UNRAVELING CANCER SIGNALING PATHWAYS USING GLOBAL PHOSPHOPROTEOMIC APPROACHES

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Over the last several decades, tremendous progress has been made in our understanding of a variety of signal transduction pathways. Most of our knowledge comes from methodical and systematic small-scale experiments. In the last several years, however, improvements in methods to enrich post-translationally modified proteins/peptides coupled with the advances in mass spectrometry allow us to build very detailed maps of signaling pathways with minimal effort. For example, it is not uncommon to identify hundreds to thousands of phosphorylated proteins in a single experiment. Coupled with quantitative methods such as SILAC, these methods can be used to characterize signaling pathways in a comprehensive fashion. Using specific examples from our laboratory, I will illustrate how we have used these strategies to explore signaling pathways initiated by specific growth factors/cytokines such as TGF-beta and thymic stromal lymphopoietin (TSLP) as well pathways that are activated by mutant kinases in breast cancer (PI3-Kinase). Overall, our data reveal the enormous complexity of even “well understood” signaling pathways.