Translation Medical Research Fund (TMRF)

The TMRF was used to link the strongest basic and clinical research across the University of Dundee (2011-2014). Funding was awarded on a competitive basis and 25 different projects have been supported including; Pump-priming (up to 20k) and Strategic projects (up to 100k), and translational medicine (non-clinical) PhD projects.

TMRF: Case Study (Pump-priming, £10k)

**Project Title** - Automation of a high-throughput MALDI TOF mass spectrometry drug discovery assay of deubiquitylase (DUB) inhibitors.

**Recipients** - Dr Matthias Trost (MRC PPU) and Dr David Gray (DDU).

Deubiquitylases (DUBs) are key regulators of the ubiquitin system which cleave ubiquitin moieties from proteins and polyubiquitin chains. DUBs have been implicated in a number of diseases including cancer and neurodegeneration, and due to their potentially druggable active sites, are considered attractive drug targets. The flexible funds awarded through TMRF enabled Dr Trost, in collaboration with Dr Gray, to facilitate the transfer of a manual screening protocol into a fully automated process quantifying in vitro DUB enzyme activity. The outputs of this work have recently been published in *Nature Communications* [Ritorto et al. (2014) Nature Comms 5:4763].

This robust high-throughput assay is now offered as a service to both academic collaborators and industrial partners, to either investigate specific compounds or entire compound libraries. Since the launch of the service in 2015, three academic and two industrial collaborations have been formed. A project, funded by MRC Technology attracting an inward investment of £100k, is about to commence screening a library of over 20,000 compounds. Furthermore, in collaboration with the Drug Discovery Unit, another project is in its initial stages to screen over 150,000 compounds against an important neurological target. Acquisition of the latest, state-of-the-art mass spectrometer, due to be installed Autumn 2015, will allow the screening assay to be 5x faster and enable the analysis of >10,000 compounds a day. An additional valuable output of this work is that it is anticipated that the knowledge gained from development of this assay will be applied to other enzyme activity assays and thus drive additional strategic projects forward.