PROTEOMICS CORE UNIT

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OVERVIEW

Recent developments in "omics" technologies have revolutionised how biomedical research is conducted. These approaches enable unbiased analyses of biological samples and can be used to generate novel hypotheses. Proteins are the molecular effectors of cells, and mRNA assessment merely represents a proxy to estimate the final levels of the protein product. Moreover, genomics does not provide information about the post-translational modifications of proteins or their interactions. Thus, direct analysis of proteins is paramount to our understanding of how cells work. Proteomics is an emerging and multidisciplinary field that aims to analyse the complex regulation of the proteome and its impact on disease. The CNIO Proteomics Core Unit provides state-of-the-art mass spectrometry-based proteomics to scientists and research groups to better understand, at the proteome level, the molecular basis of cancer.

"In 2021, we developed novel proteomic strategies that could be used to identify potential biomarkers in liquid biopsies."

RESEARCH HIGHLIGHTS

In collaboration with the Experimental Oncology Group, we used targeted proteomics to accurately identify and quantify different Kras isoforms, which provide valuable information to understand the interplay between these variants. With the DNA Replication Group, we used Affinity Purification Mass Spectrometry (AP-MS) and showed that PrimPol, a primase-polymerase, interacts with factors involved in DNA inter-strand crosslinks. These results have implications for chemotherapy based on DNA crosslinks. In collaboration with the Metabolism and Cell Signalling Group, we used proteomics to analyse expression changes in livers from RagAGTP mice and identified a failed metabolic adaptation to fasting due to a global impairment in the PPARα transcriptional programme. In addition, in collaboration with the Genomic Instability Group, we used approaches to identify RNA binding proteins and determined that arginine-rich peptides lead to a generalised displacement of factors bound to nucleic acids. These results may provide a plausible mechanism for the pathogenesis of amyotrophic lateral sclerosis. Moreover, we used proteomics, phosphoproteomics, and metabolomics to dissect the series of molecular events that regulate the establishment of naïve pluripotency in embryonic stem cells. These data demonstrated the presence of post-transcriptional regulation, which fine-tune the levels of mitochondrial proteins and enhance their oxphos capacity. Finally, the Unit implemented novel methods aiming to reveal the true identity of proteins present in small extracellular vesicles (sEVs). This is based on high resolution density gradients in conjunction with proteome correlation profiling to deconvolute the origin of proteins (FIGURE 1). Our data revealed that popular markers used to assess the purity of sEVs originate in non-vesicular fractions. This approach could have important applications for identifying potential biomarkers in liquid biopsies. ■

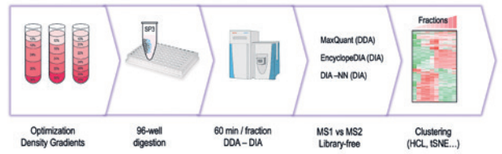

FIGURE 1 Schematic showing the workflow used to reveal the true identity of proteins present in small extracellular vesicles. This figure depicts some of the steps that have been optimised to improve the confidence of the assignments.

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