INSTITUTIONEN FÖR KEMI OCH MOLEKYLÄRBIOLOGI

Structural and Interaction Studies of the Human Protein Survivin

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Abstract

Cell division and cell death (apoptosis) are two essential processes to maintain the specific number of cells in all multicellular organisms. In humans, the misregulation of these processes leads to severe diseases, such as cancer, and neurological, inflammatory or autoimmune diseases. Proteins are the most versatile macromolecules in all living organisms and are the orchestra directors of the majority of cellular processes. Their three-dimensional structure and the interaction with other molecules are essential for their correct biological function.

This work focus on small human protein survivin which plays an important role in cell division and apoptosis, and has been extensively reported in clinical research. Our aim was to discover new interaction partners of survivin, and to study their specific binding and structure to better understand its function. We successfully used microarray peptide technology to determine new possible interaction partners and microscale thermophoresis to confirm these interactions. The direct interaction between the shugoshin-like protein family and survivin has been reported and highlights its importance in cell division.

In addition, this thesis exhibits the powerful multivariate Bayesian inference approach for data analysis by focussing on addressing X-ray crystallography problems of experimental phasing for molecular structure determination. This approach has also been successfully applied to determine the binding curve and to calculate the interaction strength between two molecules, and avoids manual treatment and human subjective bias.

Keywords: survivin, cell cycle, apoptosis, protein interactions, X-ray crystallography and Bayesian inference

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