Characterization of protein tyrosine phosphorylation pattern in different cancer cell lines - can it be used as a biomarker of disease?

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In order to make proteins in a specific cell, first a DNA strand is transcribed to RNA in a process called transcription, and then RNA is translated to protein. Making RNA from DNA, and producing protein from RNA is known as "central dogma" in biology. In some cases the proteins are not mature yet and in order to make the proteins functional they undergo so-called post-translational modifications (PTMs), enabling the proteins to exert their tasks properly. Protein phosphorylation (addition of a phosphate group to a protein) is a common PTM that has a critical role in regulating the structure and function of proteins within a cell. Phosphorylation often occurs on the amino acids serine (~ 90 %), threonine (~ 10%) and tyrosine (< 1 %). My thesis is focused on tyrosine phosphorylation (pTyr) because of its important role in regulating cellular functions involved in the formation and development of tumors. The pTyr modification is present at low concentrations in cells but can be detected with highly sensitive and selective methods using anti-pTyr antibodies that can recognize the pTyr residues on a wide range of proteins. To investigate the potential of pTyr modifications in different cancer cell lines (e.g. prostate, bladder, leukemia) as a biomarker in cancer diagnosis 1-D, 2-D gel electrophoresis, western blot and proximity ligation assay (PLA) methods were used. As the outcome of our investigations we conclude that the signals from western blotting agreed with the PLA quantification of pTyr signals per cells. The leukemia cell lines showed a considerably higher level of pTyr proteins compared to prostate and bladder cancer cell lines, where the K562 (leukemia) cell line had the highest level due to the presence of a dys-regulated fusion protein kinase. In conclusion, it might be possible to use the phosphotyrosine modifications pattern as a biomarker of disease or diagnostic tools to distinguish e.g. different stages of each tumor.