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**Title:** Exploitation of host chemokine signalling by pathogenic mycobacteria

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## Stellingen

Behorende bij het proefschrift:

“Exploitation of host chemokine signalling by pathogenic mycobacteria”

1. Pathogenic mycobacteria actively manipulate macrophage chemotaxis to maintain a continuous traffic of “ready-to-be-parasitised” host cells (**This thesis, Chapter 3 and 4**).
2. CXCR3/CXCL11 signalling not only mediates recruitment of macrophages to mycobacteria and sustains granuloma expansion, but also acts as a “remote control” that reprograms macrophages to assume a more infection-permissive phenotype (**This thesis, Chapter 3 and 4**).
3. Cxcr3.3 is not a “DRY” chemokine receptor and more “WET” labwork will be necessary to precisely characterise its proposed role in antagonising classical Cxcr3.2 signalling (**This thesis, Chapter 5**).
4. In poorly vascularised tissues, mycobacteria can take advantage of the homeostatic chemokine receptor CXCR4 to sustain granuloma-associated angiogenesis and promote bacterial growth (**This thesis, Chapter 6**).
5. Similar to in humans, the zebrafish chemokine receptor Cxcr2 engages in promiscuous interactions with multiple IL8-like ligands to recruit neutrophils (**This thesis, Chapter 7**).
6. Chemotaxis and immune competence of macrophages are tightly interdependent processes, since lysosomal function is controlled by chemotactic cues and, simultaneously, chemokine-dependent motility is sustained by lysosome trafficking.
7. The immune response to TB is multifaceted and multiple host pathways are affected during mycobacterial diseases. Understanding the exact functions of each process in the overall context may allow to develop an efficient combinatorial therapy that counteracts the pathogen on multiple fronts.
8. HIV and *Mtb* infections represent the two leading causes of death associated to a single microbe, and in both cases, the success as pathogens is linked to the capability to largely usurp a single population of immune cells.
9. Paradoxically, several microbial pathogens require macrophages to successfully parasitise the host and the host requires macrophage-driven immune defence to counteract these invaders.
10. The intricate network of chemokine ligand and receptors is comparable to the plot of an Italian soap opera: there are many characters, a lot of “apparent” redundancy, and complex promiscuous relationships between partners...
11. Virgil's text “Trojans, don't trust the horse. Whatever it is, I fear the Greeks, even those bearing gifts” (*Aeneid*, **Book II**) should be taken as a warning about the function of macrophages during infection.

17<sup>th</sup> November 2016, Vincenzo Torraca