CANCER

# A novel mouse skin array to study tumor immune phenotypes

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Human cancers can be characterized by distinct immune phenotypes – defined by the level of T-cell presence and activity in the tumor microenvironment – that help to predict response to immunotherapy. However, many questions remain regarding the development, heterogeneity or dynamics of these different tumor immune phenotypes. A new study in *Nature* reports the development of the skin tumor array by microporation (STAMP), a new preclinical approach to investigate tumor immune phenotype over time in mice.

The STAMP technique uses a laser to create an array of hundreds of pores in the dermis of the mouse. The researchers can then seed in each pore tumor cells expressing a fluorescent marker (GFP), longitudinally track individual tumors of the array using epifluorescence microscopy and analyze growth kinetics by automated computation.

In a first set of experiments, the investigators used the STAMP technique to address the role of adaptative immunity in controlling tumor growth. After implanting clonal mouse pancreatic ductal adenocarcinoma (PDAC) cancer cells into wild-type or immunodeficient RAG2-deficient mice, the investigators compared tumor growth in the two models. The results revealed that immunocompetent mice showed tumor rejection in about a third of individual tumors from the same array after 14 days, while immunodeficient mice did not show tumor rejection in the array. Similarly, tumor rejection was minimal in CD8-depleted mice, strongly suggesting that T cells are recruited into STAMP tumors to mediate rejection.

Fluorescent imaging of GFP$^+$ PDAC tumors in mice with fluorescently labeled T cells (tdTomato$^+$ T cells) revealed that tumors within a same array exhibited a combination of different immune phenotypes, including tumors that were highly infltrated by T cells (immune-inflamed), tumors that lacked T cells (immune desert) or that spatially excluded T cells to the periphery of the tumor lesion (immune excluded), as well as resolved tumor, in which eGFP$^+$ tumor cells have disappeared leaving behind a cluster of red T cells. These findings show that STAMP can establish different tumor immune phenotypes (TIPs), which mimic the phenotypes observed clinically.

Further analysis of STAMP tumors demonstrated that TIPs had unique transcriptomic profiles, were controlled by local factors within the tumor environment, were dynamic over time and could predict spontaneous or therapy-induced tumor rejection. In their report, the researchers explain that STAMP has the potential to translate therapeutic concepts into successful clinical strategies.

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