethnicity, age over 50, immune suppression, infection with Merkel cell polyomavirus (MCPyV)

Merkel cell polyomavirus (MCPyV)

Discovered in 2008. Associated with ~80% of MCC tumors by clonal integration into malignant cell genome (1). T antigen expression is required for maintenance of virus positive MCCs (2).

CD8 and CD4 T cells that recognize MCPyV viral oncoproteins can be detected in blood and tumors of MCC patients (3). CD8 infiltration into MCC tumors is correlated with improved prognosis (4).

Importantly, autologous CD8 T cell therapy has shown limited efficacy in treating MCC.

Do MCPyV-specific CD4s matter for MCC?

Using CyteFinder to identify and phenotype MCPyV-specific CD4 T cells

Sensitivity detection of rare T cells

Identification of MCPyV-specific CD4s in patient and donor PBMC

Future Directions

- Validation of this platform is underway. We are generating transgenic TCRs from TCR alpha and beta sequences that have been obtained from picked cells. We will then test their ability to bind tetramer.
- This approach using the CytePicker for identification of rare T cell populations combined with single cell RT-PCR of 24 phenotypic genes enables highly sensitive and detailed characterization of antigen-specific T cells.
- Evaluating the phenotype and functional of MCPyV-specific CD4 T cells in correlation with patient outcome will greatly enhance our understanding of the immune response against MCC.
- Transgenic TCRs can be generated from the TCR sequences obtained using this platform and used to generate therapeutic transgenic T cells for MCC patients.

References


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