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Quantitative proteomics for epigenetics: MS-based analysis of the histone post-translational modifications for basic and clinical research

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Chromatin is a highly dynamic, well-organized and yet ill-defined protein-DNA-RNA structure that controls various DNA-dependent processes. A large number of site-specific reversible and irreversible post-translational modifications of histones (hPTMs) contribute to the maintenance and modulation of chromatin plasticity, gene activation and a variety of other biological processes and disease states. Abnormalities in hPTM patterns, upstream or downstream of DNA methylation are a critical event in cancer initiation and progression as a consequence of the aberrant expression or irregular activity of the enzymes responsible for setting or removing such modifications during the transition from physiological state to tumor. For instance, genetic alterations in various histone deacetylases and demethylases loci are frequently observed in human cancers. As such, hPTMs can represent powerful biomarkers for patient stratification and to predict a specific response to epigenetic drugs. Nevertheless, a comprehensive description of how histone modifications are altered in transformed cells is missing. It is therefore crucial to accurately detect and quantify hPTMs linked with diseased states to shed light on these mechanisms and to exploit them for prognostic, diagnostic and therapeutical purposes. Recent achievements made Mass Spectrometry (MS) and quantitative Proteomics excellent tools within the arsenal of analytical strategies aiming at understanding how histone variants/PTMs and their specific interactors mediate the structural-functional state of chromatin. Our team has contributed to this common effort by setting up distinct quantitative MS-proteomics approaches combined with various biochemical methods of enrichment of chromatin and extra-chromatin proteins to facilitate the investigation of the complexity and plasticity of gene expression regulation. The talk will offer an overview of the MS-proteomics strategies developed in our group to gain novel unconventional insights into chromatin biology highlighting approaches based on the clinical applications of the abovementioned MS techniques to the analysis of breast cancer clinical samples.

Biography

Tiziana Bonaldi is Tenured Group leader at the Department of Experimental Oncology of the European Institute of Oncology, where she has been directing the Giovanni Armenise-Harvard Foundation Laboratory on “Nuclear proteomics to study multi-layer regulation of gene expression” since 2008. Following her training in Biology at the University of Milan, she obtained her PhD degree in Molecular and Cellular Biology at DiBit- San Raffaele Scientific Institute in Milan (Italy). In 2003, she was awarded a long-term EMBO Post-doctoral fellowship to work in the laboratory at the Ludwig Maximillians University of Munich (Germany). During her first Post-doc TB pioneered the use MS for the characterisation of complex patterns of histone PTMs in various loci of the genome. With a second Post-doctoral research carried out in the Department of Proteomics and Signal Transduction at the Max Planck Institute of Biochemistry in Martinsried (Germany), she published a ground-breaking study, demonstrating the power of proteomics to investigate gene expression regulatory events. Since 2008, she returned to Italy where she works as Research Unit Director at IEO focusing on the application of proteomics to study multi-layered mechanism of gene expression regulation. In 2007 she was awarded the “Armenise-Harvard Career Development Award” to support her transition to independence and in 2010 she was awarded the “International Inner Wheel for Women” for her scientific achievements.

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