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Oral Sessions

HACE1 localized in recycling endosome regulates the recycling and degradation of β_1 -adrenergic receptor via Rab11 and Rab12.

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β_1 -adrenergic receptor (β_1 AR) is a potent regulator of cardiac function. Previously, we showed that recycling endosome (RE) is key organelle of the intracellular trafficking of β_1 AR induced by ligand stimulus. Here, we found that HACE1, an E3 ligase, is localized in RE and ubiquitinates β_1 AR internalized by the ligand isoproterenol (Iso). Silencing of HACE1 by siRNA resulted in a decline of β_1 AR on the cell surface at steady state. Given that the ubiquitinated Rab11 functions as a recycling factor, ubiquitinated Rab11 mediated by HACE1 might recycle β_1 AR to the cell surface. Ubiquitination of β_1 AR was increased by Iso treatment, which was further enhanced with either bafilomycin A₁ (BafA₁), a lysosome inhibitor or MG132, a proteasome inhibitor. β_1 AR was co-localized with Rab12 at RE and lysosome and interacted with each other. The co-localization at lysosome was strengthened in the presence of BafA₁, and the interaction was enhanced by Iso stimulus. Silencing of Rab12 led to stabilization of β_1 AR with or without Iso. These data suggest that Rab11 and Rab12 were involved in the recycling and degradation of β_1 AR through ubiquitination of Rab11 and β_1 AR mediated by HACE1 in RE, respectively.