SCIENCES & BIOENGINEERING SCIENCES

The Research Group

Structural Biology Brussels

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

Junaid Ahmed

to obtain the degree of Doctor of Bioengineering Sciences

Title of the PhD thesis:
Unraveling the role of liquid-liquid phase separation in amyotrophic lateral sclerosis and prostate cancers

Promotor:
Prof. dr. Peter Tompa

The defense will take place on
Thursday, April 27, 2023 at 17h30 in auditorium D.2.01

Members of the jury

Prof. dr. ir. Eveline Peeters (VUB, chair)
Prof. dr. ir. Remy Loris (VUB, secretary)
Prof. dr. Janine Brünner (VUB)
Prof. dr. Luc Leyns (VUB)
Prof. dr. Ludo Van Den Bosch (KU Leuven)
Prof. dr. ir. Yann Sterckx (UAntwerpen)
Prof. dr. Pedro Martins (Universidade Nova de Lisboa)

Curriculum vitae

Junaid Ahmed received his first master's degree in pharmaceutical science (Pharm-D) from the University of Lahore in Pakistan. He then worked in a pharmaceutical company before enrolling in the interuniversity program in molecular biology (IPMB) at Vrije Universiteit Brussel in 2015. After graduating in 2017, he was awarded an FWO fellowship and began his PhD in the laboratory of Prof. Peter Tompa. Junaid's research has resulted in three peer-reviewed international publications, and he has presented his work at several international conferences. During his PhD, he has supervised two master thesis students, and guided different practical courses.

Abstract of the PhD research

Classically, it has been described that compartmentalization in cells can be achieved by membrane-bound organelles, e.g., the nucleus and mitochondrion. Recent advance in molecular and cell biology have unraveled a novel class of organelles called membranelles organelles (MLOs), which do not possess membranes. Some examples of MLOs are the nucleolus in the nucleus, and stress granules in the cytoplasm. These MLOs are essential for cellular functions such as sequestering of cellular material, targeting biochemical processes, and buffering protein and RNA components. In all, they play key roles in sensing and responding to environmental changes. Due to their central cellular roles, they are also frequently involved in diseases.

MLOs form by a process called liquid-liquid phase separation (LLPS), which results in demixing of a homogenous mixture into two phases, a dense and a light phase. The dense phase can contain the protein at concentrations up to 100-fold higher than the light phase.

In this thesis, LLPS was studied by focusing on the menin-androgen receptor-mixed lineage leukemia (menin-AR-MLL) protein complex in prostate cancer (PC), and dipeptide repeats (DPRs) in amyotrophic lateral sclerosis (ALS). These two systems were studied by a range of biophysical techniques as well as different *in cellulo* and *in vivo* assays. These experiments were carried out in several cell lines, e.g., HEK 293, U20S, neuro 2a and LNCAP cells, and also in *in vivo* zebrafish models.

My observations have shed light on the role of LLPS in physiological processes, such as transcription regulation, as well as in pathological processes that drive PC and ALS. In the not too far future - as I also demonstrate in my thesis -, my results may also enable us to devise novel ways of drug development, especially through targeting DPR-mediated LLPS in ALS and the menin-AR-MLL system in PC.