Frank Sargent

Winner of the 2009 FEBS Letters Young Scientist Award

It has by now become a tradition for FEBS Letters to award a yearly ten thousand euro prize to the best paper published in the journal by a young independent scientist. This year the choice has fallen upon Dr. Frank Sargent, Professor in Bacterial Physiology at the University of Dundee, Scotland, UK. The award-winning manuscript, entitled “Features of a twin-arginine signal peptide required for recognition by a Tat proofreading chaperone” [1], was selected for its significant contribution to the understanding of the mechanism of action of the twin-arginine transport system in bacteria.

What is the twin-arginine transport system?

About ten years ago, we discovered a new pathway through which proteins can cross membranes in bacteria [2]. The unique feature of the pathway is that it translocates fully folded proteins, and the targeted proteins are characterized by the presence of two arginines on an N-terminal signal peptide, which enables the recognition by the translocase machinery. The whole translocation apparatus is thereby called the Tat (twin-arginine translocation) system.

What is the novel finding in the award winning paper?

In the following years, we demonstrated that many Tat proteins have specific chaperone proteins that will recognize their signal peptides and bind to them, exerting a proofreading function [3]. The chaperone releases the Tat protein only after it has verified that the protein is fully folded and ready to be translocated. In the award winning study [1], we identify the residues within the signal peptide of the Tat protein TorA (trimethylamine N-oxide reductase) that are important for the recognition by its chaperone (TorD) and we propose a binding mechanism. This mode of recognition is likely to be a paradigm for all the Tat proteins and chaperones that have the same key residues in the signal peptide.

Why is it important to understand how a Tat protein and chaperone interact?

Protein interaction is the way that proteins speak to each other inside the cell. A specific interaction takes place amongst a huge soup of thousands of millions of proteins. In Escherichia coli there are 27 known proteins that use this export pathway, and that share similar signal peptides. However, the chaperone TorD is able to pick out TorA amongst them. It is crucial to learn how this happens.

What are your future plans regarding this project?

We are trying to solve the structure of the TorA–TorD protein complex. The structure will reveal whether the signal peptide changes conformation upon TorD binding, and will help understand how the release of the chaperone takes place. We suspect that a nucleotide, such as GTP, is involved in the release, but the mechanism is still unclear.

Why did you choose to publish your work in FEBS Letters?

I had set myself the deadline to publish this study in 2008. However, when the manuscript was ready for submission, it was already October. FEBS Letters always had the reputation to handle manuscripts rapidly, and also, the multidisciplinary aspect of the study seemed to fit well with the journal’s scope. FEBS Letters also presents structured digital abstracts for protein–protein interaction, which applied to our study. The structure digital abstract sounded like a novel idea, and I’m all in favour of new ideas. I hadn’t even thought about the Young Scientist Award until this little box popped up while I was submitting, asking if I wanted to participate!

I heard that you are also working on a “superbug” project… Can you tell us a little more?

Yes, the idea is to produce hydrogen gas from E. coli, that can be used as clean biofuel. We are trying to genetically modify the metabolism of E. coli, so as to force all the carbon sources that it uses towards the production of hydrogen gas. The genetically engineered E. coli is what we call the superbug. In parallel, we are also testing an in vitro system by purifying large quantities of hydrogenase and attaching it to an electrode. Electrons can be pumped into the enzyme from a solar cell, and the hydrogenase will produce the gas. This last strategy seems to be the most promising at the moment, as it can be more easily optimized, without the risk of unpredictable reactions from the bacterium.
What do you do in your spare time?

I spend time with my family. I enjoy taking my two young sons to play football or to watch matches. Those are the kinds of things I liked to do as a young boy, and I still do!

In your opinion, what are the perspectives for young scientists?

I feel they are very good. There are more and more fellowships available that provide space and understanding for those who are starting up a family as well as a new lab. In the UK, students finish their studies earlier than in other parts of the world, which gives them the chance to become independent scientists while they are in their late twenties or early thirties. It would be nice if the years of study were normalized around the world following the British model, also to give everyone an equal opportunity to win the FEBS Letters Young Scientist Award!

Would you have advice to give to young scientists applying for grants?

In my opinion, science is driven by the curiosity of scientists, and a new and good idea will always attract the grant referee’s attention, no matter what the governmental policies of funding are. I would say to a young scientist: “Don’t be afraid of lateral thinking, or to do something that has never been done before. Don’t be afraid of asking a question that has never been asked.” This is what we really need in science.

References


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Interview by Daniela Ruffell