2016 Research Week Proposal Instructions and Template

Posters and Presentations

Title – Biodegradable Microcarriers for Drug Delivery

Program of Study – Biomedical Sciences, Department of Biology and Chemistry

Presentation Type – Print Poster

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Category – Choose one of the following: Experimental (Theoretical)

Microcarriers are microspheres ranging from a few nanometers to some hundreds of micrometers. One thousand nanometers equal one micrometer which is roughly half a millionth of an inch. The advantages of using polymeric microcarriers include biodegradability, low toxicity, and slow release. Microcarriers for drug delivery may be formed from two general classes of polymers: the first, polyesters such as poly(lactide-*co*-glycolide) (PLGA); then the second, polyolefins such as poly(meth)acrylates. PLGA microcarriers can successfully be synthesized through a double emulsion process using sonication. These polyesters degrade *in vivo* by hydrolysis of their ester backbone into nontoxic products, which are excreted by the kidneys. The ratio of lactide to glycolide in the PLGA polymers, the molecular weight and the terminal group of the PLGA polymer determine how fast drug release occurs. Carboxyl-terminated PLGA polymers offer faster drug release compared to ester-terminated PLGA. The following provides two literature examples of how microcarriers for drug release will work. The first example, published in 2015 [1], investigated the potential of PLGA based nanocarriers as a novel strategy to enhance penetration of therapeutic molecules into white blood cells

(macrophages) as a model for HIV infection. Following infection, HIV establishes reservoirs in macrophages that are inaccessible to optimal levels of antiviral drugs thus escaping the action of anti-HIV drugs; and thus may contribute to the rebound observed after antiretroviral treatment is stopped. To allow for more effective HIV treatment, stable polyester PLGA nanoparticles (NPs), about 180 nm in size, were prepared. Their capacity to transport an active molecule into the human macrophage cell line THP-1 using bovine serum albumin (BSA), a protein, as a proof-of-concept compound was evaluated. It was shown that encapsulation of BSA into PLGA NPs increased leukocyte infiltration *in vivo*, suggesting that enhanced delivery and protection of the protein by the polymer nanocarrier occurred. The second example, published in 2005 [2], describes the use of microparticles made from Eudragit P-4135F, a pH sensitive polyacrylate, for the purpose of treating inflammatory bowel disease (IBD). Adding FK506, an immunosuppressant, anti-inflammatory drug, to the microparticles provided efficient selective colonic drug delivery to the inflamed gut tissue. The selective delivery of the FK506 was shown to improve efficiency and tolerability in treating IBD. The important aspect of the study was that the FK506 loaded microparticles were administered orally as well as subcutaneously, to infected rats, resulting in a betterment in both cases. This shows a promise that oral administration may work as well as subcutaneous application. A major explanation for this occurrence is that the Eudragit P-4135F polymer protected the encapsulated FK506 from the acidity of the stomach acids while releasing at a neutral pH. *In vitro* studies of FK506 release from Eudragit P-4135F polymer microparticles confirmed that explanation. This proposal aims at exploring the aforementioned types of microparticles in support of a potential interdisciplinary project between the medical school, biology, and chemistry.

Christian worldview integration: The Christian Gospel is the message of "good news" for how God has reconciled his image bearers to himself by offering forgiveness through the life, death, and resurrection of Jesus Christ. Moreover, further pointing to the goodness of creation, in the incarnation of Jesus, the eternal Son of God became flesh. Those who are in Christ are to be working against the disorder that exists within the world. The benefits of polymeric nanoparticle medicine could change the view of medicine in third world countries, where medicine is expensive and scarce. The Bible tell us in Mark 16:15 to spread the gospel to the whole Earth. If a nanoparticle that can be developed, by Christian's, that can be administered to those who have HIV one will be able to save their life, and the gospel can be shared with them. Also, there is design in making the nanoparticles. There are many steps that are performed in making a nanoparticle. Each step has a defined purpose in accomplishing the task of helping the nanoparticle become biocompatible. An average human cell has a membrane that is both hydrophilic and hydrophobic. This concept has to be integrated into our nanoparticle. We will use certain polymers, like PLGA and Eudragit P-4135F, and proteins, like BSA, to create the hydrophobic and hydrophilic components. God has given us a model, the cell, and has shown us that we are able to replicate this idea into a new technique for medicine. It is incredible that something that is classified as "nonliving" can form into an intelligent design to help God's people.

References

[1] A.-S. Guedj, A. J. Kell, M. Barnes, S. Stals, D. Gonçalves, D. Girard, C. Lavigne. Preparation, characterization, and safety evaluation of poly(lactide-*co*-glycolide) nanoparticles for protein delivery into macrophages. *Int. J. Nanomedicine* **10**:5965-5979 (2015).

[2] A. Lamprecht, H. Yamamoto, N. Ulbrich, H. Takeuchi, P. Maincent, Y. Kawashima. FK506 Microparticles mitigate experimental colitis with minor renal calcineurin suppression. *Pharm. Res.* **22**:193-199 (2005).