Macrophages accumulate rapidly in tumors, where they promote immune suppression, tumor growth and resistance to therapy. Strategies to inhibit macrophage accumulation by blocking their recruitment from circulation have had limited therapeutic success. We found that the majority of macrophages in aggressive solid tumors accumulate by proliferation from c-Kit dependent tissue resident macrophages, rather than by trafficking from the circulation. Tissue resident macrophages express signatures of proliferation and profound immune suppression that correlate with unfavorable outcomes in cancer patients. By comparison, bone marrow derived macrophages express mixed signatures of inflammation and immune suppression that correlate with more favorable clinical outcomes. Genetic and pharmacological inhibition of proliferation mechanisms suppressed the expansion of these macrophages, thereby limiting their accumulation in tumors and inhibiting tumor progression in mouse models of cancer. These results identify macrophage proliferation is a new target for the development of therapeutic strategies to stimulate anti-cancer immunity.