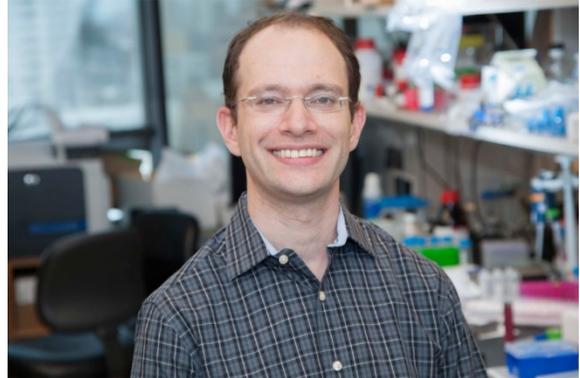## Daniel Heller, PhD

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Precision Nanomedicines for Cancer Detection and Treatment

Abstract: Our lab develops nanotechnologies to addresses problems in the diagnosis, treatment, and research of cancer and allied diseases:

Metastatic tumors are responsible for the vast majority of cancer deaths. Such tumors are often poorly accessible to nanoscale drug delivery systems because of the vascular barrier, which often prevents the targeting of the tumor site. We are investigating new targets to localize precision drugs, such as kinase inhibitors, to the metastatic tumor microenvironment. We recently developed a nanoparticle drug carrier platform with nanomolar affinity to P-selectin to localize targeted therapies in tumor-associated vasculature and away from healthy tissues to obviate dose-limiting toxicities and concomitantly improve therapeutic index. We found that the nanoparticles targeted chemotherapy, as well as MEK and PI3K inhibitors, to tumor sites in both primary and metastatic models, resulting in superior anti-tumor efficacy and the striking reduction of toxicities. Moreover, measurements of tumor tissue show prolonged inhibition of downstream effectors in the signaling pathways, constituting a significant modulation of drug pharmacokinetics. In tumors devoid of P-selectin, we found that ionizing radiation guided the nanoparticles to the disease site by inducing P-selectin expression, suggesting a potential strategy to target disparate drug classes to almost any solid tumor.

The early detection of cancer could lead to vastly improved patient outcomes. We aim to identify cancer biomarkers within the body at early disease stages, permitting detection before symptoms arise. We are developing implantable nanosensors, using the unique optical properties of carbon nanotubes, to facilitate non-invasive detection via optical detection through living tissues. The sensors could enable early detection of cancer in people at high risk for the disease, in successfully treated patients to monitor recurrence, or in patients who are undergoing treatment to inform clinical decisions.