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Resumo	Pitt-Hopkins syndrome (PTHS) is a rare neurodevelopmental monogenic disorder in the autistic spectrum caused by mutations in the Transcription Factor 4 gene. Even though the genetic etiology is known, the molecular mechanisms underlying PTHS remain poorly understood. To gain insight into the disease's pathophysiology, we set out to identify genes and pathways putatively involved in the pathology through co-expression and gene hub analyses using transcriptomic data from neural progenitor cells, neurons, and brain organoids derived from PTHS patients. Our results revealed several groups of co-expressed genes that are differentially regulated in PTHS neural cells compared to controls. These groups were enriched for genes involved in neural development and function, including synaptic transmission, membrane excitability, and cell adhesion. We identified several hub genes (highly connected nodes within gene networks that are central in these modules), including some that encode proteins involved in histone modification, synaptic vesicle trafficking, and cell signaling. Furthermore, we found that the differential expression of hub genes in PTHS neural cells was associated with altered cellular processes linked to neurodevelopment, such as cell-cell communication and irregular synaptic networks. Notably, we identified a set of hub genes related to the histone gene family, which is associated with neuronal differentiation and may contribute to PTHS pathogenesis and potentially serve as a biomarker for disease prognosis. Our results support the notion that PTHS involves alterations in neural development and function, particularly in excitatory neurons. The groups of co-expressed genes and hub genes we identified provide new insights into the molecular mechanisms underlying PTHS pathogenesis and could potentially be targeted for therapeutic intervention.

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