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How pancreatic cancer cell signaling proteins (CSPs) respond to tyrosine kinase inkibitor (TKIs) therapeutics-Peptide microarray, peparrayTM is a powerful molecular tool for CSP profiling

It is well accepted that molecular profiling of cellular proteins or nucleic acids can offer answers to causes of diseases and underlined connections of pathogenic molecules, and thus, pointing out therapeutic targets. However, protein profiling, especially at the cellular level has been challenging. There is only limited choices to allow systematic investigation of cellular protein activities, such as their responses, (i.e., sensitive, or nonresponsive or resistant, to therapeutic treatment). This presentation reports peptide microarray chip (PeparrayTM) technology developed as a powerful molecular tool for proteomic profiling of Cellular Signaling Proteins (CSPs) to interrogate CSP variations in cancer cells induced by treatment of a new generation of anti-cancer therapies, i.e., tyrosine kinase therapeutics (TKIs). Peparray chips encode a large number of receptor kinase protein (RTK) phosphotyrosine (pY) motif peptides. These are probes for capturing of phosphotyrosine binding domain proteins (PPBD), the profiling thus reveal signaling network activities, which can be translated into clinic relevant information valuable for therapeutic treatments. The case studies involving cellular protein profiling of pancreatic cancer treated with three generations of small molecule tyrosine kinase (EGFR) inhibitors (TKis): Erlotinib (TarcevaTM); Afatinib (Gilotrif TM); and the 2016 FDA approved AZD9291 (TagrissoTM). Peparray™ studies revealed molecular signature profiles of cellular conditions through proteins of commonly or differentially expressed. These proteomic profiles revealed 80 signaling proteins with Erlotinib treatment and 135 signaling proteins with Afatinib treatment and 78 signaling proteins with AZD9291 treatment. The detected signaling proteins are implicated in 38-39 cancer related KEGG pathways. Such information about functional cellular proteins provided valuable molecular signature, which reflect cancer status to allow assessment of effectiveness of cancer treatment, i.e., sensitive vs. insensitive, responsive vs. resistant. Our analysis further revealed signaling pathways responsible for therapeutic resistance. Peparray proteomic and signaling pathway results thus hold clinical significance in identifying molecular markers in therapeutic treatment of cancers and in cancer therapeutic strategy decision making. These results call for population applications for monitoring and predicting of therapeutic effectiveness, for wide spread expansion of molecular medicine as basis of precision medicine to greatly benefit human health and wellness.

Biography

Xiaolian Gao has expertise in Chemistry and Biotechnology Development, specifically technologies for massively parallel synthesis of peptides and oligonucleotides on microarray/biochip surfaces. Her team has since developed genomic and proteomic applications to analyze complex biological samples to address questions of biological functions of microRNA and long noncoding RNAs, enzymatic proteins and post-translational modified (PTM) proteins. The biochip technology has led to the establishment of platform of high throughput production of biomolecules and multiplex assay of biomolecules and their interactions.

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