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Unveiling Molecular Chaperones: A Genetic Screen for Enhancing Olfactory Receptor surface expression

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Abstract

Odor detection in mammals is mediated by olfactory receptors (ORs), the largest family of G protein-coupled receptors, expressed in olfactory sensory neurons. However, most ORs show little to no cell surface expression in non-olfactory cell types, limiting our understanding of OR-ligand interactions. For ORs to reach the cell surface, they must be translated and expressed in the endoplasmic reticulum (ER), triggering the unfolded protein response (UPR) pathway, which is necessary for OR trafficking. Our lab previously identified Receptor Transporting Protein 1 (Rtp1) as a chaperone enhancing the cell surface expression of many, but not all, ORs in heterologous cells. We hypothesize that additional chaperones co-expressed with Rtp1 are crucial for relieving UPR in the ER, thereby increasing OR cell surface expression. This study utilizes publicly available transcriptomics datasets to conduct a genetic screen aimed at identifying molecular chaperones that facilitate OR cell surface expression. Our computational pipeline identified 50 gene candidates, and through in-vitro testing using cellular assays we successfully identified four genes that enhance cell surface expression in combination with Rtp1. Additionally, we developed a tool called geLine, allowing researchers to study other genes or functions of interest in a similar screening format.

Data usage references:

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