# THE SYNTHESIS OF 2,5-DISUBSTITUTED PYRROLES FOR THE INHIBITION OF SOD1 AGGREGATION IN ALS

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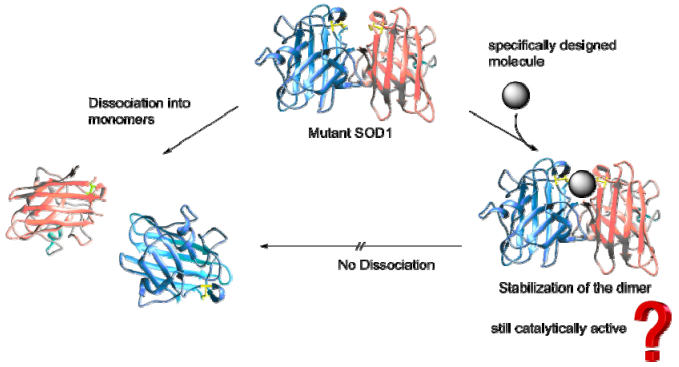
Amyotrophic lateral sclerosis (ALS) is a fatal multicausal malfunction of specific neurons which control voluntary muscles. The origin of the disease remains unknown in most cases; however, in around 10 % of all patients, ALS is inherited from a patient's parents. In these cases we talk about familial ALS (fALS)[1]. During the last decades, some pathological mutations in specific genes and/or proteins were identified to cause fALS. One example is the protein SOD1 (SuperOxide Dismutase 1). A prion-like aggregation of monomeric structures can be observed which is believed to be the prevailing reason for the ALS-associated toxicity of the mutant SOD1[2].




Our project focuses on the stabilization of the dimeric structure of the protein to retain its functionality. We identified 2,5-disubstituted pyrroles as potential aggregation inhibitors using docking studies. The substitution with aromatic acid moieties such as carboxylic acids, phosphonic acids, phosphinic acids and more will be examined to determine the suitability for an affinity-based targeting approach. Variation of the nitrogen-bound residue gives rise to a library of structures that will be examined using state of the art biophysical methods such as ITC, MST or anisotropy measurements.

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[1] L. Poppe, L. Rue, W. Robberecht, *Exp. Neurology 262*, **2014**, 138-151.

[2] S. Lee, H-Y. Kim, *Exp. Neorobiol.*, **2015**, *24(1)*, 1-7.