

FIRST PERSON

First person – Yihua Wang

First Person is a series of interviews with the first authors of a selection of papers published in Journal of Cell Science, helping early-career researchers promote themselves alongside their papers. Yihua Wang is the first author on 'Nuclear entry and export of FIH are mediated by HIF1 α and exportin1, respectively', published in Journal of Cell Science. Yihua is a Lecturer in Biological Sciences at the University of Southampton, studying cell signalling in lung fibrosis and cancer, drug target validation and gene function analysis.

How would you explain the main findings of your paper in lay terms?

Animals need oxygen for life and face the challenge of supplying enough oxygen to the organs and tissues that are using it. Cancers also require oxygen and when solid tumours grow, demand for oxygen is often greater than the supply; as a consequence, oxygen decreases to very low levels, which is termed hypoxia. Hypoxia triggers responses in cells and tissues that aim to increase oxygen supply, for example, increased blood flow. But how is hypoxia sensed inside cells? The hypoxia-inducible factors (HIFs) are key regulators for coordinating cellular responses to hypoxia. When oxygen levels are normal, the transcriptional activity of HIF is inhibited by an enzyme called factor inhibiting HIF (FIH), which is a protein hydroxylase. However, when oxygen levels are low, HIF is not inhibited by FIH and triggers the hypoxic response. This study aimed to understand more about the regulation of HIF by FIH, in particular the effect of the location of FIH within the cell. We report that FIH accumulates in the nucleus for a short time soon after hypoxia treatment. This is relevant because this is the cellular compartment where HIF is located. The results shown in this study rationalize why several earlier studies failed to detect nuclear FIH under hypoxia, since the narrow window of the nuclear impact of FIH may have been missed. The results also potentially explain why, despite FIH being largely a cytoplasmic protein in cells grown in normal oxygen levels, it has sometimes been observed in the nucleus in diseased tissues.

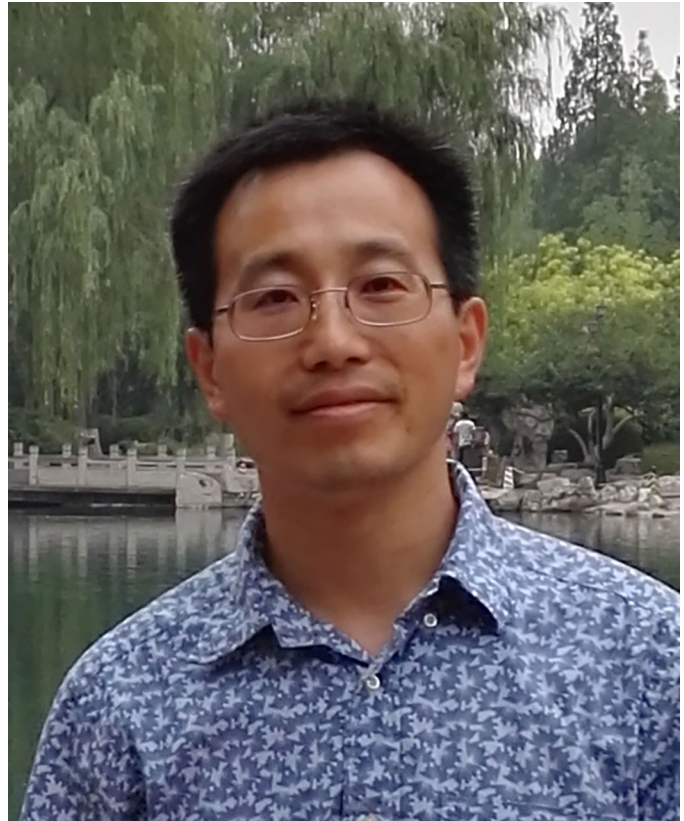
Were there any specific challenges associated with this project? If so, how did you overcome them?

An ongoing challenge we have had during this project was to understand the importance of cytoplasmic and nuclear FIH localization in terms of its biological function. Whether nuclear FIH causes or is simply associated with pathological conditions remains to be explored.

Why did you choose Journal of Cell Science for your paper?

Journal of Cell Science is a high-quality journal with a strong reputation in cell biology, and the review process is quick and fair. Also, by choosing JCS, we're hoping to share our research far and wide.

Yihua Wang's contact details: Biological Sciences, Faculty of Environmental and Life Sciences, University of Southampton, Southampton SO17 1BJ, UK.
E-mail: yihua.wang@soton.ac.uk



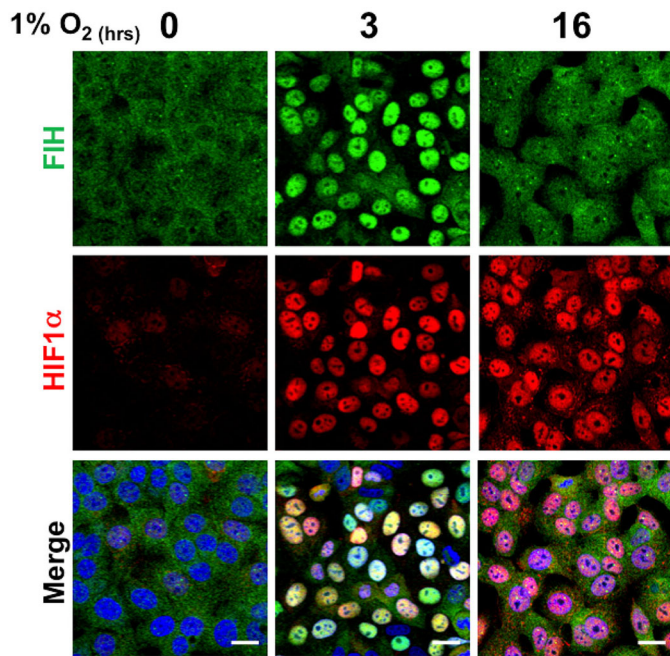
Yihua Wang

Have you had any significant mentors who have helped you beyond supervision in the lab?

I have been very lucky to have several great mentors and I am very grateful for their support. My PhD advisor Prof. Ningzhi Xu let me develop my own projects and trained me to complete them independently. My postdoc mentors Prof. Julian Downward and Prof. Xin Lu helped me further improve my ability to be an independent scientist and explore different opportunities outside the lab. I was fortunate enough to have the support from Prof. Sir Peter Ratcliffe and Prof. Chris Schofield. Their great expertise in the field of hypoxia and scientific rigor have created an invaluable environment to complete this project. I also appreciate the mentorship provided by Prof. Donna Davies, who introduced me to the idiopathic pulmonary fibrosis (IPF) field.

What's next for you?

As a relatively new recruit to Southampton, I sought to identify research links in areas of strategic importance to the University and I recognised that lung diseases offered me this opportunity. Seeking to make my current work distinct and competitive, it was immediately clear that my skills and experience were highly relevant to research on non-malignant lung disease, especially IPF, which has a prognosis worse than many cancers. Now, this allows me to connect with Southampton's internationally recognised research in respiratory disease and to rapidly establish a distinct



Immunofluorescence studies showing a striking change in FIH localization on hypoxia treatment. Clear nuclear accumulation of FIH was observed after 3 h in hypoxia, but nuclear FIH was greatly reduced after 16 h in hypoxia.

niche for myself at the University of Southampton. With the support from an Academy of Medical Sciences Springboard Award, I am now investigating the role of FIH in the development of IPF.

Reference

Wang, Y., Zhong, S., Schofield, C. J., Ratcliffe, P. J. and Lu, X. (2018) Nuclear entry and export of FIH are mediated by HIF1 α and exportin1 respectively. *J. Cell Sci.* **131**, jcs219782.