Fourth WG Meeting CA15135

BOOK OF THE ABSTRACTS

COST ACTION CA15135

Final status of WG activities within the MuTaLig COST Action

Ege University, Faculty of Pharmacy, Bornova, İzmir, Pearl of the Aegean March 5th - 6th 2020

www.mutalig.eu

ACKNOWLEDGMENTS

The MuTaLig COST Action acknowledges the following institutions and sponsors for the support given to the Organizing Committee of the Fourth WG meeting.

Scientific comittee

Prof. Dr. Stefano Alcaro- Università "Magna Græcia" di Catanzaro (Italy)

Prof. Dr. Fernanda Borges- Faculty of Sciences Campo Alegre 4169-007 Porto (Portugal)

Prof. Dr. Günay Yetik Anacak- MC member Turkey and local organizer– Ege University (Turkey)

Danijel KIKELJ – (WG1 leader) University of Ljubljana (Slovenia)

Eugenio GAUDIO – (WG2 leader) Oncology Research Institute, Bellinzona (Switzerland)

Sharon BRYANT – (WG3 leader) Inte:Ligand GmbH, Vienna (Austria)

Hanoch SENDEROWITZ – (WG4 leader) Bar-Ilan University, Ramat-Gan (Israel)

Local Organizing Comittee

- Prof. Dr. Ayfer Yalçın
- Prof. Dr. Günay Yetik Anacak
- Prof. Dr. Vildan Alptüzün
- Assoc. Prof. Dr. Gönen Özşarlak Sözer
- Assoc. Prof. Dr. Yasemin Eraç
- Assoc. Prof. Dr. Gülnur Sevin
- Assoc. Prof. Dr. Zeynep Soyer
- Assistant Prof. Dr. Hüseyin İstanbullu
- Assistant Prof. Dr. Ayşe Tarıkoğulları
- Assistant Prof. Dr. Sülünay Parlar
- Dr Gülşah Bayraktar

PhD students

- Elif Alan
- Merve Saylam
- Nazlıcan Belen
- Emine Nur Özbek

Sponsors and Institutions

Poster communication 21 – WG 2

Aminoalcoholate-driven tetracopper(II) cores as inhibitors of aggregation of β-amyloid

Aleksandra M. Bondžić,[a]* Ana V. Vujačić Nikezić,[a] Alexander M. Kirillov,[b] Bojan P. Bondžić[c]

[a] *Vinča Institute of Nuclear Sciences, University of Belgrade, Belgrade, Republic of Serbia*

[b] *Centro de Química Estrutural, Instituto Superior Técnico, University of Lisbon, Lisbon, Portugal*

[c] *Institute of Chemistry, Metallurgy and Technology, University of Belgrade, Belgrade, Republic of Serbia*

aleksandrab@vin.bg.ac.rs

The major hallmark of Alzheimer's disease is the accumulation of β-amyloid (Aβ) in the brain indicating that targeting of Aβ is good strategy for therapeutic development. In our earlier study we identified aminoalcoholate-driven tetracopper(II) core compounds namely, $[O\subset Cu_4\{N(CH_2CH_2O)_3\}_4(BOH)_4][BF_4]_2$ (**1**), $[Cu_4(\mu_4\text{-}H_2edte)(\mu_5\text{-}H_2edte)(sal)_2]_n\cdot 7nH_2O$, ($H_4edte$ = N,N,N',N'-tetrakis(2-hydroxyethyl)ethylenediamine, H_2sal = salicylic acid) (**2**), and $[\{Cu_4(\mu_3\text{-}Hbes)_4(\mu\text{-}hba)\}K(H_2O)_3]_n$, H_3bes = N,N-bis(2-hydroxyethyl)-2-aminoethanesulfonic acid (**3**), as a novel class of acetyl and butyrylcholinesterase inhibitors with IC_{50} values in low micromolar range [1].

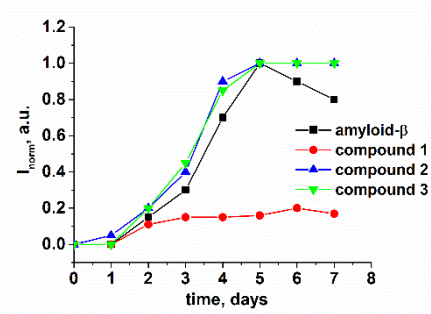

Figure 1: Fibrillation kinetics of Aβ1–40 in the absence and in the presence of compounds **1**,**2** and **3**.

In order to estimate multi target property of these compounds, we elucidated the effect of these compounds on the assembly of Aβ1–40 into amyloid fibrils, using in vitro thioflavin T (ThT) fluorescence assay. When fresh Aβ1–40 alone was incubated at 37°C, ThT fluorescence as a function of incubation time showed a sigmoidal shape (**Figure 1**). However, in the presence of **1**, ThT fluorescence did not increase, which indicated that Aβ formation was blocked. On the other hand, in the presence of **2** and **3**, changes in the fluorescence of ThT dye are not observed compared to control. Correlating this effect with structural or compositional features of investigated compounds, we concluded that the charge of the compounds might play a key role in Aβ recognition and amyloid inhibition indicating that positive charged compounds may act as multi target compounds for the treatment of Alzheimer's disease.

References

[1] Bondžić, A.; Senćanski, M.; Vujačić Nikezić, A.; Kirillova, M.; André, V.; Kirillov, A.; Bondžić, B. Aminoalcoholate-driven tetracopper(II) cores as dual acetyl and butyrylcholinesterase inhibitors: experimental and theoretical elucidation of the mechanism of action. J. Inor. Biochem. doi 10.1016/j.jinorgbio.2019.110990