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Chemokine signaling mechanisms underlying inflammation and infection control: Insights from the zebrafish model

Sommer, F.

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Author: Sommer, F.
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Propositions

accompanying the dissertation

Chemokine signaling mechanisms underlying inflammation and infection control: insights from the zebrafish model

1. The antagonistic interplay between an atypical chemokine receptor (ACKR) and a conventional receptor of the CXCR3 family modulates macrophage motility during the inflammatory response in zebrafish (**Chapter 2**).

2. The disruption of the CXCR3 signaling axis augments the bactericidal properties of lysosomes and alters intracellular vesicle trafficking dynamics preventing cell polarization during chemotaxis (**Chapter 3**).

3. Despite the extensive duplication of chemokine receptors in teleosts, ligand recognition by CCR2 and CXCR3 and the resulting macrophage responses are remarkably conserved between humans and zebrafish (**Chapter 4**).

4. The chemokine receptors CCR2 and CXCR3 work together to drive macrophage recruitment and represent attractive targets for anti-inflammatory drugs (**Chapters 2 and 4**).

5. The function of a chemokine receptor is always context dependent.

6. Elucidating the mechanisms underlying regulatory functions of the insufficiently studied ACKRs will deeply change our understanding of the chemokine system.

7. The interplay between chemotactic signaling and the endosomal-lysosomal system has critical roles in immunity, development, and cell metabolism that are just beginning to be understood.

8. The combination of *in vivo* and *in vitro* analyses in model organisms is a powerful way to pinpoint receptor-ligand pairs and establish true homologies with human chemokine systems supporting translational research.

9. We say we use zebrafish to study diseases although, strictly speaking, we should say that we are studying pathologies.

10. Communicating with the public is scientists' social obligation and one of the most important contributions of science to society.

11. The scientific community is well aware of the Impostor Syndrome but too little attention is put on the Dunning-Kruger Effect.

12. It is possible to succeed without merit. We should praise merit, not success.

Leiden, 15 October 2020