PNRR PE13 INF-ACT: Development of Immunomodulatory and Antiviral Lead Compounds

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The effects of the recent Sars-CoV-2 pandemic, even in industrialized countries at the forefront of research in the medical field, has highlighted the need to enhance the response capacity of scientific research to emergencies due to new infectious agents with a global approach including several multidisciplinary aspects, ranging from man's relationship with the surrounding environment for the study of spillovers, to virology, medical entomology, microbiology, epidemiology, and drug discovery. With this approach, the INF-ACT Extended Partnership project oriented to emerging and re-emerging infectious diseases with epidemic/pandemic potential represents a formidable opportunity offered by the National Reprise and Resilience Programme.
Our contribution to the project is in the field of drug discovery focused on the identification and development of new immunomodulatory and antiviral compounds such as:
- Identification and development of new Proteolysis Targeting Chimeras (PROTACs) for SARS-CoV2 Main Protease (Mpro) degradation, as Coronavirus antivirals, and stimulators of the cellular immune response through the generation of CD8+T-cells.
- Identification and development of small organic molecules with the ability to activate Dendritic Cells subsets that can play a specific and significant role in mounting a robust immune response without compromising immune homeostasis by binding specific receptors, like TREM2, lectins and dectin 1.
- Studies of binding of glyco-conjugates to different human pathogens-recognition receptors like carbohydrate-binding proteins (lectins), with identification of the lead compound and preliminary validation on preclinical models.
- Mitochondrial bioenergetics analyses to reveal the ability of lead compound to properly fulfill the metabolic demand of immune cells.
This presentation will show the preliminary results concerning the development of new Proteolysis Targeting Chimeras (PROTACs).

Keywords: Antivirals, Inflammation, PROTACs

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Acknowledgements:
We wish to thank MUR PNRR INF-ACT European Union - NextGenerationEU for the financial support.
Finanziato dall'Unione europea - NextGenerationEU.