SUPPLEMENTARY INFORMATION

Lymphoangiocrine signals promote cardiac growth and repair

Xiaolei Liu¹, Ester De la Cruz², Xiaowu Gu³, Laszlo Balint^{4,5}, Michael Oxendine-Burns¹, Tamara Terrones⁶, Wanshu Ma¹, Hui-Hsuan Kuo⁷, Connor Lantz⁸, Trisha Bansal¹, Edward Thorp⁸, Paul Burridge⁷, Zoltán Jakus^{4,5}, Joachim Herz^{6,9}, Ondine Cleaver³, Miguel Torres² and Guillermo Oliver^{1*}

¹Center for Vascular and Developmental Biology, Feinberg Cardiovascular and Renal Research Institute, Feinberg School of Medicine, Northwestern University, Chicago, IL 60611, USA.

²Cardiovascular Development Program, Centro Nacional de Investigaciones Cardiovasculares, CNIC, Madrid 28029, Spain.

³Department of Molecular Biology, University of Texas Southwestern Medical Center, Dallas, TX 75390, USA.

⁴Department of Physiology, Semmelweis University School of Medicine, Tuzolto utca 37-47, 1094 Budapest, Hungary.

⁵MTA-SE "Lendulet" Lymphatic Physiology Research Group of the Hungarian Academy of Sciences and the Semmelweis University, Department of Physiology, Semmelweis University School of Medicine, Tuzolto utca 37-47, 1094 Budapest, Hungary.

⁶Department of Molecular Genetics, University of Texas Southwestern Medical Center, Dallas, TX 75390, USA.

⁷Department of Pharmacology, Feinberg School of Medicine, Northwestern University, Chicago, IL 60611, USA.

⁸Department of Pathology, Feinberg Cardiovascular and Renal Research Institute, Feinberg School of Medicine, Northwestern University, Chicago, IL 60611, USA. ⁹Departments of Neuroscience and Neurology and Neurotherapeutics, University of Texas Southwestern Medical Center, Dallas, TX 75390, USA.

*Corresponding author:

Guillermo Oliver, PhD Thomas D Spies Professor of Lymphatic Metabolism Director Center for Vascular and Developmental BiologyFeinberg Cardiovascular Research Institute, Northwestern University 303 East Superior St, Simpson-Querrey Biomedical Research Center 8-519 Chicago, Illinois 60611 Phone: 312-5031651 Email: guillermo.oliver@northwestern.edu

Supplementary Information

Supplementary Figures 1-5 show lower magnification images for CM proliferation and apoptosis. Supplementary Figures 6-9 show source data for Western blots. Supplementary Figure 10 shows gating strategy for flow cytometry. **Supplementary Figure 1. Lower magnification images for Figure 2.** The representative regions of images in Fig 2c, d, e and h are shown in yellow boxes.

Supplementary Figure 2. Lower magnification images for Figure 3. The representative regions of images in Fig 3d, e, f and i are shown in yellow boxes.

Supplementary Figure 3. Lower magnification images for Extended Data Figure 11. The representative regions of images in Extended Data Fig 11a, b, c, e and g are shown in yellow boxes.

Supplementary Figure 4. Lower magnification images for Extended Data Figure 3. The representative regions of images in Extended Data Figure 3c, d, e and h are shown in yellow boxes.

Supplementary Figure 5. Lower magnification images for Extended Data Figure 9. The representative regions of images in Extended Data Figure 9a and b are shown in yellow boxes.

Supplementary Figure 6. Original western blots for Figure 3a. The uncut blot images of Fig 3a are shown in **a**. Representative images are from two separate blots together with the loading control Gapdh. Two more independent experimental repeats are shown in **b**.

Supplementary Figure 7. Original western blots for Figure 3b. The uncut blot images of Fig 3b are shown in **a**. Two more independent experimental repeats are shown in **b** and images are from three different blots with loading control on each blot.

Supplementary Figure 8. Original western blots for Extended Data Figure 8b. The uncut blot images are shown in **a**. Representative images are from three separate blots together with loading control Gapdh. Two more independent experimental repeats are shown in **b** and **c**. Each experiment was run on three separate blots with Gapdh or β -Actin as loading controls.

Supplementary Figure 9. Original western blots for Extended Data Figure 8e. The uncut blot images are shown in **a**, representative images are from three different blots with Gapdh as loading control. Two more independent experimental repeats are shown in **b** and **c** with Gapdh as loading controls.

Supplementary Figure 10. Gating strategy for Extended Data Figure 1c, d. Representative flow plots from E17.5 ventricular hearts stained with PE-labeled cardiac Troponin C and Hoechst 33342. Total cell population was gated in **a**, PE-positive CMs were gated in **b** and polyploidy was gated in **c**. Gating strategy a-b were applied to all the experiments used to quantify the percentage of CMs in Extended Data Figure 1c; gating strategy from a-c were applied to all the experiments used to quantify percentages of CM polyploidy in Extended Data Figure 1d.