

Porto, 29 October 2023

To whom it may concerns

Herein I give my assessment of the PhD thesis presented by Ms Agnieszka Olejarz-Maciej entitled " Multidirectional activity of new histamine and adenosine receptor ligands", that allows the PhD candidate to obtain the International PhD degree.

The PhD thesis document showed that the PhD student has been able to independently complete an academic project using relevant scientific methodologies, and thereby contribute with original and interesting research results in Medicinal Chemistry. The project is focused on the screening of diverse libraries to evaluate their Histamine H3 (H3R) as well as Adenosine A1 (A1R) and A2A (A2AR) receptors profile. In addition, monoamine oxidase screenings were also performed to look for multifunctional candidates for the treatment of neurodegenerative diseases. As mentioned in the thesis "the Knowledge about the structure-activity relationship in group of ligands characterized by biased signalling can help to develop new structures, which would be capable of selective activation of considered intracellular pathways"

A comprehensive study of the interest of the selected libraries towards different pharmacological targets related to degenerative disorders was realized. Highly diverse and very interesting results were obtained for some of them. These results are aligned with the main goals of the thesis. Some of them are suitable leads for future optimization in the development of new drugs to treat these diseases, which hopefully lead to development of new functional selective/multitarget ligands in the future.

The thesis is well written; the results are clearly described. The discussion and conclusions are well addressed. The key points are clearly presented and quotations and references to other works are accurately cited. Overall this work is undoubtedly of exceptional quality.

Considering that the candidate reaches with excellence all the merits required, at a level that corresponds to the international standard for PhD degrees, I strongly recommend Ms

Agnieszka Olejarz-Maciej to be awarded the International PhD degree. I am available for any additional comment or explanation.

Sincerely yours,

A handwritten signature in blue ink, reading "Maria Fernanda Martins Borges". The signature is written in a cursive, flowing style.

Prof. Dr. Maria Fernanda Martins Borges, Ph.D.
Associate Professor with Habilitation
Department of Chemistry and Biochemistry
Faculty of Sciences
University of Porto
Portugal