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The Generation of g-secretase Inhibitor-loaded PLGA-Fe3O4- Magnetic Nanoparticles

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Cardiovascular disease is the number one killer in Ireland and the wider EU. A hallmark of the disease is the obstruction to blood flow due to the build-up of vascular smooth muscle (SMCs)-like cells within the vessel wall. Treatment options include percutaneous transluminal coronary angioplasty (PTCA) and the insertion of a stent – a metal mesh tube – into the obstructed vessel to keep it open. However, the vessel can become re-occluded due to the accumulation of SMC-like cells within stented area. The introduction of the 1st generation drug-eluting stents (DES) has resulted in a paradigm shift for the treatment of in-stent restenosis with significant improvement in therapeutic outcomes. However, while polymer-coated DES have significantly reduced the incident of in-stent restenosis, current DESs lack the fundamental capacity for (i) adjustment of the drug dose and release kinetics and the (ii) ability to replenish the stent with a new drug on depletion. This limitation can be overcome by a strategy combining magnetic targeting via a uniform field-induced magnetization effect and a biocompatible magnetic nanoparticle (MNP) formulation designed for efficient entrapment and delivery of specific drugs that target the resident vascular stem cell source of the SMC.

Magnetic nanoparticles (MNP's) containing magnetite (Fe_3O_4) were fabricated, polymer coated with poly(DL-lactide- co-glycolide) polyvinyl alcohol [PLGA-PVA] and loaded with a-secretase inhibitor (GSI) of Notch signalling, DAPT using an oil in water emulsification technique. The free GSI's and GSI-loaded MNP's were assessed for drug release, the efficacy at controlling mesenchymal stem cell (MSC) growth (proliferation and apoptosis) and inhibiting myogenic differentiation under magnetic and non-magnetic conditions. The DAPT-loaded MNPs had an average hydrodynamic diameter of 351 d.nm Up to 40% of drug was released from MNPs within 48 h rising to 65% after 1 week under magnetic conditions. The Notch ligand, Jagged1 increased Hey1 mRNA levels and promoted myogenic differentiation of MSCs in vitro by increasing SMC differentiation markers, myosin heavy chain 11 (Myh11) and calponin1 (Cnn1) expression, respectively. This effect was significantly attenuated following treatment of cells with MNP's loaded with DAPT when compared to unloaded MNP's. Notch GSI loaded magnetic nanoparticles are functional at targeting vascular stem cells in vitro.

Biography:

-Roa Bashmail, Bsc. MS.Final year PhD student in the field of Biotechnology, previous qualifications in Master degree in the field of Anatomy and histology, Bachelor degree in Biochemistry.

-Excellent in culturing cells and in techniques like PCR,RNA isolation and Immunocytochemistry also good at the Flow Cytometer and High Performance Liquid Chromatography techniques.

-Excellent in socializing and good leader as well.

-Have won the award of best poster in Dublin City University in the Research day 2015 with title (**The Generation of g-secretase inhibitor-loaded PLGA-Fe_3O_4- Magnetic Nanoparticles).**