Title of the project: **Mechanical activation of deleted in liver cancer (DLC1) molecule in cancer cells**

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Note:
Please check these links to understand the rationale behind this project:
https://www.youtube.com/watch?v=SAdEJkeQJws&feature=youtu.be
https://www.imperial.ac.uk/news/187473
http://biomechanicalregulation-lab.org/

Please contact supervisor to arrange a meeting to discuss the project in detail.

Project Description:

Cells attachment to the extracellular matrix (ECM) is mediated by macromolecular structures known as focal adhesion (FAs) complexes. The protein talin is a main player in FAs, and its interaction with other molecules orchestrates several cellular processes. Talin is strategically positioned in cells, it binds the cell membrane with the N-terminal head, and the actin cytoskeleton with the other end. As a consequence of this, during each cycle of acto-myosin contraction, the talin molecule is stretched and may expose previously cryptic sites to other molecules such as deleted in liver cancer of DLC1 (one of its ligands). We observed that when talin is stretched DLC1 is unbound and inactive and it leads to increase in traction forces and migration. This is important in the context of cancer cells because DLC1 controls migration and consequently invasion. We worked with fibroblast cells for our proof of concept (Haining et al PLoS Biology 2018).

Project aim:
To test if this mechanism (talin-DLC1 binding under mechanical stimulation) is present in cancer cells and how this may affect cancer cell invasive capacity.

Research plan:
There are alternatives research plans (tailored to the student's interest) to be discussed in the first one to one meeting with the PI.

Skills that students will develop during the project:
-Set of experimental techniques including: tissue culture (primary cells and cell lines), western blot, immunofluorescence, PCR, preparation of elastic pillars.
-Work in a team with strong disciplinary background
-Deliver research hypothesis and results in a sharp and concise manner
-Active participation in group meetings – development of strong analytical thinking
-Exposure to a wide variety of biophysical techniques highly demanded in the field of cancer biology

Key techniques: Mutagenesis, cell transfection, cellular adhesion experiments, immunostaining, elastic pillars.

Publications:

- Haining AWM, Rahikainen R, Cortes E, Lachowski D, Rice AJ, von Essen M, Hytönen VP, del Río Hernández A. Mechanotransduction in talin through the interaction of the R8 domain with DLC1. PLoS Biology 2018
- Haining AWM, von Essen M, Attwood SJ, Hytonen VP, del Río Hernández A. All subdomains of the talin rod are mechanically vulnerable and may contribute to cellular mechanosensing ACS Nano 2016
- Haining AWM, Lieberthal TJ, del Río Hernández A. Talin: a mechanosensitive molecule in health and disease. FASEB J 2016.

Lab website and other links:

https://www.youtube.com/watch?v=SAdEJkeQJws&feature=youtu.be

https://www.imperial.ac.uk/news/187473

http://biomechanicalregulation-lab.org/

It is highly recommended that students read the project information in the attached pdf with the embedded figures. The group will have a dedicated open day to address all questions about the available projects, the specific aims and methodologies. Please contact supervisor 1 to arrange details.