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Cardiac Macrophage Composition Determines Dilated Cardiomyopathy Patient Outcomes

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While heart disease represents a leading cause of death, heart failure remains poorly understood. Looking at the immunology of chronic heart failure, specifically the monocyte derived CCR2+ and embryonic derived CCR2- macrophage populations, we have found that macrophage composition is associated with and predictive of clinical outcomes including cardiac function, pathological remodeling, and coronary angiogenesis. We focused on patients with dilated cardiomyopathy (n=55) who underwent placement of a left ventricular assist device (LVAD). Normal donor hearts were used as controls (n=10). We used clinical data and an immunostaining assay I designed using CD68 (pan-macrophage marker) and CCR2 antibodies to identify the macrophage populations. We showed that patients with increased numbers of monocyte derived CCR2+ macrophages display higher mortality rates and deterioration of cardiac function over time. The findings from these experiments demonstrate that manipulating macrophage composition within the diseased heart has the potential to improve the intrinsic capacity for the adult heart to heal following injury and a rationale to design novel heart failure treatments targeting cardiac macrophage subsets.