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Identification of nuclear PKR Interactome in acute Leukemia reveals a central Role for PKR in ribosome biogenesis, mRNA processing, gene expression and cell division

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The double-strand RNA-dependent kinase PKR, plays a central role in inflammatory/chronic stress-mediated pathologies such as cancer, diabetes and neuro-muscular degenerative diseases. Although a significant amount of research has been conducted to elucidate the role of PKR signaling in the cytosol where some binding partners have been reported, only recently has attention been paid to the role of PKR in the nuclear compartment. Our group previously reported that phosphorylated forms of PKR are present in the nucleus of acute leukemic cell lines, representing a reservoir of active kinase that responds to stress.

Using the CCRF-CEM acute T-cell leukemia cell line, a PKR-specific inhibitor, co-immunoprecipitation and affinity-purification mass spectrometry (AP-MS/MS), we have identified the proteins present in active and inactive PKR nuclear complexes. Data were integrated with Gene Ontology and Network analysis, in order to discriminate between proteins that specifically bind to PKR compared to indirect interactor that belong to other protein complexes. Analysis performed on networks emanating from active and inactive PKR, also highlighted those biological processes that specifically required an active PKR kinase. Results demonstrated a complex network of proteins associated with PKR in the nucleus that can be altered upon inhibition of PKR. The majority of these proteins are involved in biological processes central to pathologies in which PKR has been associated, thus offering potential molecular targets to be further exploited.

Biography

Manuela Piazzi received her Ph.D in 2009 from the University of Bologna. Following the completion of her Ph.D., she initiated her post-doctoral studies in Mass Spectrometry analysis in the laboratory of Anthony Whetton at the Universsity of Manchester, School of Enabling Science (UK), before returning to the University of Bologna, cellular Signaling laboratory, under the direction of Lucio Cocco. Currently, she is a Researcher Assistant Professor at the University of Bologna, where she is responsible for the Mass Spectrometry-Proteomic Unit of the Cell Biology Laboratory, Rizzoli Orthopedic Institute, Bologna. She has published more than 10 papers in peer-reviewed journals.

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