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**Purpose:** LIGHT (TNFSF14) is an inflammatory cytokine in the tumor necrosis factor (TNF) super-family that is involved in innate and adaptive immune responses as well as in regulation of cell survival and proliferation. We have previously shown that patients with heart failure (HF) have elevated gene expression of LIGHT in peripheral blood mononuclear cells (PBMC). The aims of the present study were to (i) study the myocardial expression of LIGHT and its receptors lymphotoxin-ß-receptor (LTßR) and herpes virus entry mediator (HVEM) in experimental and clinical HF and (ii) examine potential pathogenic effects of LIGHT.

**Methods and results:** Myocardial gene expression of LIGHT, LTßR, and HVEM was analysed by real-time RT-PCR in a rat model of post-infarction HF 2, 7, and 28 days after induction of myocardial infarction (MI). LIGHT mRNA levels were markedly elevated in the infarcted area and modestly increased in the non-ischemic part of left ventricle throughout the study period. These changes in LIGHT were accompanied by increased expression of its corresponding receptors of which LTßR was moderately increased at all time points after MI, while HVEM gene expression reached the highest levels 28 days post-MI, representing a chronic stage of HF. Immunohistochemical analysis of left ventricular tissue from explanted failing human hearts demonstrated fairly strong LIGHT and HVEM immunoreactivity in cardiomyocytes, endothelial cells, and vascular smooth muscle cells, whereas weaker LTßR immunoreactivity was observed in cardiomyocytes. Furthermore, PBMC was isolated from patients with HF and healthy controls. LIGHT stimulation for 24 hours induced a marked increase in IL-6 release from PBMC from HF patients. However, we found no such effect on PBMC from healthy controls.

**Conclusion:** Based on the important role of LIGHT in regulation of the immune response, our findings in both clinical and experimental HF suggest a role for LIGHT signalling pathways in the pathogenesis of HF.