SCIENCES & BIOENGINEERING SCIENCES

The Research Group
Structural Biology Brussels

has the honor to invite you to the public defense of the PhD thesis of

Tamás Lázár

to obtain the degree of Doctor of Bioengineering Sciences

Title of the PhD thesis:

In silico analysis of short linear peptide motifs in intrinsically disordered proteins

Promotor:
Prof. dr. Peter Tompa
Co-promotor:
Dr. Mainak Guha Roy

The defense will take place on

Friday, December 18, 2020 at 4 p.m.

The defense can be followed through a live stream. Contact Tamas.Lazar@vub.be for more information

Members of the jury

Prof. dr. Wim Vranken (VUB, chair)
Dr. Inge Van Molle (VUB, secretary)
Prof. dr. Tom Lenaerts (VUB)
Prof. dr. Sonia Longhi (AFMB laboratory, Center for the National Scientific Research, Marseille)
Prof. dr. Lennart Martens (VIB-UGent Center for Medical Biotechnology)

Curriculum vitae

Tamas Lazar obtained MSc degree in Medical Biotechnology at the Pazmany P. Catholic University and Semmelweis University in Budapest, Hungary. His Master thesis works was carried out at the Hungarian Academy of Sciences. He joined Prof. Peter Tompa's lab at VUB in April 2016. His PhD career resulted in 10 peer-reviewed papers, and he presented his work at international conferences. He is a member of the Belgian Society of Biochemistry and Molecular Biology, IDP-central, and the ELIXIR – IDP User Community.

Abstract of the PhD research

Intrinsically disordered proteins (IDPs) are difficult to superimpose for comparative analyses due to their highly dynamic nature, which is commonly characterized by conformational ensembles. IDPs function by binding partner proteins, usually via short linear peptide motifs (SLiMs) that may fold upon binding a partner, or remain "fuzzy" in the complex. Despite the general importance of in-depth characterization of their interactions, the current understanding of their binding mechanisms and specificities is still limited, their systematic analysis has not yet been attempted.

In the thesis, I detailed the development of two state-of-the-art curation projects of IDPs for open access bioinformatics databases (DisProt 8 and PED 4). I described the computational pipeline for the local, non-local and global structural comparison of IDPs, and the benefits of using intramolecular distance-based measures on various systems of fully disordered and partially disordered IDP ensembles. I carried out the first large-scale covariation analysis of mutually folded IDPs and IDPs that bind globular proteins usually via linear binding motifs. These groups of protein complexes lack strong coevolutionary signals due to the modest binding strength, as pointed out by the correlation we found between the covariation and binding affinity. I worked on two systematic analyses of SLiM-type degradation motifs (a.k.a. degrons), one on the benchmarking of peptide-protein docking tools; and another on the modulation of degradation by motif masking and the discovery of co-degrading subnetworks that we termed degronons.