



THE UNIVERSITY OF
SYDNEY

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To: Nicolaus Copernicus University in Torun
Faculty of Biological and Veterinary Science
Dean's Office
1 Lwowska Street
87-100 Torun
Poland

Review of the Habilitation Application of Dr Akos Nemecz

Dear Members of the Habilitation Committee,

In accordance with the provisions of the Act of 20 July 2018, Law on Higher Education and Science, as well as Resolution No. 37 of the Senate of the Nicolaus Copernicus University in Toruń of 26 September 2023, I have been appointed as a reviewer in the habilitation procedure of Dr Nemecz.

I am Professor Thomas Balle at the Sydney Pharmacy School, The University of Sydney. My research has focused on the structural and functional relationships of ligand gated ion channels, in particular nicotinic acetylcholine receptors. This expertise provides me with the qualifications to evaluate the scientific achievements of Dr Nemecz, whose work lies at the intersection of structural biology, neuropharmacology, and biochemistry.

This review first confirms that Dr Nemecz meets the formal eligibility criteria for habilitation, and then evaluates his scientific achievements, broader academic contributions, and future development as an educator and researcher.

Formal Eligibility and Submitted Achievement

Dr Nemecz fulfils the statutory and institutional requirements for habilitation. He was awarded the degree of Doctor of Philosophy in Chemistry and Biochemistry at the University of California, San Diego in 2011 with a dissertation on the structural determinants of ligand selectivity in nicotinic acetylcholine receptors.

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Since then, he has pursued a consistent and independent research programme supported by competitive grants and international collaborations.

For the purposes of habilitation, Dr Nemecz has submitted thematically related scientific articles published between 2011 and 2024. These articles, appearing in respected international peer-reviewed journals, constitute a coherent body of work centred on the structure, function, and pharmacological modulation of pentameric ligand gated ion channels, particularly nicotinic acetylcholine receptors.

Although separate co-author declarations have not been provided in all cases, Dr Nemecz refers to statements contained in the published works themselves and provides clarifications where possible. Based on my expertise, I note that this body of research is highly interdisciplinary and that middle author positions often reflect substantial technical and conceptual input. On this basis, the submitted achievement meets the formal requirements of originality, thematic coherence, and significance for the development of biochemistry.

Evaluation of Scientific Achievements

Dr Nemecz's publications advance understanding of receptor activation, allosteric modulation, and intracellular regulation, while also introducing nanobodies as modulators and research tools. His early work made use of prokaryotic ion channels such as ELIC and GLIC at a time when high-resolution structures of mammalian receptors were not yet available. These studies were state of the art when undertaken and remain conceptually important, even though subsequent cryo-EM work has provided direct human receptor structures. A fair limitation is that some conclusions were derived from non-mammalian receptors, which limits direct translational impact, but this reflects the state of the field rather than a shortcoming of the candidate and their research. Importantly, Dr Nemecz has since pivoted towards mammalian receptors and nanobody-based modulators, demonstrating adaptability.

Among the significant contributions are:

- Nemecz Á., Hu H., Fourati Z., Van Renterghem C., Delarue M., Corringer P-J. (2017), PLoS Biology, which systematically mapped proton sensors in GLIC.

This paper has 28 citations and is recognised as a reference point in pLGIC research.

- Hu H., Nemecz Á., Fourati Z., Van Renterghem C., Sauguet L., Corringer P-J., Delarue M. (2018), PNAS, which described a bacterial receptor stabilised in an open state. With 29 citations, this study combined electrophysiology and crystallography to provide strong mechanistic insights.

Both appear in Q1, high-impact journals, reflecting the standing of the work.

Dr Nemecz also explored the intracellular domains of mammalian nicotinic receptors using chimeric receptors. This was a well-chosen direction, even though the rapid publication of an $\alpha 7$ intracellular structure by others limited the novelty of the planned outputs. The work nonetheless demonstrates foresight and commitment to addressing important and technically challenging aspects of receptor regulation.

More recently, Dr Nemecz has focused on nanobody engineering.

Li Q., Nemecz Á. et al. (2023) in Cell and Molecular Life Sciences reported nanobodies as silent and positive allosteric modulators of $\alpha 7$ receptors. Despite being very recent, this article has already attracted 8 citations and shows rapid uptake in the community.

Nemecz D., Nowak W.A., Nemecz Á. (2024) in Journal of Medicinal Chemistry provided a comprehensive review of nanobody applications across pLGICs, positioning Dr Nemecz as a thought leader in this emerging area.

Taken together, these publications demonstrate originality, methodological rigour, and impact. They show a trajectory from foundational mechanistic work through to cutting-edge biologics, maintaining coherence around the central theme of nicotinic receptor structure and function.

Additional Academic Contributions

Teaching and supervision are present in the dossier but are less extensive than the research record. It should be emphasised that opportunity has been limited as the candidate was employed on research funding for a large period of this time. The documents list courses and seminars taught, yet it is not clear what Dr Nemecz regards as his main teaching achievements. At this stage, supervision of doctoral students is limited, with no completed PhDs listed. While understandable for his career stage, it will be important to expand this area in the coming years.

Dr Nemecz has a record of organisational involvement earlier in his career, notably in graduate student representation at UCSD and as a departmental representative at the Institut Pasteur. In his current role at Nicolaus Copernicus University, he has contributed to collaborative projects, laboratory organisation and the coordination of interdisciplinary research teams. However, evidence of broader service contributions to the academic community, such as engagement in faculty committees, conference organisation or institutional governance, is not prominent in the dossier and may warrant further elaboration.

International collaboration is a clear strength. Dr Nemecz has studied and worked in the United States and France and continues to collaborate with leading groups internationally. His integration into high-profile consortia and ability to contribute meaningfully across disciplinary boundaries is evident.

Popularisation of science is not prominent in the dossier. While not required, it may provide an additional avenue for strengthening his profile.

Critical Remarks and Questions to be Asked at the Habilitation Colloquium

The following points are offered in a constructive spirit, with the aim of supporting Dr Nemecz's future development as an academic:

- 1) The teaching record could be more clearly articulated. What is Dr Nemecz's teaching philosophy, and what would he like to achieve as an educator in biochemistry?
- 2) Beyond the number of courses taught, what does he consider his key achievements in teaching to date? Has he introduced innovative methods, developed new materials, or influenced student learning in measurable ways?
- 3) How does he plan to develop his role as a supervisor of doctoral students and postdoctoral researchers, and what strategies will he adopt to support their professional growth?
- 4) What directions does he intend to pursue in the next stage of his research? How will he consolidate his expertise and ensure continued originality and impact in the study of ligand gated ion channels, nicotinic acetylcholine receptors, and nanobody-based modulators?
- 5) How does he see his potential role in contributing to the broader academic life and governance of the university outside of his research activities?

These are not criticisms but points for reflection and discussion during the habilitation colloquium.



Summary and Conclusion

The habilitation dossier of Dr Nemecz presents a strong and coherent body of work in Natural Sciences/Biological Sciences. His research has addressed fundamental mechanisms of receptor activation and modulation and has progressed to the development of innovative nanobody-based tools. The scientific merit is evidenced by publications in high-impact journals and a solid citation record, with several highly cited works recognised as references in the field. His recent nanobody work demonstrates originality and translational promise.

Teaching and supervision are less well developed, and I encourage Dr Nemecz to articulate his philosophy and plans more clearly. Nevertheless, his international collaborations, interdisciplinary expertise, and demonstrated scientific leadership show academic maturity.

In conclusion, I find that the scientific achievements of Dr Nemecz constitute a significant and original contribution to the discipline of biochemistry and that they meet the statutory and institutional requirements for the award of the degree of doktor habilitowany.

I therefore issue a **positive recommendation** for the conferment of the habilitation degree.

Yours sincerely,

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