**Title:** Investigating the molecular mechanisms of viral haemorrhage using interdisciplinary biochemical, ‘omics, and cardiovascular biology approaches

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**Background:** Dengue is a growing health and economic concern in low- and mid-income countries, with the number of infections increasing each year and about half of the world population potentially at risk. The relatively rare but entirely unpredictable and potentially lethal bleeding complications pose extra strain on the health systems and affected families in these countries. Understanding the largely unknown mechanisms at the basis of dengue haemorrhagic disease is key to predict its emergence, provide adequate care and develop new drugs. Pericytes are important support cells that maintain the integrity of the vascular endothelium. These cells are implicated in a number of vascular leakage syndromes, including diabetic retinopathy, but their contribution to viral haemorrhage has not been investigated.

**Aims:** We aim to ascertain whether the pericytes are compromised by a dengue virus protein, NS1, which is released in the blood stream of infected people in large quantity and is already known to disrupt the lining of the blood vessels (endothelial cell layer), increasing its permeability. If NS1 does in fact disrupt the pericytes, as well as the endothelial cell layer, the effect on the vessel leakiness would be greatly amplified and would better explain the massive and sudden haemorrhage observed in these patients.

**Methods:** In this project, the student will investigate the role of syndecan-1 in this process by assessing the expression of this molecule in the NS1 treated endothelial cells and pericytes in vitro by immunocytochemistry and western blot and the effect of the co-culture of these cells on the endothelial expression of this protein. To do so, they will perform primary mammalian cell culture (single cell type and co-cultures), immunocytochemistry and western blot and functional assays (proliferation, apoptosis, migration).

**Clinical Perspective:** The elucidation of this mechanism might shed some light on the underpinning mechanisms associated with the natural repair machinery and help identify new interventions for patients affected by these diseases.