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Sommario	<p>Studies on membrane trafficking have expanded massively over the last 40 years. During this time, research has led to an understanding of the molecular mechanisms underlying membrane trafficking pathways, providing crucial insights into several fundamental events. Although we have gained detailed knowledge about the molecular organization of membrane trafficking machineries there is a lack of a global view of its function, organization and regulation. In addition, many genes of the membrane trafficking machinery have been associated with diseases. In the majority of cases, disease manifestation is tissue-specific despite the ubiquitous expression of the causal gene. Explanations for this phenomenon may be found either in the specific requirements and demands of a cell within a given tissue or in differences in the expression of disease gene interactors. The main aim of this project was to delineate sets of co-expressed membrane trafficking genes and proteins (membrane trafficking modules; MTMs) across tissues. For this purpose we curated a list of 1,261 genes that have been described as part of membrane trafficking machineries in different cellular organelles, around which we have developed a bioinformatics pipeline in order to address two specific questions: a) are membrane trafficking genes organized in MTMs, defined as communities of co-expressed genes,</p>

and are they associated with general cellular functions? b) do disease genes have specific membrane-trafficking co-expressed communities in those tissues that are affected by the disease? To address these questions we used data from the Genotype-Tissue Expression (GTEx) project, a catalog of human tissue-specific gene expression patterns obtained from “non-diseased” tissues sampled from recently deceased human donors. With regards to the first question, we analyzed the expression patterns of the trafficking genes in twenty-five different tissues and used weighted correlation network analysis (WGCNA) to derive highly preserved MTMs. We have analyzed in more detail one that includes genes apparently involved in collagen secretion. Instead for the second question we applied differential co-expression before the WGCNA to generate tissue-specific MTMs to understand how specific membrane trafficking gene modules might be organized in human tissues.

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Localizzazioni e accesso

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