MOBILISE - Monoamine oxidase B inhibitors as novel drugs targeting NLRP3 inflammasome

Although the number of anti-inflammatory drugs has increased during the past decade, there is still an urgent need to develop novel alternatives that overcome limitations of current treatments. The most used therapies, such as non-steroidal anti-inflammatory drugs, non-analgesic anti-inflammatory drugs or colchicine, often present severe side-effects. In addition, in recent years biologicals have appeared, but they are extremely expensive. Therefore, novel therapeutic approaches with lower toxicity, higher tolerance and lower price must be developed to treat autoinflammatory and autoimmune diseases. Since the NLRP3 inflammasome is a key contributor of inflammatory diseases (including gout, pseudogout, metabolic arthropathies and multiple sclerosis), its targeting has become very relevant for the development of novel therapeutics. As part of our ERC project STePS, we discovered a novel activation pathway to the NLRP3 inflammasome, which opens new opportunities to use an existing line of compounds for radically new medical indications. Within STePS, we uncovered the activation of the NLRP3 inflammasome by the enzyme Monoamine Oxidase B (MAO-B) through ROS production, positioning MAO-B as a promising target to treat autoinflammatory and autoimmune diseases. Given that there are several MAO-B inhibitors (iMAO-B) currently used in the clinic for treatment against Parkinson disease, the use of iMAO-B represent a major opportunity to develop new therapies at low risk and a fraction of the cost. This ERC PoC MOBILISE will assess the technical and commercial feasibility of repositioning iMAO-B as a novel treatment of gout and other NLRP3 inflammasome-driven diseases. Within MOBILISE, we aim to explore the efficacy in vivo of iMAO-B, solidify our IP protection, perform an extensive market and competitor analysis and develop a detail business plan to define the optimal commercialisation route for MAO-B inhibitors in gout and other autoinflammatory diseases.

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