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Computational approaches to target glyco-immune checkpoints in CAR T cell: opportunities for novel small-molecule therapeutics



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Chimeric Antigen Receptor (CAR) T-cell therapy has transformed treatment outcomes in hematological malignancies, yet its long-term efficacy is often hindered by T-cell exhaustion and therapy-induced toxicities. Inhibitory immune checkpoints, such as PD 1/PD-L1 and sialoglycan-binding Siglecs, are known contributors to the functional decline of T cells within the tumor microenvironment. While monoclonal antibody-mediated checkpoint blockade has been explored in combination with CAR T-cells, the application of small-molecule inhibitors—particularly those with known safety and pharmacological profiles—remains largely unexplored in this context. These small molecules offer a promising alternative due to their potential for oral bioavailability, lower cost, and modifiable pharmacokinetics. In parallel, managing CAR T-cell-associated toxicities such as cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) remains a critical challenge. IL-6 and IL-1, primarily secreted by monocytes and macrophages, are key drivers of these conditions. The identification of alternative small-molecule inhibitors targeting immune checkpoints and pro-inflammatory cytokine receptors, such as PD-L1, Siglecs, and IL-1R1, through advanced computational drug design, may offer a dual therapeutic benefit: improving the functional resilience of CAR T-cells while minimizing treatment-related toxicities. This integrated strategy remains a largely untapped avenue in the optimization of CAR T-cell therapies.

Short Bio

Patrícia Sobral is a PhD candidate in Sustainable Chemistry at FCT NOVA, with academic training in Applied Chemistry (BSc) and Pharmaceutical and Therapeutic Chemistry (MSc). Her research focuses on the interface of chemoinformatics and cancer immunology, and she is an active member of the Chemoinformatics group at LAQV and Glycoimmunology research group at UCIBIO. Before starting her doctoral studies, Patrícia worked for three years in the pharmaceutical industry, gaining valuable experience in drug development processes. She has contributed to several scientific projects, including *DCMatters*, which explored vaccine-based therapies for advanced tumors; *ProDGNE*, a European initiative developing treatments for GNE Myopathy; and is currently involved in the *CAR-T Matters* project, which aims to advance CAR-T cell immunotherapies

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Webinar Host

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