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Metabolism and lipid mediators as regulators of innate immune cell function: implications for inflammation and immune responses

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Stellingen behorende bij het proefschrift

Metabolism and Lipid Mediators as Regulators of Innate Immune Cell Function Implications for Inflammation and Immune Responses

1. The metabolic needs of immune cells are highly context dependent. To identify suitable therapeutic metabolic targets, it is important to study the needs of each type of immune cell in each specific pathological framework. [This Thesis]
2. IgG antibodies against the spike protein of SARS-CoV-2 induce a metabolic reprogramming in macrophages that primes them for hyperinflammatory responses. [This Thesis]
3. Different IgA subclasses induce a distinct inflammatory potential in macrophages supported by distinct metabolic rewiring. [This Thesis]
4. Both Th1 and Th2 polarization are dependent on COX-2 activity in dendritic cells, while additional PGE₂ synthase activity downstream of COX-2 is specifically required for Th2 responses induced by helminths. [This Thesis]
5. The use of preclinical models, such as mice and *in vitro* cell cultures, makes it challenging to translate experimental results into clinical applications, as these models cannot always entirely capture the complex metabolic conditions seen in humans and in disease. Data should be obtained directly from patients to properly confirm and elucidate the immunometabolic drivers behind each pathology. [Adapted from Hu *et al.*, Sig Transduct Target Ther, 2024]
6. Thus far, strategies to improve vaccine efficacy have mostly focused on changing adjuvants, formulations, and immunization routes, without directly addressing the metabolic constraints of immune cells or the microenvironment. Targeting immune cell metabolism will be a critical step towards optimizing vaccine performance. [Adapted from Møller *et al.*, Cell Mol Immunol, 2021]
7. Only by combining lipidomics, metabolomics, and proteomics with functional immune cell-based assays will we be able to properly decipher the role of lipid metabolism in immune regulation and uncover new pathways to treat immune-related diseases. [Adapted from Reinalda *et al.*, Chembiochem, 2025]
8. While AI/ Large Language Models are tools that present some usefulness in science, they ultimately lack the semantic understanding unique to the human brain. We should neither overestimate nor rely too deeply on AI, seeing as it cannot, and should not, replace proper scientific work, writing, and reasoning done by an actual person. [Adapted from Li *et al.*, Extracell Vesicle, 2026]
9. Saying a pathway is regulated by the amount of substrate is the same as saying the pathway is not regulated. [Inspired by Prof. Dr. Ana Ponces-Freire, Portuguese biochemist and enzymologist]
10. Knowledge and wisdom should be drawn from several different places. If we take them from only one source, we condemn ourselves to a rigid and stale manner of thinking. [Adapted from "Avatar: The Last Airbender", Uncle Iroh (Mako), (2006)]
11. A vital ingredient to success is not knowing that what you are trying to achieve is impossible. [Adapted from "Equal Rites", Terry Pratchett, (1987)]
12. The meaning of life lies in consciously rebelling against the absurdity of life itself. One must imagine Sisyphus happy. [Adapted from "The Myth of Sisyphus", Albert Camus, (1942)]