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JCS PRIZE

2018 Winner: Samantha Stehbens

Michael Way (Editor-in-Chief)

We are pleased to announce that the winner of the 2018 JCS Prize is Samantha Stehbens for her paper entitled 'FGFR2-activating mutations disrupt cell polarity to potentiate migration and invasion in endometrial cancer' (Stehbens et al., 2018).

The prize, $1000, is awarded annually to the first author of the paper that is judged by the Editors and Editorial Board to be the best eligible paper published in the Journal of Cell Science that year.

Samantha Stehbens is a cell biologist dissecting the molecular mechanisms of cell motility using high-resolution, quantitative microscopy. Born and raised in Queensland, Australia, she did her graduate studies under Prof. Alpha Yap, at the University of Queensland's Institute for Molecular Bioscience. It had long been recognized that cadherins function in close cooperation with the cytoskeleton, particularly with actin. Less appreciated was the capacity for cadherins to also interact with microtubules and their associated proteins. Samantha's graduate work defined how microtubules target cadherin-based cell–cell adhesions to regulate cortical actomyosin contractility through the GTPase Rho, to reinforce cell–cell junctions (Stehbens et al., 2006). As microtubules had previously been implicated in the delivery of Rho-GEFs to the cortex, she then systematically screened for junctional Rho-GEFs that depend on dynamic microtubules, identifying the cytokinetic GEF Ect2. This was the first identification of a non-mitotic role of the centralspindlin complex, which is mostly studied in the context of cytokinesis (Ratheesh et al., 2012). During this period, Samantha discovered her love of microscopy and what one can learn about biology, simply from watching.

In 2009, she relocated to The University of California San Francisco, to work with Prof. Torsten Wittmann. This move was strategic, allowing her to develop knowledge of high-resolution microscopy techniques and microscope hardware. When she joined the lab, Torsten presented her with the observation that the microtubule +TIP CLASP that, specifically, decorates microtubule clusters around focal adhesions at the leading edge of migrating HaCaT keratinocytes. Although it was well established that microtubules target focal adhesions and mediate their disassembly, the molecular mechanisms remained elusive. Together they identified that microtubule-dependent targeting and tethering at focal adhesions is mediated through CLASPs to induce adhesion turnover, and establish local exocytosis of MT1-MMP to degrade matrix during cell migration. Microtubules deliver MMPs then act locally to cut cell-matrix attachments, initiating focal adhesion disassembly from the outside-in (Stehbens et al., 2014). This work combined the application of quantitative live-cell protein dynamics by using both spinning disc confocal and TIRF-M (Total Internal Reflection Microscopy) and the new super-resolution imaging technique scanning angle interference microscopy (SAIM), in collaboration with Matthew Paszek, then a postdoc in the lab of Valerie Weaver. While at UCSF she was able to collaborate with spanning fields from ion channels in the brain to autophagy in breast cancer, highlighting the breadth of application and the impact of using microscopy in order to understand complex biology processes.

Inspired by the potential in using quantitative imaging methods to better understand mechanisms of tumour cell growth and invasion, Samantha purposely directed the next phase of her post-doctoral training towards understanding models of cancer cell biology. To

achieve this, she joined Prof. Pamela Pollock's laboratory at the newly opened Translational Research Institute in Woolloongabba, Australia. Prof. Pollock had discovered a subset of endometrial (uterine) cancer patients, who have activating mutations in FGFR2b, and wanted to investigate why these patients showed poorer cancer survival than those lacking the mutation. Following the installation of a custom-designed spinning disc confocal microscope, based on the instrument she used at UCSF, Samantha combined 2D and 3D acini models, and discovered that FGFR-activating mutations results in a loss of cell polarity, potentiating migration and invasion (Stehbens et al., 2018). Her findings suggest that micro metastatic disease can be present at the time of tumour resection and that these patients may benefit from FGFR inhibitors as an adjuvant therapy. Samantha was recently recruited back to the University of Queensland to the Diamantina Institute, to work with Prof. Nikolas Haass, a clinician researcher who uses 3D models to understand melanoma heterogeneity. With a focus on the regulation of mechanochemical processes that control microtubules, Samantha aims to explore how a cell integrates biomechanical signals to change its shape in order to move within a fluctuating environment and exploits this to become metastatic.

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