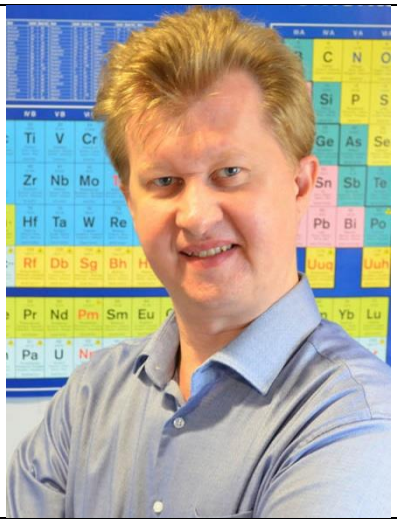

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Biography

Vladimir Torbeev received his Ph.D. degree in Chemistry from the University of Chicago under direction of Prof. Stephen B. H. Kent for the work dedicated to total chemical synthesis and biophysical studies of HIV-1 protease. Then, he performed postdoctoral studies in the group of Prof. Donald Hilvert at ETH Zurich working on molecular mechanism of misfolding and aggregation of β2-microglobulin. Since March 2014 he is a group leader at Institut de Science et d'Ingénierie Supramoléculaires and an assistant professor at the University of Strasbourg. His current areas of research are intrinsically disordered proteins, protein design, protein misfolding and aggregation and development of novel approaches for chemical synthesis of protein libraries.

Abstract title: Making order out of protein disorder

Intrinsically disordered proteins (IDPs) are highly abundant in eukaryotes and play key roles in molecular recognition, regulation and signalling. Gene transcription machinery is particularly rich in IDPs with most of the transcription factors possessing IDP domains. Thus, IDPs represent attractive targets to interfere with gene transcription. However, regulating the functions of IDPs by classical approaches using small molecules is challenging because IDPs do not have well-defined hydrophobic binding pockets. Furthermore, due to their malleable nature the structural characterization of IDPs is also difficult. Recently, my team introduced an approach to interfere with the complex formation formed by IDPs via conformational editing of an intrinsically disordered domain itself through the introduction of conformationally constrained non-canonical α-methylated amino acids [1,2]. A modified variant of the disordered activation domain 1 (AD1) from activator for thyroid and retinoid receptors (ACTR) was discovered that possessed an enhanced affinity to the nuclear coactivator binding domain (NCBD) of the cancer-related transcriptional co-activator CBP. In addition, using the best binding ACTR variant, we succeeded to crystallize the ACTR/NCBD complex for the first time and determined its high accuracy X-ray structure. Our results provide insights with atomic precision into properties of the "fuzzy" ACTR/NCBD protein complex - a truly peculiar class of protein complexes.

References:
[1] Schmidtgall et al. *Chem. Commun.* **2017**, *53*, 7369
[2] Bauer et al. *ChemRxiv* **2019**, doi: 10.26434/chemrxiv.10113128.v1