CRUK Cambridge Centre MRes rotation project

Rotation Project Title (short please)	**Cellular roles of TCF25**
Head of Laboratory (PI) Name	Svetlana Khoronenkova
Second supervisor if applicable	Luca Pellegrini
Programme	Cellular and Molecular programme
Supervisor's Email	sk870@cam.ac.uk
Lab Location	*Department of Biochemistry, Tennis Court Road, Cambridge*

Project Outline	**Human cells repair thousands of DNA lesions each day, which arise from the intrinsic chemical instability of DNA and also environmental factors. If left unrepaired, lesions can interfere with DNA replication and gene transcription, leading to cell death, mutations and disease. Therefore, the efficient detection, signalling and repair of DNA lesions, collectively known as the DNA damage response, lie at the heart of genome stability and provides the first line of cellular defence against cancer and other diseases.** **Our laboratory is interested in identifying novel factors that are essential for the cell's ability to faithfully respond to DNA damage and facilitate its repair. We recently identified several novel factors of uncharacterized function that confer resistance to a variety of DNA damaging treatments. In this rotation project, we aim to unravel the cellular roles of TCF25, a predicted basic helix-loop-helix (bHLH) transcription factor, and its functions in the DNA damage response. Importantly, expression of *TCF25* is deregulated in many cancers including breast, ovary, and prostate.**
Experimental plan	**The aim of this rotation project is to investigate the transcriptional regulatory functions of TCF25 and the importance of its DNA damage-dependent control. To identify binding sites of TCF25 to chromatin, the applicant will optimise and utilise ChIP-seq (chromatin immunoprecipitation sequencing) of TCF25. Following bioinformatic analyses, the chromatin binding sites of TCF25 identified by ChIP-seq will be confirmed by quantitative RT-PCR (qRT-PCR). The effects of DNA damaging treatments on the chromatin binding activities and specificity of TCF25 will be assessed using microarray analyses and qRT-PCR.**
Main Techniques	The applicant will become proficient in several experimental techniques, develop critical scientific thinking and improve their writing and presentation skills. Techniques to be utilised include mammalian tissue culture, SDS-polyacrylamide gel electrophoresis and western blotting, RNA isolation, chromatin immunoprecipitation sequencing (ChIP-seq), quantitative real-time PCR (qRT-PCR) and microarray analyses.
Key References	1. Khoronenkova S & Dianov G (2015) ATM prevents DSB formation by coordinating SSB repair and cell cycle progression. *Proc Natl Acad Sc*i 112, 3997. 2. Khoronenkova S *et al.* (2012) ATM-dependent down-regulation of USP7/HAUSP by PPM1G activates p53 response to DNA damage. *Mol Cell* 45, 801.