Interrogating NLRP3 inflammasome activation mechanisms

Project partners
Universität Freiburg, Université de Strasbourg
Project duration / Awarded funding
01/03/2024 – 31/12/2024 / 37,620,17€
Short description of the project
Inflammasomes are intracellular sensors of pathogens and danger signals. The NLRP3 inflammasome is involved in host defence against cancer and infection, but is also a major instigator of pathological inflammation in several diseases. Understanding its elusive mechanism of activation is one of the biggest open questions in the field of immunology and is a crucial step towards therapeutic targeting of NLRP3. Using different approaches, both groups involved in this project have individually made substantial contributions towards this goal. In this project, first steps were taken towards joining forces between the groups in Freiburg and Strasbourg to combine their complementary expertise and unique methods to specifically tackle the problem of NLPR3 activation mechanism. Novel pharmacologic NLRP3 activators developed in Freiburg were jointly investigated in Strasbourg and Freiburg to elucidate their mode of action including their impact on intracellular NLRP3 trafficking.
Concrete implementation of the project (What was the funding used for?)
• Consumables for cell cultures and experiments • Custom synthesis of the drug-like substances to be tested • Core facility fees
Project result(s) and continuation of collaboration
The project was successfully executed as planned. The results suggest that the new NLRP3 activating drugs we developed have a mode-of-action more proximal than any other known activator. Genetic screening results suggest our new activators rely on the core components of the NLRP3 inflammasome, but no other specific gene products. Microscopy results further showed that, similar to classical activators, the new substances cause recruitment of NLRP3 to cellular vesicles.
Further information (links, articles, photos)