## Macrophage ATP citrate lyase deficiency stabilizes atherosclerotic plaques

## Jan Van den Bossche

Department of Molecular Cell Biology and Immunology, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands.

## Contact e-mail: j.vandenbossche@amsterdamumc.nl | Twitter: @immunometlab

A growing number of findings highlight the crucial role of metabolic reprogramming in macrophage activation during many different diseases<sup>1</sup>. Jan Van den Bossche entered the exciting immunometabolism field when he discovered that mitochondrial dysfunction in inflammatory macrophages prevents their repolarization, and that metabolic features of macrophages can be targeted to reshape their function<sup>2</sup>. Follow-up research from his group demonstrated how diet-induced changes in systemic metabolism *in vivo* translate into altered macrophage metabolism and function<sup>3</sup>. More recent work investigated the role of ATP citrate lyase (ACLY) in macrophages in atherosclerosis, cancer and other inflammatory conditions<sup>4-6</sup>. Currently, Jan's team investigates fundamental and translational aspects of immunometabolites including succinate, itaconate and 2-hydroxyglutarate<sup>7,8</sup> and develops new tools to profile immunometabolism *in vitro*, as well as *ex vivo* using single-cell approaches<sup>9,10</sup>.

## References

[1] Van den Bossche et al. Macrophage Immunometabolism; Where Are We (Going)? Trends in Immunology. 2017 doi: 10.1016/j.it.2017.03.001

[2] Van den Bossche et al. Mitochondrial dysfunction prevents repolarization of inflammatory macrophages. Cell Reports. 2016 doi: 10.1016/j.celrep.2016.09.008

[3] Baardman et al. A Defective Pentose Phosphate Pathway Reduces Inflammatory Macrophage Responses during Hypercholesterolemia. Cell Reports. 2018 doi: 10.1016/j.celrep.2018.10.092

[4] Baardman et al. Macrophage ATP citrate lyase deficiency stabilizes atherosclerotic plaques. Nature Communications. 2020 doi: 10.1038/s41467-020-20141-z

[5] Verberk et al. Myeloid ATP citrate lyase regulates macrophage inflammatory responses in vitro without altering inflammatory disease outcomes. Frontiers in Immunology. 2021 doi: 10.3389/fimmu.2021.669920

[6] de Goede et al. Myeloid-specific Acly deletion alters macrophage phenotype in vitro and in vivo without affecting tumor growth. Cancers. 2021 doi: 10.3390/cancers13123054

[7] de Goede et al. Let's enter the wonderful world of immunometabolites. Trends in Endocrinology and Metabolism. 2019 doi: 10.1016/j.tem.2019.03.004

[8] Harber et al. Succinate is an inflammation-induced immunoregulatory metabolite in macrophages. Metabolites. 2020 doi: 10.3390/metabo10090372

[9] Artyomov, Van den Bossche. Immunometabolism in the single-cell era. Cell Metabolism. 2020 doi:

10.1016/j.cmet.2020.09.013

[10] Hartmann et al. Single-cell metabolic profiling of human cytotoxic T cells. Nature Biotechnology. 2021 doi: 10.1038/s41587-020-0651-8