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The control of protein synthesis in health and disease

Reporting

Project Information

PROTEIN SYNTHESIS

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Final Report Summary - PROTEIN SYNTHESIS (The control of protein synthesis in health and disease)

The proteins that are the most difficult to evaluate structurally are those which have several large, well-structured units connected by flexible linking strands. You can think of them like a plate of spaghetti and meatballs. The meatballs are big and obvious, but the spaghetti is so random and sprawling that the fine details of each strand go unnoticed. When it comes to protein structure elucidation, there is a gap in the

market for anyone willing to do battle with these challenging opponents. Their enormous size coupled with the randomness of the linking strands mean there is no single technique which can provide information on the overall structure. Biologists are beginning to look at the working life of our cells – how molecules are moved around, metabolised and synthesised – with continually increasing resolution. But on the other hand, another breed of scientists, structural biologists, are looking at the structures of enormous protein architectures. Scientists are good at both things separately, but it is sometimes hard to relate the fine details to the bigger picture; the spaghetti to the meatballs.

Did someone call for a physicist? Bartosz Rozycki, a Marie Curie fellow, currently based at the Max Planck Institute of Colloids and Interfaces, Germany, is trying to bridge that gap. Rozycki's background is in theoretical physics, which he studied first in his native Poland, and then in Germany and at the National Institutes of Health (NIH), USA. As a student he got interested in biology, and he is now using his specialist knowledge to probe deeper than ever before into some of these most challenging of protein structures. Rozycki is particularly interested in the lengthily-named Endosomal Sorting Complex Required for Transport (ESCRT for short), a protein complex of more than 2,000 amino acids, consisting of tightly-defined regions connected by stringy peptide loops. The ESCRT sorts proteins expressed on cells' surfaces into particular vesicles, which Rozycki calls the "trash cans of the cell." Periodically, these proteins get damaged or need to be swapped, so the ESCRT sorts out the chaff, packages it into vesicles and sends them off to be metabolised. That might sound like a pretty complex task for an inanimate protein to do – and it is. Scientists have been puzzling over how the packaging up process works for some time, but without knowing the structure of ESCRT they can only make guesses. What is more, ESCRT is a protein complex known to be hi-jacked by envelope viruses like HIV when, having done their dastardly work, they need to make an exit from a cell. They cannot escape from the cell without a disguise, and so they use ESCRT to package themselves into vesicles which can bud out from the cell membrane unnoticed. Again, if scientists could unravel the mechanisms, new insights into the disease pathways could be unveiled and new therapeutic strategies envisaged.

Related documents

final1-protein-synthesis-report.docx

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