

CaSR--GSH Interaction: Finding an Effective Antagonist

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As the second leading cause of death, cancer has negatively impacted the lives of millions across the globe both directly and indirectly. In this study, we propose targeting the CaSR (calcium-sensing receptor)—GSH (glutathione) interaction with quinazolinone-containing compounds, which recent computational studies have shown to have high binding affinity and structural specificity to CaSR. CaSR—GSH mediated interactions are expected to increase proliferation of endothelial cells and, therefore, vascularization of cancerous tissue. We hypothesize that quinazolinone derivatives can bind to CaSR and outcompete endogenous agonists, thereby, abrogating GSH-mediated CaSR activation and stunting cancer cell proliferation. Computational drug repurposing methodology was used to create a compound library of quinazolinone-containing drugs, which were screened for binding potential to CaSR using AutoDock Vina. The highest ranked drug based on binding affinity, intermolecular interactions, and binding site was chosen for in vitro validation. Luciferase assays were performed on a stably transfected line of HEK-293 cells to determine efficacy of the drug in inhibiting CaSR activation. In this study, we highlight the potential of Idelalisib as an inhibitor of CaSR—GSH mediated downstream signaling responses such as endothelial cell proliferation in silico and in vitro and provide further evidence for the pre-clinical development of quinazolinone-containing compounds as CaSR inhibitors.

Awards Won:

Third Award of \$1,000