



Precision Imaging Beacon of Excellence Studentship Form

Supervisors	Dr Luca Marciani (40%) Medicine / Nottingham Digestive Diseases Centre Dr Martin Garnett (15%) Dr P Gershkovich (15%) Dr S Stolnik (15%) School of Pharmacy Professor Robin Spiller (15%) Medicine / Nottingham Digestive Diseases Centre		
Start date	September 2018	Duration	3 years
Project	Impact of the colon environment on drug absorption from modified release oral formulations		
Abstract	<p>BACKGROUND: Orally administered modified release formulations can be designed to deliver the active pharmaceutical ingredient (drug) to specific regions of the gastrointestinal tract, particularly the colon. However, we propose that co-administration with agents that may modify colonic transit time and the fluid distribution in the colon (for example poorly absorbed sugar alcohols or bulking hydrogels) may affect significantly the formulation behaviour, drug release and absorption and, in turn, therapeutic effect.</p> <p>Developments in MRI imaging and recent applications to pharmaceutical sciences from our group are opening up the possibility to revolutionise knowledge of the impact of the gastrointestinal fluid distribution on drug dissolution and absorption profiles. This has great impact potential on bioequivalence studies and industrial practices, from drug design to drug absorption predictive modelling and the development of new drug formulations.</p> <p>PROJECT: In this PhD project we aim to undertake mechanistic studies using licenced modified release medicines (e.g. mesalamine, quinine), in conjunction with commonly used over the counter agents that modify the colon environment (e.g. mannitol, lactulose, ispaghula) and correlate the MRI insights on gut transit, volumes and intestinal water distribution with data on drug plasma concentration. We will apply pharmacokinetic analysis and, from deconvolution of oral plasma-concentration profiles, obtain and compare drug absorption profiles in different colon environment conditions. The absorption will furthermore be compared to drug permeability behaviour in an in vitro cell culture model, following a co-application with agents that modify the colon environment.</p> <p>CANDIDATE: The ideal candidate for this PhD project will be a student with an excellent background in pharmaceutical sciences and biopharmaceutics and some experience on physicochemical characterization of the lower intestine, including active pharmaceutical ingredients stability in the colonic environment.</p> <p>FIT WITH THE PRECISION IMAGING BEACON STUDENTSHIP PROGRAMME: New Cross Discipline: This studentship will seed a completely new cross disciplinary interaction at UoN, bridging areas of UoN expertise and excellence.</p> <p>Research Question: The effect of co-administration of common poorly absorbed sugar alcohols and bulking hydrogels on drug pharmacokinetic is poorly understood. Addressing this knowledge gap using imaging will improve formulation design and prediction of bioperformance with a direct effect on industrial practices and, ultimately, improved therapeutic effect for patients. This fits well with the Beacon themes of metabolic and physiological imaging</p>		

	<p>and effective translation, with aspects of prediction, mechanism evaluation and guidance for therapy.</p> <p>Strategic value: We have a rapidly growing imaging programme investigating the dissolution of immediate release drug formulations in the stomach and small bowel which has generated a recent FDA programme grant with the University of Michigan. This Precision Imaging Beacon studentship will not only enable us to develop the new relationship with the School of Pharmacy but also to be first to extend these studies to the modified release formulations and the colon, a vastly unexplored area with the potential to make us the world leading laboratory for these imaging studies, a genuine step change with further prestigious grant income downstream.</p> <p>Training: The supervisors here have proven successful track record of training postgraduate students. The student here will benefit from a comprehensive training package that fulfils exquisitely the added value of interdisciplinary strategic skills. The student will become comfortable working alongside colleagues from other disciplines; the links with Michigan will give an international dimension to the student's training. This experience will equip the student with an interdisciplinary core provision, cross-cutting from MRI, computing and image analysis to knowledge transfer, from regulatory matters to human research. He/she will be enrolled on the FHMS n-Trans PhD programme with additional computing, physics, pharmacy and MRI modules to provide a truly multi-disciplinary training and wide portfolio of cross-cutting skills. They will benefit from exposure to ongoing research projects and joining meetings and discussions. Our students are encouraged to present their work at international conferences and to write up their own work and submit it for publication as first authors at the earliest opportunity, with guidance and peer support from the team. This develops critical thinking and communication skills. This student will develop an outstanding and internationally competitive CV.</p>
Queries	Please contact PI-Beacon@nottingham.ac.uk
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