Insights into macrophage migration in tuberculosis from the zebrafish

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Award: Pioneer Award
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We have developed the zebrafish as a facile, genetically tractable and optically transparent model for the study of host-pathogen interactions in tuberculosis. The ability to observe in unprecedented detail the steps of tuberculosis in a single animal and to perturb these through genetic manipulation has proved to be powerful. We have had surprising insights that suggest entirely new approaches to TB treatment, which are now in clinical studies. I will focus on the very earliest steps of the host-pathogen interface when mycobacteria first infect the host. Our findings suggest that they manipulate host macrophage migration so as to avoid microbicidal macrophages and instead use permissive macrophages to traverse host epithelial barriers. We have uncovered the details of these host evasion strategies and their mechanism which I will present. These findings provide an explanation for longstanding observations about human TB that have been puzzling.