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Biofilm dispersing NO-donor Cephalosporins activated by β -Lactamase

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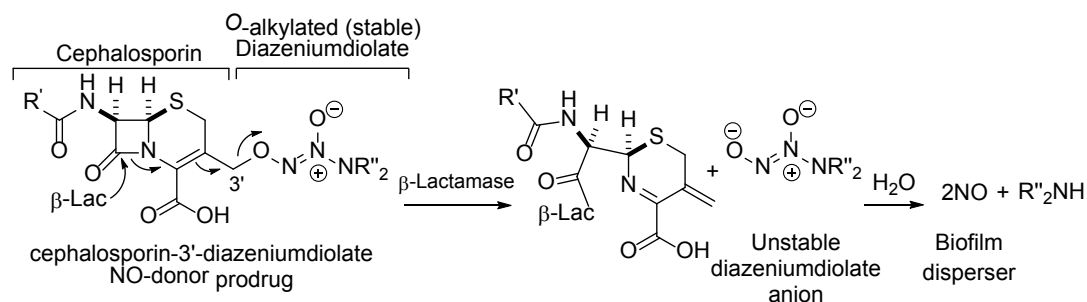
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Low concentrations of nitric oxide (NO) have been shown to act as a signal that induces biofilm bacteria to disperse and revert to the free-swimming (planktonic) form. This finding unveiled an exciting new anti-biofilm paradigm; i.e. use of NO-donor compounds in combination with antibiotics to clear chronic biofilm infections, since it is well-known that planktonic bacteria are up to 1000x more susceptible to antibiotics and host immune defences than their better-protected biofilm counterparts. Based on this discovery, we have designed, synthesized and provided in vitro proof-of-concept validation for a novel class of cephalosporin-based NO-donor prodrugs (DEA-CPs) that can provide biofilm-targeted NO delivery. The targeted NO signal from DEA-CPs (activated by β -lactamases) induces biofilms to disperse and when used in combination with clinical antibiotics the compounds are able to clear biofilms. The seminar will highlight key results in this area, including our latest efforts to translate DEA-CPs for use against chronic respiratory *P. aeruginosa* biofilms in cystic fibrosis patients.



Biography

Martin qualified in medicine from Newcastle University in 1982 and has worked as a GP since 1986. He obtained a Masters qualification in public health at Cambridge University in 1997. He has had a longstanding interest in applying evidence-based medicine to prescribing and therapeutics. He has previously worked for the National Prescribing Centre and the Department of Medicines Management at Keele University. From 1999, he has worked as a part-time GP in Conwy, North Wales, and initially worked as Medical Director for Conwy Local Health Board. Following the reorganisation of health services in Wales in 2009 he became Deputy then Acting Medical Director for the Health Board which manages all primary and secondary care NHS services in North Wales. He helped to organise and run the Diploma in Therapeutics at Cardiff University between 2005 and 2010. He chaired the New Medicines Group for Wales from inauguration in 2007 through to 2010. He is a Clinical Adviser on prescribing and evidence-based medicine for the Royal College of GPs, and is member of one of NICE's technology appraisal committees.

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