PACE Award Profile: Xiretsa

Progressing membrane-remodelling conjugated electrolytes as a novel class of antibiotic

Project title: Development of anti-infective conjugated electrolytes (ACEs) as a novel class of antibiotic

As bacteria develop resistance against existing antibiotics, it is becoming important to identify novel structural classes that act in new ways. Fulfilling these needs, Xiretsa has developed small molecules termed anti-infective conjugated electrolytes (ACEs), which have no structural similarity with other classes of antibiotics and are therefore unlikely to be affected by existing bacterial resistance mechanisms.

ACEs work by inducing membrane remodelling, which is known to be highly specific to bacteria, and has low susceptibility to resistance development. ACEs are also fast- and long-acting (aiding clinical deployment), have low cytotoxicity, do not cause hemolysis, and have activity against the biofilms that cause recurrent and difficult-to-treat infections.

Xiretsa has already undertaken structure-activity relationship studies, which laid the foundation for a partnership with the RTI Chemistry Center for Combating Antibiotic Resistant Bacteria – as part of which over 40 novel ACEs will be designed and synthesised. With funding and support from PACE, this project will be developed further. This will involve characterising these ACEs, designing and synthesising promising derivatives, assessing the *in vitro* and *in vivo* performance of three potential leads, and elucidating additional structure–activity relationships to aid lead optimisation.

Should this project be successful, it will deliver a new antibiotic that circumvents even the most resistant bacterial strains, such as those causing bloodstream and lower respiratory infections. Moreover, because of Xiretsa's focus on developing a fast-acting, long-acting antibiotic, the patient experience will also be improved, because infections will be resolved quickly, and the physical and mental stress caused by frequent hospital injections will be minimised.