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Interaction network of human FOX protein family

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Abstract

The study of protein-protein interaction has provided immense insight into protein functions. Widely used in large-scale proteomic studies, one-step purification using endogenous antibodies or one epitope tag still has its limitations, especially when used to detect interacting proteins in the presence of abundant non-specific binding proteins. In an effort to understand the diverse regulation and functions of FOrkhead boX (FOX) family proteins, we have used a modified Tandem Affinity Purification followed by MASS spectrometry (TAP-MASS) method to study 37 human FOX family members, which comprise all of the 19 FOX subfamilies, from both soluble and chromatin fractions. With a total of 102 TAP-MASS assays, we have identified 17,894 FOX interacting proteins. The data analysis has been performed with several different filtration algorithms and incorporated the protein CCI network, a protein interaction network based on 3,290 endogenous purifications, to get a linearized complex distribution. In this way, we have uncovered ~2,000 high confidential FOX-interacting proteins and several high confidential FOX-interacting complexes, which have been further validated by functional annotations and biochemical analysis.

With this proteomic data set, we have found that FOX proteins form heterodimers across subfamilies and co-regulate each other's transcriptional activities. Moreover, we have discovered that a number of FOX family members bind to homeobox proteins or other transcription factors and these interactions correlate with the abilities of these FOX proteins to induce cell proliferation, EMT and tumorigenesis. Together, our findings suggest that FOX family proteins have many previously underappreciated roles in regulating cellular functions.

Biography

Xu Li obtained his Ph.D degree from University of Southern California School of Pharmacy in 2009. After a brief postdoctoral research on cancer signaling and drug discovery at the City of Hope National Cancer Center, Dr. Li joined the Department of Experimental Radiation Oncology, MD Anderson Cancer Center in 2011. His research focuses on using large scale mass spectrometry-based proteomics to identify novel molecular markers and drug targets for cancer therapeutics. He has published 11 peer reviewed articles in journals including Science Signaling, Genes & Development and Journal of Biological Chemistry.