DRF: Thesis SL-DRF-19-0564

RESEARCH FIELD

Structural biology / Life Sciences

TITLE

Intrinsically disordered proteins and their role in stress response

ABSTRACT

Intrinsically disordered proteins (IDPs) represent a significant population of all proteomes, for which standard structural biology is not adapted due to inherent conformational disorder. The development of meaningful descriptions of the behaviour of IDPs is a key challenge for contemporary structural biology. In order to understand how these proteins carry out their function, atomic resolution ‘movies’ of the dynamics and interaction modes of these proteins are necessary. The PhD candidate will join an active group in this field, combining high field NMR spectroscopy, with single molecule fluorescence spectroscopy (FRET), small angle X-ray and neutron scattering as well as state of the art molecular simulation, to develop a complete picture of the structural and dynamical basis of molecular function and malfunction in IDPs. It has recently been discovered that some IDPs may play a yet more intriguing role, in protecting organisms against stress, for example by inducing liquid-liquid phase separation to form membraneless organelles within the cell, a process that has recently been discovered to control numerous essential cellular processes. In particular, Tardigrades are microscopic aquatic organisms that have been observed to exhibit tolerance to long-term exposure to extreme conditions, such as dessication, extreme pressure, radiation and temperature. IDPs that are overexpressed in Tardigrades (T-IDPs) appear to be responsible for this stress response. We will investigate the molecular basis of the protective function of T-IDPs which is currently unknown. This will be the first study of the dynamics of T-IDPs at atomic resolution, over the entire range of temperatures and stress conditions that induce these protective phase transitions.Intrinsically disordered proteins (IDPs) represent a significant population of all proteomes, for which standard structural biology is not adapted due to inherent conformational disorder. The development of meaningful descriptions of the behaviour of IDPs is a key challenge for contemporary structural biology. In order to understand how these proteins carry out their function, atomic resolution ‘movies’ of the dynamics and interaction modes of these proteins are necessary. The PhD candidate will join an active group in this field, combining high field NMR spectroscopy, with single molecule fluorescence spectroscopy (FRET), small angle X-ray and neutron scattering as well as state of the art molecular simulation, to develop a complete picture of the structural and dynamical basis of molecular function and malfunction in IDPs. It has recently been discovered that some IDPs may play a yet more intriguing role, in protecting organisms against stress, for example by inducing liquid-liquid phase separation to form membraneless organelles within the cell, a process that has recently been discovered to control numerous essential cellular processes. In particular, Tardigrades are microscopic aquatic organisms that have been observed to exhibit tolerance to long-term exposure to extreme conditions, such as dessication, extreme pressure, radiation and temperature. IDPs that are overexpressed in Tardigrades (T-IDPs) appear to be responsible for this stress response. We will investigate the molecular basis of the protective function of T-IDPs which is currently unknown. This will be the first study of the dynamics of T-IDPs at atomic resolution, over the entire range of temperatures and stress conditions that induce these protective phase transitions.

LOCATION

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Place: Grenoble
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