Exploring Alternative Immune Therapeutics

The field of immunotherapy has experienced clinical success with molecules targeting immune checkpoints like PD-1/PD-L1, yet not all exhibit significant potential. The immune system and its checkpoints engage in complex crosstalk, further complicating these interactions.

In this research, we characterized pAC65, a macrocyclic peptide demonstrating inhibitory potential comparable to FDA-approved monoclonal antibodies. To structurally analyze this peptide, we obtained high-quality crystals, providing insights into its interactions with PD-L1. The peptide's potency was assessed through HTRF, resulting in an EC_{50} value of 0.58 nM, like the FDA-approved therapeutic antibody atezolizumab (EC_{50} = 0.14 nM). In comparison with previously published macrocyclic peptides, we observed an almost 600-fold increase in potency.

Furthermore, we conducted cell-based assays, revealing that pAC65 induced the expression of PD-1 on T lymphocytes, akin to the effects observed with the therapeutic antibody atezolizumab. The 3D structure of the pAC65/PD-L1 complex has been successfully deposited in the PDB database (PDB ID: ALX8).

In this presentation, I will discuss the results and future directions of our research.