Lymphatic vessels in mice and humans: Alike yet different

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In an international collaboration, researchers from Uppsala University have mapped the lymph node lymphatic vessels in mice and humans down to the level of individual cells. The results may eventually help scientists to discover new methods for strengthening the immune system against viruses and cancer. Their work has been published in the journal *Frontiers of Cardiovascular Research*.

The unique microenvironment of the lymph nodes plays an important role in maintaining an efficient immune system. When we have an infection, the lymph nodes swell and release activated white blood cells into the body through the lymphatic vessels. It is important to understand how these vessels work if we are to develop new drugs to improve the immune system; for example, new vaccines.

Previous research has shown that the specialized cells that make the lymphatic vessels, known as lymphatic endothelial cells, both communicate with white blood cells and actively assist in regulating the immune system. Until now, however, researchers have only understood the importance of a few of the genes that control the versatility of these cells.

Our immune system is involved in a range of different diseases, including chronic inflammatory diseases such as psoriasis, atherosclerosis and cancer. In order to study the role of the immune system in disease mechanisms, many scientists use model systems, including mice.

"By using model systems, we researchers can test the function of various genes and evaluate treatment strategies, all of which provides us with valuable knowledge. However, in order to translate findings from mouse models to humans we need a better understanding of the similarities and differences between the signaling pathways and genes that control cell function in the different species," explains Maria Ulvmar, a researcher who led the study at Uppsala University's Department of Immunology, Genetics and Pathology.

The research teams that conducted the study analyzed the activity of genes in individual cells in mice and humans. Based on the gene activity profiles, they were able to demonstrate that both species have five distinct and similar groups of lymphatic endothelial cells in the lymph nodes, two of which were previously unknown. This discovery, complements previous published analysis of the lymphatic vessels in the lymph nodes and will help the scientific understanding of how immune cells enter and leave the lymph nodes and how their activity is regulated.

The results support the proposition that basic vessel functionality is the same in mice and humans. At the same time, researchers noted crucial differences in gene activity between the two species. This discovery is important for future research.

"This new knowledge will make it possible for my team and other researchers to focus our research

on the genes expressed in humans and eventually identify new ways to strengthen the immune system against viral diseases and cancer for example. My team is currently looking at how the lymph node endothelium changes in cancer and contributes to metastases in breast cancer. This an exciting new area of research and we are looking forward to new advances in our understanding of organ-specific and immune-regulating functions of the lymphatic endothelial cells over the next few years," says Maria Ulvmar.

More information: Menglan Xiang et al. A Single-Cell Transcriptional Roadmap of the Mouse and Human Lymph Node Lymphatic Vasculature, *Frontiers in Cardiovascular Medicine* (2020). DOI: 10.3389/fcvm.2020.00052

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