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Internalization and degradation of natriuretic peptide receptor-A is stimulated by ligand binding

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Background

Natriuretic peptide receptor-A (NPR-A) is a transmembrane receptor guanylyl cyclase that binds and mediates the effects of atrial and B-type natriuretic peptides (ANP/BNP). Internalization and ligand-dependent degradation of NPR-A is controversial, in part due to the use of ligand binding studies to predict the cellular location of the receptor. Here, we used a more direct sequential immunoprecipitation-western blot assay to demonstrate that long-term ANP exposure increases NPR-A degradation in primary, immortalized, and transfected cells.

Results

A separate novel extracellular epitope antibody-binding assay indicated that NPR-A is internalized under basal conditions and that this rate is increased about two-fold by ANP exposure. siRNA knock down of clathrin and dominant negative inhibition of dynamin failed to inhibit ANP-dependent NPR-A degradation, whereas dominant negative dynamin expression reduced the rate of NPR-A internalization about 40%.

Conclusion

These data indicate that NPR-A is basally internalized by a dynamin-dependent pathway and that prolonged ANP exposure stimulates both NPR-A internalization and degradation.

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