DMM Prize 2018 winner: Wenqing Zhou

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Disease Models & Mechanisms (DMM) is delighted to announce that the winner of the DMM Prize 2018 is Wenqing Zhou, for her paper entitled ‘Neutrophil-specific knockout demonstrates a role for mitochondria in regulating neutrophil motility in zebrafish’ (Zhou et al., 2018a). The prize of $1000 is awarded to the first author of the paper that is judged by the journal’s editors to be the most outstanding contribution to the journal that year. To be considered for the prize, the first author must be a student or a postdoc of no more than 5 years standing.

Outstanding contribution

Wenqing Zhou grew up in a small town in South Central China and received her bachelor’s degree in biotechnology from Central South University, China. In the third year of undergraduate study, she joined Dr Xueduan Liu’s lab, where she learned to isolate bacterial strains from the environment and utilize those strains to increase the metal extraction efficiency from mineral. During that time, she was deeply attracted by those ‘tiny but magic microbes’.

After graduation, in 2011, Wenqing joined the master’s program at the Institute of Microbiology, Chinese Academy of Sciences, and began to study the antibiotic resistance of pathogens with the guidance of Dr Jie Feng. Streptococcus pneumoniae, one of the most common pathogens in the respiratory tract, is widely resistant to macrolide antibiotics because of the dissemination of transposon Tn2010, which carries two different macrolide-resistance genes. She identified that transformation is the predominant way to transfer Tn2010 between S. pneumoniae, and that the acquisition of Tn2010 has a negligible fitness cost, which may explain the widespread distribution of the transposon (Zhou et al., 2014).

The experience in Dr Feng’s lab made her understand what research is, and she really enjoyed the process, so she decided to pursue an academic career. After graduation, she began her PhD under the direction of Dr Qing Deng at Purdue University, IN, USA, in 2014. In Dr Deng’s lab, her first project was to determine the role of microRNA in the response of neutrophils to inflammation. She identified that miR-223 in epithelial cells regulates neutrophilic inflammation. miR-223 is known as a myeloid-enriched microRNA, and its expression is highest in neutrophils. However, she found that the augmented neutrophilic inflammation in miR-223-deficient zebrafish is mainly due to the over-activation of NF-κB in the basal layer of the surface epithelium. The intrinsic regulation of NF-κB in epithelial cells by miR-223 was further confirmed in human cells. This work provided a direct connection between miR-223 and the canonical NF-κB pathway, and highlighted an overlooked relevance of epithelial cells in dampening neutrophil activation (Zhou et al., 2018b).

Neutrophils are fast-moving cells and primarily rely on glycolysis for adenosine triphosphate (ATP) availability. Whether mitochondria regulate neutrophil motility in vivo remained obscure. Wenqing’s second project focused on mitochondria and neutrophil migration. She optimized the original method developed by Dr Len Zon’s group (Ablain et al., 2015) and established a gateway system harboring the CRISPR/Cas9 elements for tissue-specific knockout to disrupt mitochondrial function genetically in zebrafish (Zhou et al., 2018a). With this system, she found that neutrophil-specific disruption of mitochondrial DNA polymerase, polg, significantly reduces the velocity of neutrophil interstitial migration. In addition,
inhibiting the mitochondrial electron transport chain or the enzymes that reduce mitochondrial reactive oxygen species (ROS) also inhibited neutrophil motility. Furthermore, the research demonstrated that the reduced cell motility resulting from neutrophil-specific knockout of sod1 mRNA overexpression or by treating with scavengers of ROS. Together, their work established the first in vivo evidence that mitochondria regulate neutrophil motility, and provided insights into immune deficiency seen in patients with primary mitochondrial disorders. Technically, the group has used the tissue-specific-knockout approach to discover the function of genes, especially those that are developmentally essential, in neutrophils. This is the first successful example of using this technique to make scientific discoveries. They have further demonstrated the specificity of the knockout by mRNA and chemical rescue (Zhou et al., 2018a).

Currently, Wenqing is characterizing the stable zebrafish lines that she generated with neutrophil-specific knockout, and trying to provide a full understanding of the pathway regulated by mitochondria in neutrophil migration. She will finish her PhD work in the spring of 2019 and start to look for a postdoctoral position.

References


