Metabolic Assessment of Therapies for the Development of Drug-Eluting Stents

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Drug-eluting stents (DES) have been associated with late-stent thrombosis and subacute-stent failure. The thrombosis related mortality rate urgently requires improved therapeutic options. These therapies are tasked to reduce neointimal hyperplasia whilst encouraging endothelialisation. This study assessed the metabolic activity of a number of different drugs with application in DESs.

Curcumin, ferulic acid, exendin-4, magnolol, everolimus and paclitaxel of varying concentrations (1-100µM, 0.5-500µM, 1-50nM, 3.75µM-375µM, 10-100µM, 1-100µM, respectively) were assessed upon dosing porcine coronary artery endothelial cells (PCAEC) and smooth muscle cells (PCASMC) and human coronary artery smooth muscle cells (HCASMCs) and umbilical vein endothelial cells (HUVECs). A metabolic activity assay (WST-8) was independently conducted upon 24, 48, 72 and 144h of treatment and was compared to untreated cells. Samples were studied in triplicates.

The metabolic activity indicated that curcumin and magnolol induced cytotoxic effects/reduced metabolic activity on ECs at the majority of concentrations. Curcumin at 1, 5 and 10µM caused a slight increase in metabolic activity on both SMCs. 5µM of ferulic acid boosted PCAEC metabolic activity and maintained SMC activity. Exendin-4 showed significant increase in metabolic activity of PCAECs and HUVECs at 144h, suggesting time dependant dosage. It was noted that ECs were more sensitive to commercially-used anti-proliferative controls (paclitaxel and everolimus).

This assessment demonstrated an initial judgement and promising strategy to identify ideal drugs for DESs. Certain concentrations for ferulic Acid and exendin-4 have shown ideal metabolic activities and will be subjected to further assessment, including their effect on cell metabolic activity and phenotype under dynamic flow conditions.