Coming Events

Due to COVID-19, please check to see if the listed events have been postponed or canceled.

2022

Imaging, Diffraction and Crystallography – Where John Spence's Legacy Leads Us
October 11–13, 2022
Tempe, AZ
phy.asu.edu/spencesymp

XVI CIASEM Congress: 16th Inter-American Congress on Microscopy
October 25–28, 2022
Oaxaca, Mexico and Virtual
ciasem2022.com

Neuroscience 2022
November 12–16, 2022
San Diego, CA
www.sfn.org/meetings/neuroscience-2022

2022 MRS Fall Meeting
November 27–December 2, 2022
Boston, MA
and
December 6–8, 2022
Virtual
mrs.org/meetings-events/fall-meetings-exhibits/2022-mrs-fall-meeting-exhibit

Cell Bio 2022
December 3–7, 2022
Washington, DC
www.ascb.org/cellbio2022

2023

2023 MRS Spring Meeting & Exhibit
April 10–14, 2023
San Francisco, CA
mrs.org/meetings-events/spring-meetings-exhibits/2023-mrs-spring-meeting

IUMAS-8: 8th Meeting of the International Union of Microbeam Analysis Societies
June 11–16, 2023
Banff, Alberta, Canada
iumas8.wixsite.com/iumas8/events/8th-meeting-of-the-international-union-of-microbeam-analysis-societies

Microscopy & Microanalysis 2023
July 24–28, 2023
Minneapolis, MN
www.microscopy.org/events/future.cfm

2024

Microscopy & Microanalysis 2024
July 28–August 1, 2024
Cleveland, OH
www.microscopy.org/events/future.cfm

Carmichael's Concise Review

Migrating Into a Cell-Dense Tissue

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Cell dissemination into tissues is fundamental for the formation and maintenance of complex organisms. Frequently, migrating cells find the path of least resistance through the extracellular matrix (ECM). Migration through pores and tracks in the ECM has been well studied, but migrating cells also move into and through confining cell-dense tissues, a process that is not well understood. Recently this important aspect of cell migration was studied by an international team lead by Daria Siekhaus. The first author was Maria Akhmanova.

Examples of cell migration through cell-dense environments include neural crest cells moving into tissues during vertebrate development to form different tissue types, immune cells entering organs to regulate tissue function and combat infection, and cancer cells traversing into other organs during metastasis. To study this aspect of cell migration, Akhmanova et al. used early *Drosophila* development as a model system. Specifically, they examined when macrophages follow guidance cues and invade the cells destined to give rise to the embryo (the germ band, GB) at an entry point between the basal side of the ectoderm and the mesodermal surface (Figure 1). During this invasion, macrophages move as a chain and maintain the separation of the ectoderm and mesoderm established by the pioneer cell. Although integrins and other factors are involved, how the dynamic properties of surrounding cells influence macrophage tissue invasion remains unclear.

Akhmanova et al. tracked macrophage nuclei, the stiffest of the organelles. As the first macrophage invaded, one or two ectodermal cells adjacent to the entry point became round, indicating that mitosis of those cells was beginning. In some cases, two connected smaller, rounded daughter cells had already formed. Further study showed that macrophage entry always occurred during the division or rounding of a flanking ectodermal cell. The fact that macrophages enter the GB tissue only when an adjacent ectodermal cell is dividing suggested that this is a permissive event.

Next, they examined whether ectodermal division is required for macrophage entry. Upon pharmacological inhibition of cell division, macrophages did not invade

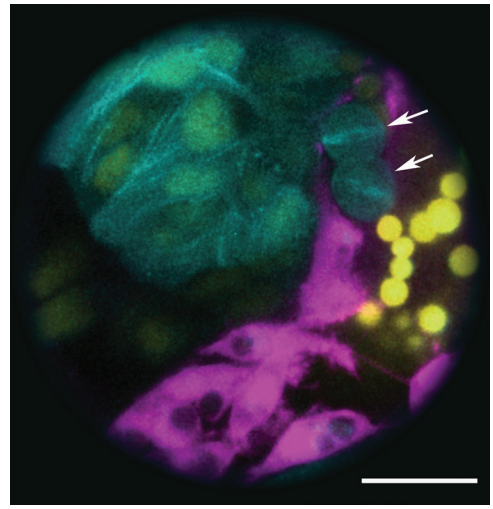

Figure 1: Macrophages (magenta) invade into cell-packed tissue (cyan) in the *Drosophila* embryo next to the rounded dividing cells (arrows). Invasion requires division of a germ band cell at the invasion site because it releases adhesion between cells, allowing the first macrophage to penetrate in between cells. Scale bar = 20 μm.

doi:10.1017/S1551929522001031

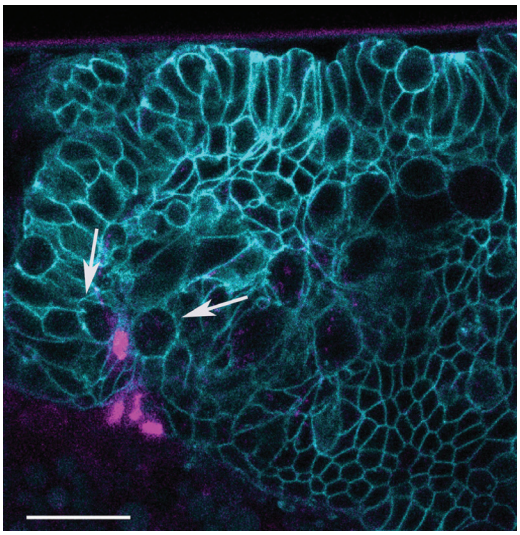

Figure 2: Macrophages (magenta) invade into cell-packed tissue (cyan) in the *Drosophila* embryo next to the dividing cells (arrows), which have a round shape. Invasion requires division of a tissue cell at the invasion site, which "opens the door" for the first macrophage to enter. Scale bar = 20 µm.

at all, or they entered next to the few remaining ectodermal cells that rounded as if they were going to divide. These results were confirmed by RNA interference (RNAi) to knockdown division just in the ectodermal cells. These and other results strongly suggest that the timing of ectodermal cell division is a rate-limiting factor for macrophage invasion.

The basal side of the ectoderm is adjacent to the mesoderm. Akhmanova et al. showed that focal adhesions (FA) formed by integrins are located at this interface and that they could impede macrophage entry. They used markers for FA to examine the temporal and spatial dynamics of FA in the GB. A series of experiments lead to the conclusion that FA disassembly at the entry point correlates with the penetration of the macrophage between the tissues. Further RNAi knockdown studies revealed that disassembly of the FA during mitosis is the main mechanism by which cell division "opens the door" for macrophage infiltration (Figure 2).

Akhmanova et al. appear to have demonstrated conclusively that ectodermal cell division is the crucial variable affecting the rate of entry of the first *Drosophila* macrophage into the GB and that other macrophages follow. Their finding suggests that regulation of division during development, inflammation, or tumor growth could affect the number and placement of immune cells in tissues in a wide range of normal and disease states.

References

[1] M Akhmanova et al., *Science* 376 (2022) https://doi.org/10.1126/science.abj0425.

[2] This is a link to a clever claymation animation that illustrates the concepts presented in this publication: https://www.youtube.com/watch?v=zwoD6Ns-amc.

[3] The author gratefully acknowledges Drs. Maria Akhmanova and Daria Siekhaus for reviewing this article.

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