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Breast cancer cell cycle through the proteomics perspective

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Abstract

The mammalian cell cycle is a tightly regulated process that must be obeyed by every cell in order to divide and proliferate. It consists of four distinct stages: G1, S, G2 and M. The progression from one stage to another is enabled by biological control mechanisms called checkpoints that ensure that the processes characteristic to each cell stage have been executed accurately. The transition from the G1 stage to S is particularly relevant to cancer, as cancer cells evolved the ability to evade the restriction point and continue through the cell cycle even in the presence of extensive DNA damage. The goal of our research is to use proteomic and mass spectrometry (MS) technologies to bring new insights into the fundamental biological mechanisms that are responsible for driving aberrant cancer cells into division, even when molecular checkpoints such as the G1/S restriction point are in place. Our model system consists of two representative breast cancer cell lines, MCF-7 estrogen receptor positive (ER+) and SKBR-3 epidermal growth factor receptor positive (EGFR/Her2+), and a non-tumorigenic cell line, MCF-10. From over 5000 proteins identified by data dependent liquid chromatography-MS, differential expression analysis performed by spectral counting has revealed dozens of protein clusters that can be matched to all hallmarks of cancer: self-sufficiency of growth signals, insensitivity to antigrowth signals,unlimited replicative potential, evasion of apoptosis, metastasis, sustained angiogenesis, deregulation of metabolism and evasion of immune destruction. Key members of these protein clusters display biomarker potential or the properties of attractive drug targets.

Biography

Iulia Lazar has earned her Ph.D in 1997 from Brigham Young University, and completed postdoctoral studies at Oak Ridge National Laboratory (1998-2000). Currently, she is an Associate Professor at Virginia Polytechnic Institute and State University. Her research is focused onproteomics, breast cancer cell cycle, biomarker discovery and the development of microfluidic and mass spectrometry technologies for the interrogation of biological systems.Dr. Lazar is a member of ACS and ASMS, served on over 20 NIH/NSF review panels and reviewed for 18 scientific journals. She reported her work at over 100 symposia and published over 40 manuscripts and book chapters.