2 Aims

The aim of the current work was to characterize the final fate of intracellular retained NDI-causing V2R mutants. Little is known about the degradation pathways of GPCRs that are retained in post-ER compartments, specifically the ERGIC and Golgi apparatus. Most of the studies addressing cellular protein turnover were performed in yeast or in mammalian cells expressing wild-type receptors or mutant ER-retained proteins. Additionally, the dependence of the dominant ERAD pathway in relation to the localization of the misfolded domain within substrate proteins is not well characterized. The present work focused on the role of mammalian ERAD as a reaction to misfolded proteins bearing mutations in cytosolic, transmembrane and ER-luminal domains.