*Deadline for application: 3rd January 2019*

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| **Division** | Cellular and Molecular Pathology |
| **Supervisor** | Paolo D'Avino |
| **Project title** | Characterization of the roles of PP1 phosphatases in cytokinesis |
| **Project abstract for advert**<br><br>(Max 100 words) | Cell division faithfully partitions the genomic information between the two daughter cells and errors in this process have been implicated in many human diseases. Most mitotic events are regulated by phosphorylation and, although mitotic kinases have been studied is some detail, very little is known about their counteracting phosphatases. We have recently characterised the protein interaction network in the last phase of mitosis, cytokinesis, and found that PP1 phosphatases were the most abundant and frequent. The aim of this project is to characterize the roles of these phosphatases during cytokinesis using a multi-systems approach combining gene editing, quantitative proteomics, and multi-dimensional high resolution microscopy. |
| **Full details**<br><br>(Max 250 words. Will be published on Departmental website; do not include confidential information) | Cell division faithfully partitions the genomic information between the two daughter cells and errors in this process have been implicated in many human diseases, such as chromosomal syndromes, sterility and cancer. Thus, a thorough understanding of the mechanisms controlling cell division may lead to the development of novel therapeutic treatments for these diseases. As the genome is compacted into chromosomes during mitosis, cell division events are regulated mainly through post-translational modifications (PTMs), such as ubiquitin-mediated protein degradation and phosphorylation/de-phosphorylation.<br><br>Although the identity and function of mitotic kinases have been studied is some detail, very little is known about their counteracting phosphatases. In a recent survey of the protein interaction network (i.e. interactome) in the last phase of mitosis, cytokinesis, we discovered that members of the PP1 family were the most abundant and frequent phosphatases of the interactome. The aim of this project is to characterise the function of these phosphatases using a multi-systems approach combining gene editing, quantitative proteomics, and multi-dimensional high resolution microscopy. We will generate by gene editing a collection of RPE-1 cell lines containing catalytic and regulatory PP1 subunit genes tagged with an auxin-inducible degron (AID) in tandem with GFP. We will then use these cell lines to analyse the dynamics of each PP1 subunit and to dissect their roles after AID-mediated depletion at specific mitotic stages. We will also use quantitative proteomics to identify their interactomes and to analyse changes in the cytokinesis phospho-proteome after targeted depletion of each subunit. |
| **Image(s) related to project**<br><br>(For use in adverts and on Departmental website) | |

**Department of Pathology fully-funded PhD studentships: project proposal form**

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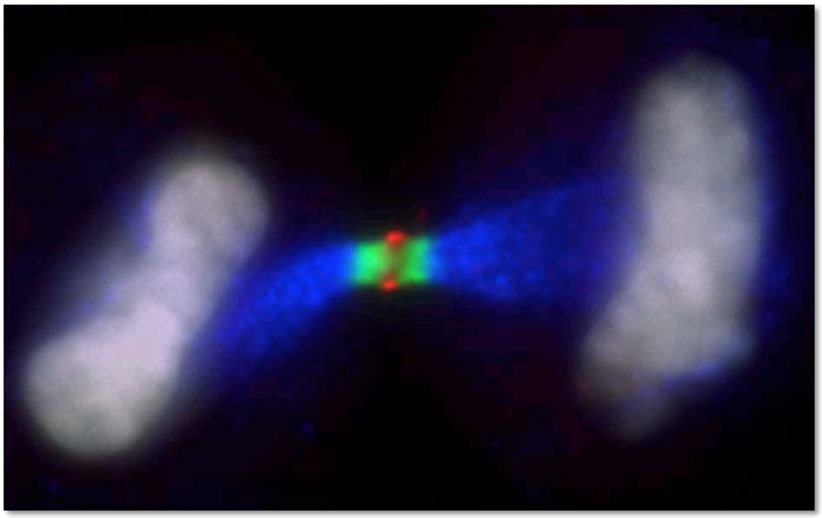
| |  |
| **5 recent publications** | • Bassi I.Z., Audusseau, M., Riparbelli, M.G., Callaini, G. and **D'Avino P.P**. (2013) Citron kinase controls a molecular network required for midbody formation in cytokinesis. ***Proceedings of the National Academy of Sciences USA***, 110(24):9782-9787.<br>• McKenzie C., Bassi I.Z., Debski J., Gottardo M., Callaini, G., Dadlez M. and **D'Avino P.P**. (2016) Cross-regulation between Aurora B and Citron kinase controls midbody architecture in cytokinesis. ***Open Biology***, 6: 160019 (doi: 10.1098/rsob.160019).<br>• Capalbo, L., Mela, I., Abad, M.A., Jeyaprakash A.A., Edwardson, J.M. and **D'Avino P.P.** (2016) Coordinated regulation of the ESCRT-III component CHMP4C by the chromosomal passenger complex and centralspindlin during cytokinesis. ***Open Biology,*** 6: 160248 (doi: 10.1098/rsob.160248)<br>• McKenzie, C. and **D'Avino P.P.** (2016) Investigating cytokinesis failure as a strategy in cancer therapy. ***Oncotarget***, 7(52):87323-87341 (doi: 10.18632/oncotarget.13556)<br>• **D'Avino P.P.** and Capalbo L. (2016) Regulation of midbody formation and function by mitotic kinases. ***Seminars in Cell and Developmental Biology***, 53:57-63.<br>• **D'Avino P.P.** (2017). Citron kinase - renaissance of a neglected mitotic kinase. **Journal of Cell Science,** 130(10): 1701-1708; doi: 10.1242/jcs.200253 |