2016 Webb-Waring Biomedical Research Awards
Investigator Research Profile

Sabrina L. Spencer, Ph.D.

University of Colorado, Boulder

Dr. Spencer is currently an assistant professor in the department of chemistry and biochemistry at the University of Colorado at Boulder. She completed postdoctoral training in chemical & systems biology at Stanford University. Dr. Spencer earned her Ph.D. in computational & systems biology at the Massachusetts Institute of Technology and her M.S. in human genetics at the University of Michigan.

Select Honors

Dr. Spencer has been the recipient of a Henzl-Gabor Young Women in Science Travel Fellowship, a Damon Runyon Cancer Research Foundation Postdoctoral Fellowship, an American Cancer Society Robert Forsland Postdoctoral Fellowship, a prize for best 2013 publication in the Department of Chemical and Systems Biology (Stanford University), a K22 Career Development Award from the National Cancer Institute (NIH), a Searle Scholar Award and a Kimmel Scholar Award.

Medical Focus

Mammalian cells have two fundamentally different states—proliferative and quiescent—but current understanding of how and why cells switch between these states is limited. Generally, cancer cells divide uncontrollably, and many current cancer therapies target this characteristic. However, the ability of cancer cells to pause and enter a quiescent, dormant or slow-dividing state during times of stress is increasingly appreciated as a key feature of malignancy, since slow-dividing cells are thought to be particularly drug resistant. It has been difficult to test this hypothesis because there has been no way to prospectively identify or isolate these slow-dividing cells from a heterogeneous population. Additionally, a critical cause-and-effect question remains unanswered: whether cells that escape therapy are quiescent at the time of treatment (thus indicating that quiescence confers stress resistance), or whether quiescence is the cells' response to the stress of drug treatment. A fundamental understanding of the causes and consequences of cellular quiescence has been elusive due to a lack of tools for identifying and isolating quiescent cells.

Research Proposal

Dr. Spencer's team has previously developed a novel biosensor for detecting living, quiescent cells, thus giving her the tools needed to identify, isolate, and characterize them. Her research proposal will leverage this unique technology to explore the causes and consequences of this slow-dividing cell population to answer the fundamental questions: do slow-dividing cells arise as a result of internal cell stress, and are slow-dividing cells more drug-resistant? She has previously noted that slow-cycling cells have elevated levels of p21, a protein known to cause cell-cycle arrest in response to DNA damage. Therefore, the first aim of her proposal will test the hypothesis that spontaneous errors in DNA replication are one trigger for the slow-cycling state. To complement this hypothesis-driven approach, her team will isolate the slow-cycling cells by flow cytometry and perform RNA-seq to identify other cell stresses that may induce the slow-cycling state. Thirdly, her team will use cancer cell lines to test the hypothesis that slow-cycling cells are indeed more stress and drug-resistant than the majority of the cells. If indeed the slow-dividing state confers drug resistance, any sources of cell stress that her team can identify, such as DNA damage, will suggest new therapeutic hypotheses to investigate, either by eliminating this stress and returning cells to drug sensitivity, or by deepening this stress for a synergistic lethal effect when combined with a cancer therapeutic. This knowledge will generate leads for

the biological nodes that would be most effective for pharmaceutical companies to target therapeutically, with the goal of eliminating drug-resistant cells to kill 100% of cells in a tumor.