Iron rich tumor associated macrophages promote tumor growth and immune suppression

Macrophages play important roles in immune responses and local tissue homeostasis. Their immunological roles can be pro-inflammatory or anti-inflammatory, depending on the context. The molecular basis of the location-specific specialization remains poorly understood. Tumor associated macrophages (TAMs) are the most abundant leukocytes in many solid tumors and contribute to the establishment of an immunosuppressive tumor microenvironment through multiple mechanisms. Here we identify a population of iron rich tumor associated macrophages (iTAMs) in murine fibrosarcoma. These macrophages have high intracellular iron content, express a heme metabolism gene signature, selectively express the endothelin receptor B (EdnrB) and can be found in many human solid tumor subtypes. We show protumoral activity of iTAMs when cotransplanted with murine fibrosarcoma cell line through functional experiments in mice. Further, we demonstrate decreased tumor burden after genetic ablation and pharmacological inhibition of EdnrB. Overall, iTAMs are a novel tumor macrophage subset with protumor and immune suppression activity that can be targeted to improve antitumor response.