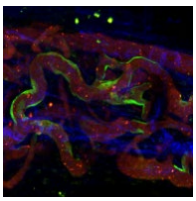
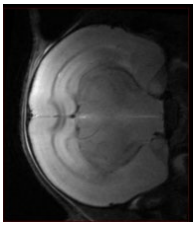
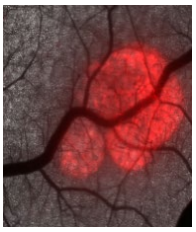
6EME ECOLE D'IMAGERIE

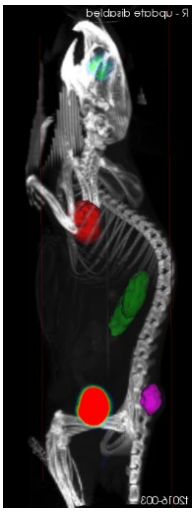
DU PETIT ANIMAL APPLIQUEE AU CANCER

12 au 16 juin 2022, Toulouse









Jeudi 16 juin à 14h – Amphi Gallais (205 route de Narbonne)

Conférence ouverte à toute la communauté scientifique

Surveillance of *in situ* tumor arrays reveals early environmental control of cancer Immunity

Christine MOUSSION

Principal Scientist, Cancer Immunology, Genentech

The immune phenotype of a tumor is a key predictor of its response to immunotherapy. Patients who respond to immune checkpoint blockade generally present with tumors that are infiltrated by activated T cells, a tumor immune phenotype (TIP) referred to as 'immune inflamed'. However, not all 'immune inflamed' tumors respond to therapy, and most of the patients present with unresponsive tumors that lack T cells ('immune desert') or that spatially exclude T cells in the periphery of the tumor lesion ('immune excluded'). Despite the importance of these TIPs, little is known about their development, heterogeneity or dynamics due to the technical difficulty of tracking these features in patients or in preclinical models. Here, we introduce STAMP (skin tumor array by micro-poration), an approach that combines in vivo non-invasive, high-throughput time-lapse imaging with excisional biopsies and next generation sequencing to characterize the initiation of a tumor and its immunological niche, as well as providing the ability to follow tumor evolution and fate during immunotherapy. STAMP involves the seeding of hundreds of clonal tumors in the superficial dermis of a single mouse ear that can be visualized simultaneously in situ over weeks to months. Surprisingly, we found genetically identical tumors could give rise to all three basic TIPs (inflamed, excluded and desert), whose transcriptional signatures were very similar to those found in human cancer patients. Although individual tumors of the same array were populated by the same T cell receptor clonotypes, local regression or progression of individual tumors were associated with distinct patterns of spatial organization of the T cells. Experimental depletion of myeloid and fibroblast subsets indicated that the tumor microenvironment, rather than tumor genetics or T cell clonotypes, played a predominant role in determining individual tumor fate among the array. In situ imaging of 14K tumors revealed that immune phenotypes were not static over-time but could rather evolve with tumor growth and response to treatment. Therapy-induced or spontaneous early conversion to the immune inflamed phenotype correlated with tumor regression and enhanced cytotoxic T cell activity. Therefore, STAMP provides a flexible approach to study the relationship between tumor evolution, immune cell dynamics, and tumor microenvironment with therapeutic response to immunotherapy.

Inscription obligatoire par mail : Cancéropôle GSO avant le 13 juin