salk
Where cures begin.

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THE CHALLENGE

Scientific research has taught us that cancer is a disease of aging and not actually one disease, but many. Knowing the molecular defects that produce a particular cancer subtype can indicate which drugs should be used to treat it most effectively. Yet, we must overcome major challenges to better treat cancer patients. For example, we only have molecular targets for a handful of cancers. Additionally, the cells within a single cancer often have differing molecular defects that we must target individually. Clearly, we need innovative strategies to chart the molecular interactions and genetic underpinnings of cancers. Such knowledge will generate the new therapies that will enable us to live with, rather than die from, these diseases.

THE APPROACH

Geoffrey Wahl's team is using state-of-the-art approaches to better understand breast and pancreas cancers in order to develop more individualized therapies. First, his lab is studying whether the most aggressive forms of breast cancer are fueled by deranged versions of the stem cells that generate the mammary gland. They are using the most sophisticated molecular and tumor modeling approaches to determine whether the risk factors for breast cancer, such as obesity, actually cause adult cells to reprogram themselves into more plastic, stem-like variants that generate metastatic tumors. Important differences between reprogrammed tumor cells and normal cells may reveal uniquely targetable vulnerabilities.

Secondly, some cancers, like pancreatic, are encased in a protective covering of cells that both prevents drugs from reaching the tumor cells and provide substances that fuel cancer growth. The protective covering arises due to interactions between the cancer cells and the normal cells that surround it. Like breast cancers, pancreatic cancers also "evolve" from one mutant rogue cell. How this evolution occurs, and how the original "initiated" cell generates the diverse types of variant cells within the cancer, remains unknown. The Wahl lab is using advanced methods that interrogate the individual cells formed at each stage of evolution from normal to cancer to understand how the process occurs, to identify vulnerable intervals amenable to interception. Already, their studies are uncovering rare cell types generated during the cancer evolution that produce substances that may be helpful for slowing tumor development or in aiding the immune system to fight the growing cancer before it has a chance to spread.

THE INNOVATIONS AND DISCOVERIES

- Wahl's lab discovered striking similarities between genetic signatures found in certain types of human breast cancer and those of stem cells in breast tissue in mouse embryos. The findings may lead to new ways to predict and personalize the diagnosis and treatment of some of the most aggressive forms of breast cancer.
- His lab examined mammary development, cell by cell, to provide a road map from the fetus to the adult to show how the mammary gland arises. This provided the first comprehensive analysis of all the genes that are expressed during mammary development. And they provided the first single-cell-resolution map of how the chromatin changes in each cell during development. Together, these studies provide a road map for understanding how normal processes are perturbed in the genesis of breast cancer.
- Wahl's team found that a rare type of cell generated during pancreatitis, a harbinger of pancreatic cancer, appears to act by secreting substances that aid the healing of the damaged pancreas. Harnessing this knowledge may provide a way of preventing pancreatitis from turning cancerous, or of slowing the progression of pancreatic cancer.

For more information, please visit:
WWW.SALK.EDU/SCIENTIST/GEOFFREY-WAHL

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