DISTINCT STRUCTURAL REQUISITES OF THE ANGIOTENSIN II AT_1 RECEPTOR FOR DIFFERENT SIGNAL TRANSDUCTION PATHWAYS: ANALYSIS BY MUTATION OF α-HELIX PROLINE RESIDUES

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The angiotensin II receptor type 1 (AT_1) belongs to GPCRs family. In addition to classical signaling pathway by activation of G protein, the binding of AngII to AT_1 receptor also leads to activation of mitogen-activated protein kinase (MAPK) pathways, such as ERK phosphorylation. Up to date, studies of AT_1 structural requirements involved in alternative functional pathways have been limited. We have generated two proline mutants of AT_1 receptor (P82A and P162A) aiming at to comparatively investigate the behavior of these mutants on distinct pathways. Wild type and mutant-transfected 293T cells were used to perform acidification rate assays and western blotting to access activation of the classical and ERK pathways, respectively. Our results showed that Pro^{82} has a crucial participation in classical signal transduction, as the acidification rate was severely impaired, but not in ERK activation. Our data contribute to provide evidence that different structural features from the receptor are required to trigger distinct functional events. Financial support: FAPESP, FAEPA, CAPES, CNPq.