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Type	Oral communication
Session	Gene regulation, transcriptomics and epigenomics
Title	A computational pipeline for functional analysis of alternative splicing events
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Motivation

Thanks to the advancement in RNA sequencing (RNA-Seq), it is now possible to deeply investigate the alternative transcriptome of cells among experimental conditions and biological contexts. Although many bioinformatic tools are available for detecting alternative splicing events (ASEs), a computational workflow for the functional characterization of the downstream consequences of ASEs is still missing.

Methods

We propose a reproducible bioinformatic pipeline providing a network representation of the ASE downstream effects in terms of differential protein-protein interactions between two different biological conditions. The pipeline is divided into three modules: the first one processes raw RNA-Seq data to perform differential gene expression and splicing analysis at both isoform- and event-based levels. The second module annotates isoforms interested by a significant switch and exons characterized by a skipping event with protein and protein domain information, respectively. The third module builds a protein-protein interaction network integrating those annotations with protein-protein and domain-domain interaction data from online databases. Then, all pairwise interactions are weighted based on the expression of isoforms containing the interacting protein domains. Finally, it displays the predicted ASE downstream consequences on protein interactions using a network formalism.

Results

This pipeline was tested on RNA-Seq data from MCF-7 breast cancer cell lines treated with ESRP1/2-targeting siRNAs, or with control. Consistently with the role of ESRP1/2 in controlling the epithelial-to-mesenchymal process, regulated genes and interactions were enriched in cell adhesion regulation, extracellular matrix remodeling and tissue morphogenesis. The results showed consistency between the network interactions and the current literature, but also highlighted novel candidate factors regulated by the ESRP1/2 pathway.

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