Nonvenous Origin of Lymphatic Vessels (p 1649)

Martinez-Corral et al discover that the mammalian lymphatic system doesn’t solely develop from blood vessels as previously thought.

It is currently believed that during embryogenesis, lymph vessels arise from veins by the transdifferentiation of venous endothelial cells into lymphatic endothelial cells (LECs). However, research in chickens and frogs suggests LECs could also be derived from a secondary source. Martinez-Corral and colleagues have now found evidence of a nonvenous source of LECs in mammals as well. They showed that in the lumbar region of embryonic mice, dermal lymph vessels arise independently from subcutaneous vessels, suggesting the two might have different origins. To confirm this suspicion, they performed lineage tracing experiments, in which they genetically labeled venous endothelial cells—identified by expression of the protein Tie2—such that the cells and all their progeny would fluoresce green. They found, however, that many LECs were not fluorescent, indicating that they had not arisen solely from these venous endothelial cells. The team also showed that deleting a critical LEC driver—Prox1—specifically from the Tie2 lineage, did not eliminate all LECs, providing further evidence of an alternative origin. These findings increase our understanding of the origins of lymphatic vessels, which could potentially aid the development of new therapeutic lymphatic regeneration approaches in the future.

Li et al find that cold-induced RNA binding protein regulates repolarization of the heart.

The Cold-Induced RNA binding Protein (CIRP) is rapidly upregulated in response to stresses such as low temperature, hypoxia, and UV exposure, but the protein has also been implicated in a number of physiological processes such as circadian regulation of gene expression and proinflammatory responses. Li and colleagues have now investigated the function of CIRP in the heart. The team engineered rats in which the gene encoding CIRP was homozgyously deleted and found that the animals’ hearts exhibited a distinctly reduced QT interval—the time it takes for electrical depolarization and repolarization during a single heartbeat. The team went on to show that this unusual electrical activity in the knockout mice was associated with an increase in the expression of the subunits of the potassium channel that contribute to the repolarization of the heart. They also showed that in normal cells CIRP bound to the mRNAs of these channel subunits—most likely suppressing their expression. The finding that CIRP regulates repolarization of the heart provides new understanding of the electrophysiological mechanisms at work both during normal functioning of the heart as well as under pathological conditions such as arrythmia.

Iron deficiency promotes the development of pulmonary hypertension in rats, report Cotroneo et al.

Patients with pulmonary hypertension commonly exhibit low iron levels in the blood, and such iron deficiency is associated with poorer disease prognoses. However, whether iron deficiency contributes to or is merely a consequence of pulmonary hypertension is a matter of debate. Cotroneo and colleagues now present evidence suggesting that iron deficiency alone can promote pulmonary hypertension, at least in rats. To examine the role of iron-deficiency, Cotroneo and colleagues restricted the dietary iron intake in otherwise healthy rats and found that over the course of four weeks the animals developed multiple symptoms of pulmonary hypertension including increased pulmonary blood pressure, right ventricular hypertrophy, enlargement of the heart, infiltration of inflammatory cells, and a profound remodeling of the pulmonary vasculature—with blood vessels displaying smaller lumens and hypertrophy of the walls. They also noted altered metabolic activity in pulmonary vessels—such as increased glucose uptake and reduced mitochondrial activity—suggesting a switch from aerobic to anaerobic respiration. When the rats were given a dose of intravenous iron, however, these symptoms were reversed. Based on these observations, the authors suggest that ongoing clinical evaluations of iron supplementation in pulmonary hypertension patients could yield promising results.

Written by Ruth Williams

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