

**GENETICALLY ENGINEERED MYELOID CELLS (GEMYS)  
AS A PLATFORM TO ENHANCE ANTITUMOR IMMUNITY**

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**Background** Immune suppression is a major hurdle in cancer immunotherapy for solid tumors. Innate myeloid cells are key regulators of the immune system and can dampen the antitumor response against cancer. We have identified that bone marrow-derived myeloid cells play an immunosuppressive role in the metastatic microenvironment, limiting immune surveillance and facilitating the growth of tumor cells. We hypothesized that targeting the myeloid-mediated immune suppression program in the metastatic and primary tumor microenvironment could facilitate antitumor immune activation and be a successful immunotherapeutic approach.

**Methods** To take advantage of the unique capability of myeloid cells to home to and infiltrate tumor and metastatic sites, we designed an immunotherapeutic approach in which we generate genetically engineered myeloid cells (GEMys) as a platform to locally deliver modulatory factors into the tumor and metastatic microenvironment.

**Results** Mice treated with IL-12-secreting GEMys (IL12-GEMys) exhibited a robust IFN $\gamma$  response associated with increased expression of antigen processing and presentation machinery as well as numbers of T and NK cells expressing markers associated with activation and cytotoxicity. These microenvironmental changes were associated with reduced metastasis, delayed tumor growth, and increased survival. When combined with chemotherapy pre-conditioning, IL12-GEMys cured mice of established tumors and generated long-lived T cell memory, as these mice were immune to subsequent tumor challenge. We are currently working on translating these exciting findings into the human setting.

**Conclusions** This work demonstrates that IL12-GEMys can functionally modulate the core program of immune suppression in the pre-metastatic niche to successfully rebalance the dysregulated metastatic microenvironment in cancer. This approach holds promise to limit metastatic progression in patients with high risk and advanced cancers.

**REFERENCES**

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