Inducing Cellular Adhesion via Membrane Targeting of Rap1 Pathway Effectors for Development of Bone Marrow Mobilizing Drug for Chemotherapy Patients

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Rap1 is key protein in regulating a cell signaling pathway that controls cell adhesion to its environment. Being able to manipulate and shutdown this pathway would yield immense benefits for chemotherapy patients. Rap1 inhibition may allow for delocalization of patient bone marrow into the bloodstream for harvesting and later reintroduction once patient has undergone drug therapy that would otherwise damage or destroy the marrow. While attempts to develop a drug to inhibit this pathway by directly targeting Rap1 have generally failed due to Rap1's involvement in numerous other pathways, this project is the among the first studies to investigate two downstream effectors, RapL and RIAM, for drug targeting to disrupt the adhesion pathway. Before any drug development can commence, however, it is necessary to prove that these are viable drug targets. To do so we engineered DNA that encoded membrane targeting varieties of RapL and RIAM the wild types. We then transfected our synthesized DNA into human endothelial kidney cells and performed a collagen well plate adhesion assay to test the effectiveness of our membrane targeting proteins. The adhesion assay conducted our transfected cells revealed that membrane-targeting varieties of RapL and RIAM significantly outperformed the wild types. Adhesive cell counts increased by 39.554% and 56.155% respectively. Our results prove that RapL and RIAM can promote adhesion independent of Rap1 and are thus viable drug targets. Because of this essential verification, drug development for inhibiting these two protein may now commence in the hopes of alleviating bone marrow damage in chemotherapy patients.

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