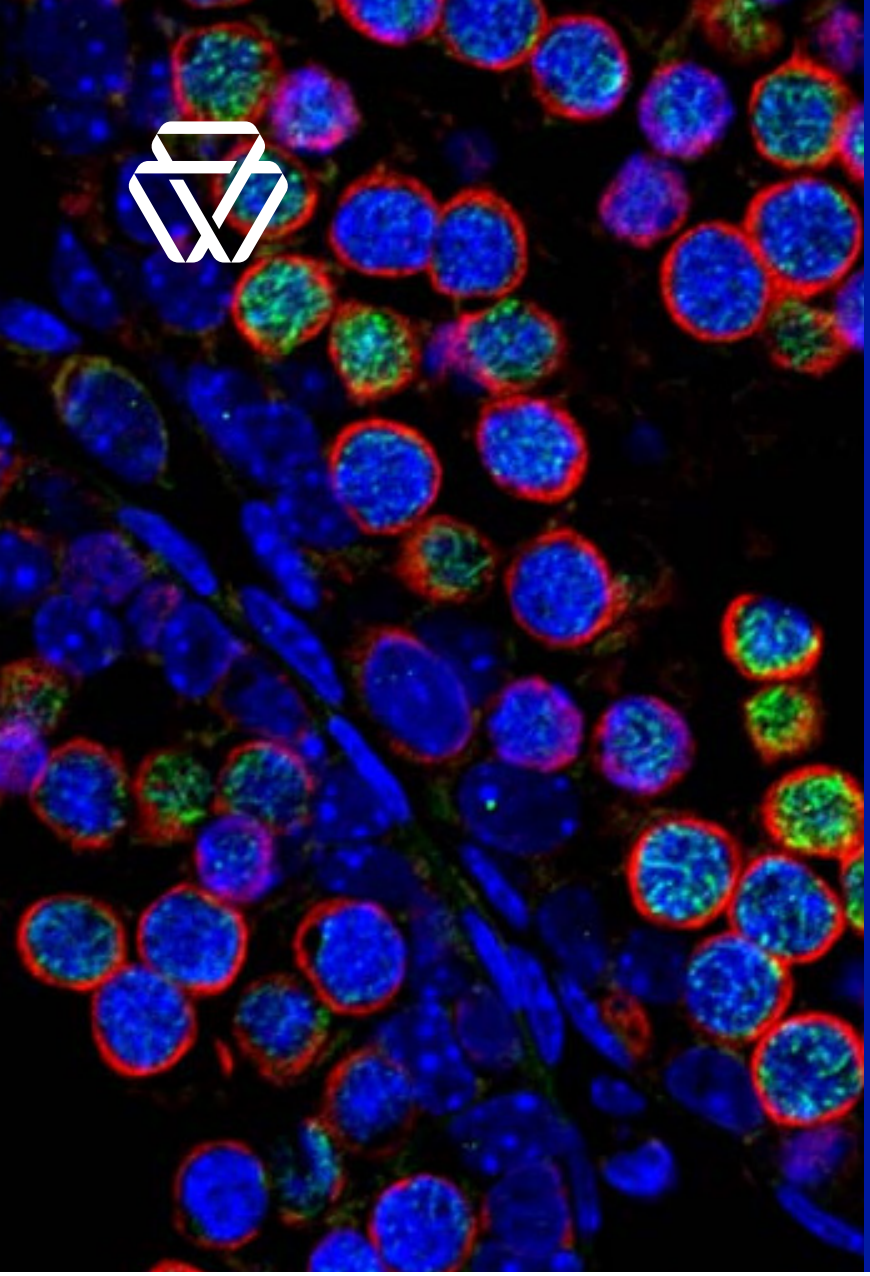

Cancer: therapeutic insights from foundational studies

Advances in cancer therapies are built upon foundational research into how cancers arise, develop, and spread. The foundational work of Whitehead Institute researchers will ultimately benefit patients whose cancers evade current therapies. Research focuses include metastasis, or the spread of cancer throughout the body, which often makes cancer more deadly; and immunotherapy, which harnesses the body's immune system to destroy cancer cells.

Valhalla Fellow **Tobiloba Oni** works on tools to boost the immune system's response to pancreatic cancer, which has a low survival rate and poor response to immunotherapies. Oni is investigating new strategies to make pancreatic cancer cells more responsive to immunotherapy by targeting proteins and sugar molecules on the cell surface, which shield these cancer cells from immune attack.

Whitehead Fellow **Aditya Raguram** studies how large molecules are transferred between cells in the body and how we can harness these processes to more effectively deliver therapeutic molecules into diseased cells. Raguram is particularly interested in the delivery of genome editing technologies. His work could lead to new therapeutic strategies for cancers, as well as genetic disorders and a variety of other conditions.

“This research provides new insights into how cancers develop and become aggressive and deadly—knowledge that could be used to prevent cancers.”

Founding Member **Robert Weinberg** studies how cancers metastasize, with the ultimate goal of prevention. One focus is on how cancer cells enter a particular “quasi-mesenchymal” state that Weinberg and others have found best enables the cells to proliferate after disseminating to distant tissues, allowing them to form life-threatening metastatic tumors. Recently, Weinberg lab researchers identified several genes responsible for keeping breast cancer cells in this state in mice, shedding light on the genetic drivers of metastasis.

Valhalla Fellow **Kipp Weiskopf** researches how macrophages, a type of white blood cell that consumes harmful objects and cells, behave within tumors, where they are often suppressed or even contribute to cancer growth. Weiskopf is searching for genes that will instead trigger macrophages to recognize and attack cancer cells. Drugs that block certain signals on cancer cells’ surfaces allow macrophages to recognize the cells as harmful and destroy them. Weiskopf and colleagues found that when other cancer therapies are used in combination with these drugs, it improves their efficacy. Weiskopf is currently applying these strategies to solid tumors such as lung, colorectal, and ovarian cancer, as well as blood cancers such as lymphoma.

Member **Jonathan Weissman** and collaborators developed an approach to track cancer cells through their generations, building a family tree. The researchers use the cells’ relationships to reconstruct how and when cancers evolved important traits. With this approach, they have studied how metastatic cancer spreads through the body and tracked lung cancer through its entire progression, identifying its most common trajectories. This research provides new insights into how cancers develop and become aggressive and deadly—knowledge that could be used to prevent cancers from making these evolutionary leaps.

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