Freedom for your own thoughts

How ‘ribosomes’ – the cell’s protein factories – work and execute all the different stages of protein synthesis in a fine-tuned and coordinated fashion, are being investigated by Suparna Sanyal, professor at the Department of Cell and Molecular Biology. Her research team is also studying the function of the translation factors, which ensure the genetic code is translated from messenger RNAs into proteins. One of her projects is about how antibiotics block protein synthesis and thereby stop bacterial infections.

“We are investigating the molecular mechanisms of protein synthesis. These studies are particularly important for combating antibiotic-resistance in bacteria that cause serious diseases such as tuberculosis. In the future, these studies could aid the design of new drugs against pathogenic microbes,” explains Suparna Sanyal.

The research team has also been able to produce peptides and proteins synthetically in the test tube, by reconstituting a protein synthesis system with individually purified components of the bacterial protein synthesis machinery. This is an important first step towards constructing artificial cells.

“You can add any DNA or RNA in this system and get an active protein. We have been able to build a test-tube model protein synthesis system that has virtually the same accuracy as in living cells. It covers all the stages and processes in protein synthesis, but is much easier to study than in the living cells,” says Suparna Sanyal.

Correctly folded peptide chains are essential for this test-tube protein synthesis system to work. A breakthrough came when the research team was able to show the importance of the ribosome in correct protein folding. It is well known that misfolded proteins give rise to amyloid diseases, for example Alzheimer’s and Parkinson’s diseases, and prion diseases such as scrapie, BSE and Creutzfeldt-Jakob disease. Amyloid diseases occur globally, and the number of cases is increasing.

“Prion proteins are infectious. When misfolded, they can form amyloid fibrils that can damage the brain. If we find a solution to the prion diseases, it might also be a solution to widespread diseases such as Alzheimer’s, Parkinson’s and cystic fibrosis, all of which are due to misfolded proteins,” says Suparna Sanyal.

Though this team is involved mainly in fundamental research, the long-term goal is to solve the riddle of prion and dementia diseases. Why proteins become misfolded, and how misfolding can be prevented, is what they are now trying to understand by constructing newly synthesized proteins in the test tube. To this end, the research team has also produced a bacterium with a His-tagged ribosome. It has become very popular, with over 100 institutions worldwide using it to purify ribosomes in a single step with ordinary affinity columns. Another big challenging project is to understand the role of GTP hydrolysis in protein synthesis.

In addition to all the research projects, Suparna Sanyal coordinates two Master’s programmes in biotechnology. She thinks Uppsala University combines research and education very well. As a PhD student in India, she read a lot of the literature by Uppsala researchers such as Måns Ehrenberg and Chuck Kurland. She spent two years as a postdoc in Lund before coming to Uppsala, where she has been for 16 years now. She returns to Kolkata, her home town in India, about twice a year to visit her family and friends. She also has research collaborations with the universities and research institutes there. While she can sometimes miss Indian culture and her friends, she feels very much at home here in Uppsala. When she is not researching, she likes reading. She leads and sings in the Uppsala Indian choir, which she started with her husband, senior lecturer Biplab Sanyal. And she appreciates Swedish folk music. As for research, she comments that no other system trains people as good as in research to handle failure. It is an immense privilege to be a researcher.

“As a researcher, you benefit from having the freedom for your own thoughts – and that is wonderful,” says Suparna Sanyal.