Ship-1 inhibitors for prophylactic treatment and/or prevention of infectious diseases

CNIC

Dr. Carlos del Fresno

PROFILE

Within **CNIC** (*Spanish National Center for Cardiovascular Research*) the **Immunobiology lab,** led by Dr. David Sancho, focus on the study of myeloid cells, in particular macrophages and dendritic cells, trying to understand cellular, molecular and metabolic features related to the capacity of these cells to modulate immunity. These studies cover relevant pathologies such as metabolic disorders (obesity), cancer and infections of diverse etiology.

SPEAKER

After his degree in Biology, **Dr. Carlos del Fresno** performed his doctoral thesis in the Research Unit of La Paz Hospital, Madrid, where he obtained his PhD in Biochemistry, Biomedicine and Molecular Biology. Since 2013 he takes part of the Immunobiology laboratory at the Spanish National Center for Cardiovascular Research (CNIC). Altogether he can credit more than 12 years as biomedical researcher.

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PRODUCT

Ship-1 inhibitors for prophylactic treatment and/or prevention of infectious diseases

MECHANISM OF ACTION

SHIP-1 inhibitors are small molecules that specifically target the phosphatase SHIP-1. It is well described that the inhibition of this molecule boosts immunogenic processes. Our novelty is the application of SHIP-1 inhibitors in the context of the prophylaxis generated by the trained immunity. This trained mechanism prompts prophylactic immune responses against infections, that are boosted by the SHIP-1 inhibitors.

Trained immunity is a recently described process by which innate immune cells, such as macrophages, develop a state that allows them to perform improved inflammatory responses against infections. Of note, this state is long-lasting. A key molecular pathway to generate this prophylactic trained state is the PI3K/Akt, and the SHIP-1 phosphatase inhibits this pathway. Therefore, the underlying mechanism of our product is the inhibition of a trained immunity repressor. Thus, we have described that SHIP-1 inhibitors improve the prophylaxis generated by inducers of trained immunity, allowing better outcomes after infections.

TARGET INDICATIONS

The therapeutic area where SHIP-1 inhibitors can be applied in combination with the prophylactic effect of trained immunity is to fight infections. Due to the wide-ranging effect of this prophylaxis against virus, bacteria and fungi, there is a broad potential application of our product in the clinical practice. Importantly, this prophylactic effect could be extended to other non-infectious pathologies such as cancer.

CURRENT STATUS

- In 2018 we published the basis for the development of our product (Saz-Leal, et al., Cell Reports, 2018). There, we showed that both the genetic deletion of SHIP-1 or its chemical inhibition, improved trained immune responses triggered by ß-glucans.
- These ß-glucans are compounds of fungal origin that are well known for their capacity to induce trained immunity. We showed that their combination with SHIP-1 inhibitors, protected mice against lethal infections in a prophylactic manner.
- We confirmed that these SHIP-1 inhibitors also enhanced inflammatory responses in human blood cells, supporting their potential use in the clinical practice. Thus, those SHIP-1 inhibitors constitute the product we are presenting in here.

INNOVATIVE ASPECTS

- To the best of our knowledge, our product is the only chemical with the capacity of improving trained immune responses.
- As indicated before, trained immunity is a quite novel process that is still under intense investigation, in an attempt to understand it deeply. Based on our solid expertise in SHIP-1, immunity and infectious processes, we were the first research group to publish the capacity of improving trained immune responses.

IPR

The technology is currently protected under international application PCT/EP2019/064871 entitled 'Enhanced trained immunity in myeloid cells by SHIP-1 inhibition' filed on the 6th June 2019. The patent applicants are the CNIC, Syracuse University and the Research Foundation for the State University of New York.

PARTNERING OPPORTUNITIES

We are looking for a partner interested in a license of the patent application. We would like to explore diverse ways of cooperation with pharmaceutical partners ranging from extending our knowledge on the effect of SHIP-1 inhibitors in additional pathological settings where trained immunity could be important, to testing our product in clinical trials.