Purpose: Chronic heart failure (HF) is in part characterized by immune activation and inflammation, potentially contributing to the development and progression of this disorder. The homeostatic chemokines CCL19 and CCL21 are, via their receptor CCR7, important regulators of lymphocyte and dendritic cell trafficking during immune surveillance. The aims of the present study were to examine the expression of this chemokine system in patients with HF and study CCR7−/− mice in a model for post-myocardial infarction (MI) HF.

Methods and Results: Our main findings were that: (i) As determined by enzyme immunoassays, HF patients in NYHA classes II-IV had elevated circulating levels of both CCL19 and CCL21 as compared to healthy controls. (ii) Immunohistochemistry of explanted failing hearts localized CCR7, CCL19, and CCL21 expression to cardiac myocytes, but staining of endothelial and smooth muscle cells was also observed. (iii) CCR7−/− mice showed increased heart weights to tibial length ratios compared to wild type mice, indicating effects on myocardial growth. In accordance with this, echocardiography demonstrated increased left ventricular chamber size, but preserved myocardial function in CCR7−/− mice. (iv) When subjected to MI, both CCR7 and wild type mice, responded with a similar degree of myocardial remodeling (i.e., increased ventricular weights and dimensions). However, we found significantly lower gene expression of atrial natriuretic peptide in left ventricle of CCR7−/− mice, indicating an effect on cardiac function.

Conclusion: Our findings in patients with chronic HF suggest that the CCL19/CCL21/CCR7-axis may play a role in this disorder. Although, the precise pathophysiological role remains to be determined, the cardiac phenotype of CCR7−/− mice suggests that CCL19 and CCL21 can play a role in regulating myocardial growth. Moreover, loss of CCR7 may contribute to preservation of myocardial function post-MI.