# PostDoc Job Opportunity

| DUBLIN CITY UNIVERSITY | First Name | Last Name | email | Institute | Address |
|---|---|---|---|---|---|
| PI name & contact details: | Paul | Cahill | paul.cahill@dcu.ie | DUBLIN CITY UNIVERSITY | Glasnevin, Dublin 9, Ireland. |
| School: | Biotechnology | | | | |
| Research Centre / group affiliation: | Vascular Biology & Therapeutics | | | | |
| Research group / centre website: | http://www.sfi.ie/assets/media/files/researcher_files/cahill_paul.pdf | | | | |

**Brief summary of research group / centre activity:**

The Vascular Biology & Therapeutics group at DCU both examine the putative role of key developmental gene regulatory networks in dictating resident vascular stem cell self-renewal and transition to vascular lineage and their ultimate contribution to vascular diseases and develop targeted strategies against these networks using magnetic nanoparticle drug delivery platforms for novel therapeutic delivery.

**Description of postdoctoral project on offer:**

**Title: Magnetic Nanoparticle delivery of novel therapeutics to bare metal stents for the treatment of in-stent restenosis.**

Restenosis is a major complication of coronary angioplasty, at least in part due to the fact that the origin of the vascular smooth muscle cells responsible for occlusion is somewhat controversial. Two important and distinct resident vacsular stem cell populations have recently been implicated in vascular disease progression in murine models and include Sca1 positive (Sca1+) adventitial progenitor cells (APC) that reside at the medial adventitial boundary, and myosin heavy chain (MHC) negative mesenchymal-like stem cells called multipotent vascular stem cells (MVSC) that reside in the tunica media. Both of these stem cell types proliferate and differentiate into vSMC that invade the intima in vascular injury models. Several factors have been described as positive and negative regulators of stem cell self-renewal, differentiation and growth, and these notably include the morphogen sonic hedgehog (Shh). Transient Shh activity promotes stem cell self-renewal in normal tissues, whereas continuous Shh activation is associated with the initiation of stem cell growth and differentiation of many types of cells. Of particular interest, we have shown that smooth muscle α-actin negative, Shh-positive cells that co-localize with the APC population at the medial-adventitial boundary of normal vessels only to later appear within the α−actin positive medial and intimal layers following injury. Hedgehog signaling is triggered by binding of the secreted Shh ligand with the transmembrane receptor Patched (Ptch) and is subsequently mediated by transcriptional effectors belonging to the Gli family. Components of the Hedgehog pathway are induced after vascular injury in vivo and a Hedgehog- Notch signaling axis controls vSMC growth and phenotype in vitro. Crucially, we have recently shown that inhibition of hedgehog signaling using Ptch1 siRNA in situ within the vessel wall attenuates intimal-medial thickening following iatrogenic injury.

This project will demonstrate the putative role of Hedgehog signaling components, notably ptch1 and Gli-target genes in controlling APC Sca1+ cell fate by demonstrating Hh control of their self-renewal

**Please indicate the core skills or disciplines that are required for this position:**

Stem Cell Biology – Isolation of embryonic and adult stem cells, iPS cells

Vascular Biology – Vascular stem and mural cell culture

Cell Biology – Protein expression, functional assays

Molecular Biology – Gene silencing, gene expression, miRNA's

Pharmacology – Pharmacokinetics/Pharmacodynamics

Nanomedicine – SEM, TEM, DLS analytical assays

Nanomaterials – Fabrication, characterisation