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Universiteit Leiden



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Title: Regulatory mechanisms of innate immune signaling in zebrafish embryos

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Stellingen

Behorende bij het proefschrift

Regulatory mechanisms of innate immune signaling in zebrafish embryos

1. Ptpn6 functions as a negative regulator in innate immune responses of zebrafish embryos (Chapter 2 & 3).
2. A proper function of negative regulators in the immune system is indispensable for an effective immune response against bacterial pathogens (Chapter 2).
3. During the process of mycobacterial granuloma formation in zebrafish embryos, infected macrophages undergo a major reprogramming of their cellular identity accompanied by a loss of typical macrophage marker gene expression (Chapter 3).
4. Increased granuloma formation during mycobacterium infection of *ptpn6*-deficient zebrafish embryos is primarily due to increased expression of matrix metalloproteinase genes (Chapter 3).
5. Knockdown of the infection-inducible microRNA-146 in zebrafish embryos does not have a major impact on pro-inflammatory gene expression, but suggest a function for this microRNA in regulating lipid metabolism during inflammation (Chapter 4).
6. Simultaneous analysis of host and pathogen by dual RNA-Seq is the next challenge in transcriptomics with great potential to increase understanding of the molecular mechanisms underlying infectious diseases. (Westermann et al., 2012, Nature Reviews Microbiology)
7. The wide clinical use of glucocorticoids as anti-inflammatory drugs warrants further research into their possible pro-inflammatory side effects in particular patient groups.
8. The mechanisms underlying the pathologies of autoimmune and inflammatory diseases are likely to be linked to dysregulation of microRNAs, since the majority of innate immune genes are predicted to be regulated by microRNAs and since many of these microRNAs show altered expression in patient materials. (O'Neill et al., 2011, Nature Reviews Immunology).
9. The innate immune system plays a bigger role in autoimmune and autoinflammatory diseases than previously thought. (Beutler 2009, Immunology Reviews).
10. Convincing people to use the zebrafish as a laboratory animal can be more challenging in the countries where zebrafish originates from than anywhere else.
11. If you succeed in extracting RNA on your first day in the lab, you can have a molecular biology career.
12. It is better to know some of the questions than all of the answers.

Zakia Kanwal
Leiden, December 12, 2012