

Metastasis accounts for 90% of all human cancer related deaths and involves a complex process in which cancer cells invade adjacent tissues and vasculature (intravasation) resulting in their dissemination away from the primary tumor site to distant organs. Matrix metalloproteinase 9 (MMP-9) is a secreted type IV collagenase known for its role in multiple pathological processes such as cancer invasion, metastasis, and angiogenesis. When the role of MMP-9 in cancer progression was first elucidated, targeting its catalytic domain became a primary interest in molecular drug discovery by generating synthetic collagen-mimicking hydroxamate compounds which would facilitate chelation of the zinc ion in the active site upon binding. Although novel in design, these compounds performed poorly in clinical trials due to their lack of specificity for the catalytic domain of MMP-9. To circumvent the problems encountered by previous scientists during clinical trials, our lab has decided to target the hemopexin domain of MMP-9, the least conserved domain of this family of enzymes to allow for a more specific drug treatment for combating cancer dissemination. Through use of an in silico docking approach for discerning the binding affinity between small molecules and MMP exosites, our lab has identified a novel compound which binds to the hemopexin domain of MMP-9, along with displays potent inhibition of MMP-9-mediated cancer cell migration. I plan to dissect the molecular mechanism of the identified derivate on targeting MMP-9 mediated cancer dissemination in addition to discerning the specificity and binding affinity of the identified compound to the hemopexin domain of MMP-9.