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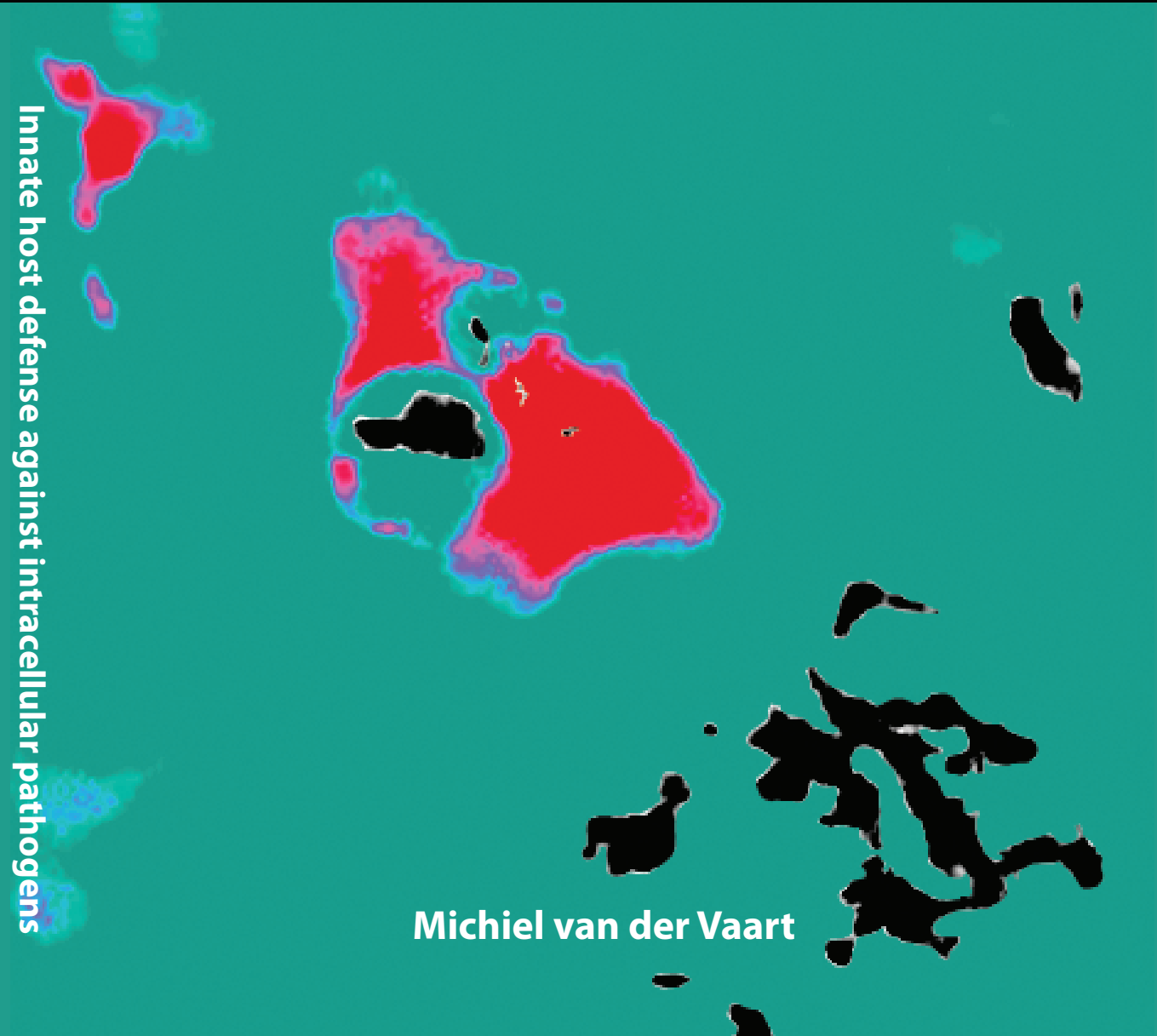
Michiel van der Vaart

Innate host defense against intracellular pathogens

Innate host defense against intracellular pathogens

This thesis focuses on the recognition of pathogenic bacteria and the defense mechanisms that are activated during the innate immune response to infection. Detection of pathogens, such as bacteria, viruses, and parasites, depends on receptors that bind to evolutionary conserved structures on their surface. The most extensively studied class of immune receptors is the Toll-like receptor (**TLR**) family, which signals via adaptor molecules such as myeloid differentiation factor 88 (**MyD88**) to initiate gene expression and activate the appropriate response upon recognition of a pathogen. We have used the zebrafish as a model organism to study how MyD88 orchestrates the immune response against intracellular bacterial pathogens like *Mycobacterium marinum*, the causative agent of tuberculosis disease (**TB**) in fish. We found that several defense mechanisms against TB are highly dependent on MyD88, including **autophagy**, cytokine and chemokine production, and the generation of microbe killing radicals. These findings in the zebrafish model will hopefully aid in the development of new therapeutic strategies against multi-drug resistant tuberculosis infections.

Innate host defense against intracellular pathogens



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