Targeting MMP-9 in Cancer Treatment: Computational Design and Experimental Validation of Potent, Safe Antitumor Agents

Matrix metalloproteinase-9 (MMP-9) is an enzyme that plays a key role in cancer progression, helping tumors invade surrounding tissues and spread to distant organs. This makes MMP-9 inhibition an attractive strategy for anticancer therapies. Yet despite more than thirty years of research, every experimental drug designed to block MMP-9 has failed in clinical trials. The main reasons were either adverse side effects or no measurable improvement in patient survival. Careful analysis revealed that all of these candidates shared a common weakness: poor pharmacokinetic and safety properties — in other words, unfavorable ways in which the body absorbs, distributes, and metabolizes them. These disappointing outcomes highlight the urgent need for a new generation of MMP-9 inhibitors that not only demonstrate strong specificity and potency against the enzyme, but also possess favorable pharmacokinetic and safety profiles, greatly improving their chances of success in clinical development.

Our project aims to overcome these barriers and substantially accelerate the discovery process through advanced AI-aided drug design. We envision that using state-of-the-art medicinal chemistry software, incorporating retrosynthesis and forward-synthesis algorithms, will enable the creation of unprecedented yet synthesizable chemical entities. The workflow will begin with computational calculations to generate hundreds to thousands of new molecular structures and immediately predict how well they bind to the MMP-9 enzyme, while also screening them for pharmacokinetic criteria. These drug candidates will then be further evaluated using molecular docking to assess binding affinity and selectivity, and molecular dynamics simulations to estimate binding stability. This means we can focus only on compounds with the highest likelihood of success — those that combine strong activity against MMP-9, selectivity over other MMP isoforms, and favorable drug-like and safety properties. The most promising compounds will be synthesized in the laboratory and tested in cell-based experiments to confirm their anticancer potential.

By integrating modern computational tools with laboratory validation, this project seeks to accelerate the discovery of safe and effective MMP-9 inhibitors. We expect that our approach will not only yield promising drug candidates for cancer therapy but also demonstrate a faster and more efficient way to design new medicines.