Significant advances in breast cancer prevention and treatment have come from strategies based on knowledge of mammary cell biology and the unique molecular fingerprints of individual tumors. Despite such advances, however, more than 40,000 patients in the United States and about 500,000 worldwide will die of breast cancer in the next 12 months. In too many cases, treatment failures resulting from emergence of drug-resistant cells and metastases will shorten lifespan and reduce quality of life. The overarching issue the Wahl lab addresses is whether a better understanding of the stem-like cells Wahl and others have found in many breast cancers could provide clues to the development of more effective treatment strategies.

During the 1800s pathologists and developmental biologists emphasized that understanding cancer requires deep knowledge of the principles governing the development of the tissue of origin in which the cancer will arise. Thus, even in the 19th century, scientists appreciated that cancer is a caricature of normal development. Wahl’s group therefore expended considerable effort studying the development of the mouse mammary gland in the hope that it would provide insight into the types of cells and processes that are perturbed in the generation of human breast cancers.

His team recently reported the first identification, isolation and characterization of mouse fetal mammary stem cells (fMaSCs) and their associated gene expression profiles. Significantly, they found that many growth regulatory pathways present in fMaSCs appear to be enriched in specific patients with aggressive and frequently chemoresistant basal-like and triple-negative cancers. This is important, as these cancers currently lack molecular targets around which to build personalized therapeutic agents, such as Herceptin for those breast cancers that overexpress Her2 (a growth factor receptor that Herceptin inactivates). The researchers tested whether currently available targeted therapeutic agents directed against some fMaSC growth factor pathways would inhibit their growth and found that the agents tested worked well to inhibit fMaSC growth.

Wahl and his group are now doing the work needed to extend these studies to the clinic in the hope that this basic research can be translated to the bedside to help patients with breast cancers that currently lack targeted therapeutic strategies. An implication of the work is that cells that fuel cancer progression may revert to, or acquire, gene expression characteristics initially found in the stem cells of the embryonic tissue of origin.

For more information, please visit www.salk.edu/faculty/wahl