Selective autophagy in host defense against mycobacterial infection

Zhang, R.

Propositions

Accompanying the PhD thesis

"Selective autophagy in host defense against mycobacterial infection"

1. Enhancing the activity of selective autophagy receptors or proteins that stimulate autophagy is a promising host-directed approach to improve the treatment of tuberculosis. (Chapters 2 and 4).
2. The lysosomal protein Dram1 is required for autophagic targeting of mycobacteria and acidification of the subcellular compartments where these bacteria reside. (Chapter 2).
3. Deficiency in Dram1 increases pyroptotic cell death of mycobacterium-infected macrophages and thereby exacerbates tuberculosis disease symptoms. (Chapter 2).
4. Dram1 influences metabolic processes during health and disease not only by promoting autophagosome-lysosome fusion, but also by modulating the transcription of metabolic pathway genes. (Chapter 3).
5. At least two members of the selective autophagy receptor family, Optineurin and p62, are required for the zebrafish host to restrict mycobacterial infection. (Chapter 4).
6. Although Lc3-II and p62 protein levels are trusted indicators of autophagic activity, the use of fluorescently tagged versions of these proteins is more informative about the cellular relevance of autophagic processes.
7. More research is required into how mycobacteria manipulate host cell death pathways, because the mode of cell death is a major factor in tuberculosis progression and currently more than twenty different forms of regulated cell death have been identified.
8. While selective autophagy receptors are known to function by direct autophagic targeting bacteria as well as by delivery of neo-antimicrobial ubiquitinated peptides, it remains to be discovered to what extent each of these mechanisms contribute to control of mycobacterial infection *in vivo*.
9. The use of CRISPR/Cas9 technology is to be preferred over ENU mutagenesis not only because of greater efficiency and precision, but also because of the lower risk of off-target effects.
10. Luckily, my Chinese is still better than my English after nearly 5 years of international life.
11. There are no limits to knowledge, because one can learn more than ever imagined when standing on the shoulders of great people.

8 November 2018, Rui Zhang