AMYGING – Holistically sustainable multi-modal β-amyloid imaging

AMYGING aims at developing a sustainable nanoparticulate bimodal imaging system for early stage detection of misfolded Aβ-amyloid, exploiting the tremendous potential of the *Danio rerio* (zebrafish) model as an effective high-throughput screening platform for the identification of next-generation imaging agents (IAs).The envisaged IAs will be endowed with high sensitivity and specificity, with a high potential for the detection of soluble oligomers of amyloids in body fluids, allowing as such for an early-stage detection of Aβ-oligomers in the CSF of AD patients. The urgent need for novel tools able to detect pathological protein aggregates combined with the low biopharmaceutical properties of already existing agents, e.g., thioflavin T - ThT, render the search of novel fluorescent probes necessary. The PhD student develop ThT improved analogues and novel fluorescent probes. Highly conjugated heterocyclic scaffolds, e.g., the pyrroloquinoxaline scaffold, will be suitably decorated with a set of substituents, including electron-withdrawing and releasing substituents, a variety of aliphatic and (hetero)aromatic substituents, acid and/or basic functionalities. The substituents will be placed at different positions of the heterocyclic system, in order to optimize the conjugation features responsible for the fluorescence properties. Additionally, the combination of heterocyclic moieties, e.g., pyrroloquinoxaline and quinoline motifs, with polyphenolic monomers and oligomers through the use different linkers, which might even play the role of fluorescence-modulating substituents will be explored. The fluorescence of the resulting compounds will be then evaluated in different media in the presence/absence of Aβ-oligomers. A small number of selected and optimized fluorescent probes will be selected for AMYGING's nanoparticulate sensor. Standard organic chemistry approaches and synthetic methodologies developed ad hoc will be exploited for the construction of specific structural motifs exploiting the proven experience in the field of organic and heterocyclic chemistry and method development in batch and under continuous flow conditions.

References

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