PI profile

## Ellie Tzima

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| https://www.well.ox.ac.uk/people/ellie-tzima/@@haiku.profiles.portrait/f93e28a49c2b423d9f7a7e7a4b1b7ffb/@@images/image/w1140?c33eac19-ba8e-4208-b18c-3da9f3093a56 | **Professor Ellie Tzima**  **Titles**: Professor of Cardiovascular Science, Senior Fellow, Group Leader / PI  **Location**: Henry Wellcome Building of Genomic Medicine  **Department**: Cardiovascular Medicine  **Group**: Vascular Mechanotransduction  **Webpage**: <https://www.well.ox.ac.uk/people/ellie-tzima>  **Email**: ellie@well.ox.ac.uk |

### GMS themes:

### Research Overview

From the moment the heart starts beating, endothelial cells that line blood vessels are subjected to haemodynamic (or mechanical) forces due to blood flow. Mechanical forces are crucial not only for normal development of the embryonic heart and vascular system, but also play an important role in maintaining homeostasis on the adult organism. Mechanical forces, however, can also be instigators of vascular pathologies, such as atherosclerosis. Our research focuses on the role of mechanotransduction in regulating cardiovascular function in health and disease. We use a multi-disciplinary approach that includes expertise in bioengineering, molecular and cell biology and physiology to understand mechanisms of mechanotransduction. The aim is not only to understand at a fundamental level how cells sense mechanical force and transduce it into biochemical signalling, but also to identify the molecular mechanisms by which mechanical forces regulate cardiac and vessel function. This should facilitate development of therapeutics that ultimately promote beneficial signalling or disrupt pathological responses. We have recently identified a pathway by which endothelial cells sense and respond to blood flow (Mehta et al, Nature 2020; Mehta et al, Science Advances 2021) that dictates development of atherosclerosis and cardiovascular disease. We plan to extend these studies to understand the molecular mechanisms responsible using a combination of in vitro and in vivo approaches.

Project areas: cardiovascular science and molecular, cell & systems biology, mechanotransduction, shear stress, cardiovascular disease, endothelium, intercellular junctions, integrins, PECAM, Rho GTPases, tRNA synthetases, protein translation, redox signaling, angiogenesis, vascular remodeling and myocardial infarction.

### Specific project proposals:

Please contact directly for further information.

*These pages were reviewed/updated:* ***10/06/2022***

Project proposal

# **Title**: How do cells respond to mechanical forces?

Supervisors: Professor Ellie Tzima, Professor John Reader, Dr Vedanta Mehta

Wet/dry lab mix (approx): 80% wet/ 20% dry

### Description:

Cells are constantly exposed to forces that dictate their function. In blood vessels, endothelial cells that line arteries are exposed to forces due to flowing blood; these forces are critical determinants of their physiologial functions but can also instigate development of diseases, such as atherosclerotic plaques and cardiovascular disease. The mechanisms by which cells sense and respond to mechanical forces is a mystery in biology and has implications in a number of diseases, including cancer, immune cell dysfunctions and neurobiology. We have bespoke in vitro systems that allow us to apply different forces on cultured cells and complement these studies with transgenic mouse models in vivo. We generate large datasets from RNA sequencing and proteomics with the ultimate goal of understanding at the genetic, molecular and physiological level how cells respond to forces.

### Training Opportunities:

The DPhil will be based at the Wellcome Centre for Human Genetics. The student will get to experience and learn a wide array of *in vitro* and in *vivo* techniques. These include cell culture, transfections, western blotting, co-immunoprecipitation, qPCR, dissection of animal tissue, staining, confocal microscopy and analysis of RNA sequencing and mass spec proteomic data. Training in scientific writing and presentation skills will be provided, and writing of reviews and presentation at conferences will be strongly encouraged.

### Background reading / references:

Please include references as desired. Suggested format:

* 1 Mehta, V. *et al.* Mechanical forces regulate endothelial-to-mesenchymal transition and atherosclerosis via an Alk5-Shc mechanotransduction pathway. *Sci Adv* **7**, doi:10.1126/sciadv.abg5060 (2021).
* 2 Sweet, D. T. *et al.* Endothelial Shc regulates arteriogenesis through dual control of arterial specification and inflammation via the notch and nuclear factor-kappa-light-chain-enhancer of activated B-cell pathways. *Circ Res* **113**, 32-39, doi:10.1161/CIRCRESAHA.113.301407 (2013).
* 3 Liu, Y., Sweet, D. T., Irani-Tehrani, M., Maeda, N. & Tzima, E. Shc coordinates signals from intercellular junctions and integrins to regulate flow-induced inflammation. *J Cell Biol* **182**, 185-196, doi:10.1083/jcb.200709176 (2008).