

Project Title: Selectin-Mediated Delivery of Polymeric siRNA Nanoparticles to Metastatic Tumors

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Description:

Over 90% of cancer-related deaths are due to metastasis, the spread of cancer cells from a primary tumor to anatomically distant organs such as brain and bone. While primary tumors can typically be treated via surgery, radiation and chemotherapy, metastases are very difficult to detect and treat, and typically lead to a poor patient prognosis. siRNA therapeutics have enormous potential to silence genes that contribute to metastasis, however local delivery of siRNA of metastatic tumors remains a challenge, as the majority of siRNA nanoparticles localize to the liver upon delivery. In this project, we will utilize a novel approach (Mitchell, PNAS, 2014) to attach polymeric nanoparticles to cells in the bloodstream, as an entirely new means to localize siRNA therapeutics to metastatic tumors. Polymeric siRNA nanoparticles will be functionalized with selectins, which rapidly bind to cells in blood such as white blood cells and circulating cancer cells. **We will harness the innate ability of these cells to migrate to metastatic tumors as an entirely new means to localize siRNA within tumors, to reduce tumor size and enhance survival.** Students will gain experience in nanoparticle synthesis, siRNA delivery, cell culture, and working with animals including mice.

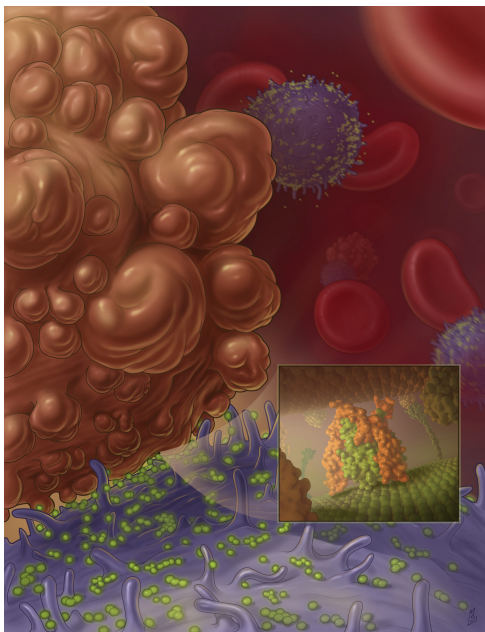


Figure 1: Selectin-coated nanoparticles (green) can be directly attached to white blood cells in the bloodstream, as an entirely new means to deliver siRNA nanoparticles to metastatic tumors in the body that cannot typically be targeted. Reference: Mitchell, PNAS, 2014.