PW01-88 - **VISUALIZATION AND QUANTIFICATION OF APP INTRACELLULAR DOMAIN (AICD) MEDIATED NUCLEAR SIGNALING BY BIMOLECULAR FLUORESCENCE COMPLEMENTATION**

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Although several targets of APP intracellular domain (AICD) mediated transcriptional gene regulation have been published, the role of AICD in nuclear signaling in health and (Alzheimer´s) disease remains under debate. We previously demonstrated that AICD forms nuclear complexes with two other proteins, Fe65 and Tip60, called AFT complexes. Functionally, these co-localization areas likely represent sites of transcription. However, it is currently unknown how the formation of these complexes is regulated.

Bimolecular fluorescence complementation (BiFC) is a recently developped technique to visualize protein/protein interaction. We established a detection system based on BIFC to study the intracellular interaction of AICD, Fe65 and Tip60 in cell culture. By means of confocal microscopy the subcellular localization of the proteins was studied. The influence of several genetic mutations for familial Alzheimer´s disease as well as for caspase cleavage and phosphorylation sites was quantified by fluorescence assisted cell sorting (FACS).

Using our BiFC visualization system, we could verify known findings such as APP/APP dimerization in the membrane and the interaction of AICD, Fe65 and Tip60 in the nucleus. Our system furthermore revealed the regulatory effect of familial AD and caspase cleavage site mutations on AFT complex formation.

AFT complex formation can be effectively visualized and quantified by means of our novel BiFC constructs, thus opening new insights into the functions of the amyloid precursor protein APP.

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