# REGIONAL CENTRE FOR BIOTECHNOLOGY

## Seminar series

# *Role of Semaphorin3D in Cardiovascular development and disease*

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**3:00 PM**
**Seminar Room**

# Abstract

Class 3 semaphorins are secreted molecules that primarily signal through neuropilin and/or plexin coreceptor complexes. Semaphorins were originally identified as axon guidance molecules, but have since been implicated in multiple biological processes including cardiovascular patterning. The proepicardial organ is an important transient structure that contributes cells to various cardiac lineages. However, its contribution to the coronary endothelium has been disputed, with conflicting data arising in chick and mouse. Here we resolve this conflict by identifying a new proepicardial marker, Semaphorin3D (Sema3D) that genetically delineate heretofore uncharacterized proepicardial subcompartments. In contrast to previously fate-mapped Tbx18/WT-1 -expressing cells that give rise to vascular smooth muscle, Sema3D-expressing proepicardial cells give rise to coronary vascular endothelium in vivo. Furthermore, Sema3D+ proepicardial cells contribute to the early sinus venosus, a tissue linked to vascular endothelial formation at later stages. In a separate study, we showed that Sema3D is crucial for normal patterning of the pulmonary veins. Prevailing models suggest that total anomalous pulmonary venous return (TAPVR) occurs when the midpharyngeal endothelial strand, the precursor of the common pulmonary vein, fails to form at the proper location on the dorsal surface of the embryonic common atrium. However, analysis of Sema3D mutant embryos shows that TAPVR occurs despite normal formation of the midpharyngeal endothelial strand. Rather, the emerging venous plexus destined to form the pulmonary veins fails to anastomose uniquely with the properly formed midpharyngeal endothelial strand, and forming endothelial tubes penetrate a boundary normally produced by Sema3D expression, resulting in aberrant connections. These results identify Sema3D as a critical pulmonary venous patterning cue and provide experimental evidence for an alternate developmental model to explain abnormal pulmonary venous connections.