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Sumoylation of the β_2ARinfluences receptor internalisation, desensitisation and downstream signaling

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Introduction: Beta 2 adrenergic receptor (β_2AR) signalling can be modulated by a variety of post-translational modifications (PTMs) which include phosphorylation, ubiquitination, palmitoylation and glycosylation [1]. Following sequence analysis of the β_2AR, we discovered a putative site for SUMOylation, a previously unknown type of modification for this receptor. Our aim was to verify whether the β_2AR can be SUMOylated and how this modification affects receptor signaling and desensitization.

Method: Using peptide array we have delineated a putative SUMO site on β_2AR. Using both wild type and SUMO-null β_2AR mutants we have investigated downstream signaling of the β_2AR using western blotting. We have "forced" SUMOylation of the receptor via overexpression of the SUMO E3 ligase PIASy.

Results: We have identified a novel site of SUMOylation on the β_2AR and shown that this modification robustly alters downstream signaling in a model cell-line. Specifically, we have demonstrated that SUMOylation reduces β_2AR phosphorylation by PKA, altering the receptor driven phospho-ERK response, inhibits β_2AR ubiquitination and degradation, and delays β_2AR internalisation.

Conclusion: We report for the first time that the β_2AR can be SUMOylated and that this retards desensitization and receptor degradation. We speculate that this mechanism may be relevant to heart disease and have developed a β_2AR SUMO-site specific antibody to investigate this possibility.

References:

1. Shenoy S *et al*. (2006). *J Bio Chem* 1261-1273.