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Abstract Title: Extracellular ST6Gal-1 inhibits MCSF-mediated monocyte maturation into macrophages

Resident macrophages are diverse populations of specialized immune cells present in almost every organ of the body, and play essential roles in both the onset and resolution of inflammation, and in maintaining immune homeostasis at steady state. Macrophage colony stimulating factor (MCSF) is the main cytokine responsible for maintaining resident macrophage populations and is important for the maturation of inflammatory monocytes into macrophages in response to inflammatory stimuli. Recent studies have identified extracellular ST6Gal-1 as a modulator of cell development and/or activation in both the innate and adaptive arms of the immune system. Here we identify an additional setting in which extracellular ST6Gal-1 can influence innate immune cell maturation; extracellular ST6Gal-1 can inhibit MCSF-dependent maturation of monocytes into mature M0 macrophages. Cells grown in the presence of extracellular ST6Gal-1 display a repertoire of cell surface proteins more similar to monocytes than macrophages and are less responsive to subsequent inflammatory stimuli. Interrogation of intracellular MCSF signaling revealed decreased response to MCSF in the presence of extracellular ST6Gal-1. Furthermore, we have observed increased numbers of resident macrophage populations in the peritoneal cavity and gastrointestinal tract of mice lacking functional ST6Gal-1 protein, supporting a role for ST6Gal-1 in monocyte-macrophage functionality and homeostasis in vivo. These results further elucidate an emerging role for extracellular ST6Gal-1 in maintaining immune cell homeostasis and guiding appropriate inflammatory responses.