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MUR PNRR National Center for Gene Therapy and Drugs based on RNA Technology

Spoke 6: RNA drug development

veRNAdì

A webinar series about RNA

to share projects and competences, increase networking, discuss issues and new ideas, and disseminate results

Every last Friday of the month

https://rb.gy/y40y6

XVI veRNAdì: July 25, 2025, 15:00

Novel encoded adjuvants for genetic vaccines

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Over the past three decades, we assisted to the development of a novel vaccine technology called Genetic Vaccination (GV) which uses genes encoding the antigen(s) rather than the antigen in its proteinaceous form. However, the immune system is governed by a highly diversified network of entities, resulting in a robust and resilient system which changes its properties along the time and space axes. For this reason, the administration of encoded antigen alone results in suboptimal immune response. Understanding the underlying mechanisms would advance our ability to selectively activate and control it. To establish a more potent and durable adaptive immunity, here we describe a synthetic immunology approach to identify and characterize genetic encoded immune adjuvants capable of enhancing the strength, duration and quality of the adaptive immunity induced by Genetic Vaccines. By interpolating single cell data from immune cells with a bioinformatics analysis, we selected 80 potential genetic adjuvant candidates to be screened in vivo in the form of mRNA-LNP. We co-deliver the mRNA encoded antigen of interest with a second mRNA encoding the potential genetic adjuvant, both of them formulated in lipo-nanoparticles (mRNA-LNP) to ensure a spatio-temporal coordinated expression in vivo. In this way, we have identified several immunomodulators that significantly enhance the immunogenicity of genetic vaccines for cancer and infectious diseases. These data confirm the feasibility of using mRNA encoded immunomodulatory molecules to improve immunogenicity and efficacy of mRNA vaccines. Through an in-depth analysis of the mechanisms of action of the immunomodulators, we aim to develop a comprehensive map of the molecular circuits involved in the induction of optimal adaptive immunity by mRNA based genetic vaccination for rapid clinical translation.