Knowledge about RNA might be used in cancer therapy and new antibiotics

RNA is more important to all living organisms than was once thought. Anders Virtanen’s research team has looked at how RNA is regulated. They found links between a small tail on RNA, longevity and carcinogenesis.

In the cell, mRNA determines which genes are expressed as proteins. Of particular interest to Anders Virtanen’s research team is a tail known as the poly(A) tail, which is present on each mRNA. The tail regulates the mRNA molecule’s activity, synthesis and breakdown. In the mid-1990s, he discovered an enzyme that degrades the poly(A) tail. The enzyme has become something of a trademark for him. Since its discovery, they have studied how the enzyme works and moves. However, it was some time before they established its physiological significance.

“It turned out that this particular enzyme, poly(A)-specific ribonuclease, is important in controlling the length of telomeres. Telomeres are the extreme ends of our chromosomes. They are involved in central processes, such as aging, and in carcinogenesis,” says Anders Virtanen.

Cancer cells often have long telomeres because of the greatly raised levels of telomerase, the enzyme that synthesizes them. The cells become ‘immortal’ because they can divide an abnormal number of times without dying. One potential cancer therapy would therefore be to regulate the levels of telomerase in cancer cells. The unexpected discovery of the link between the enzyme poly(A)-specific ribonuclease and telomeres sprang from a phone call from a doctor in Canada just over two years ago.

“He called and told me that he had found a patient lacking the enzyme poly(A)-specific ribonuclease. Totally mind-boggling! We had been waiting so long for it. Even more amazing, the patient is still alive.

The patient has no bone marrow, and her nervous system is poorly developed. She has a much smaller brain than normal and is just over a metre tall. Nevertheless, she has survived to the age of 20,” says Anders Virtanen.

Few individuals are able to survive with this type of genetic defect. It has been virtually impossible for me to find this type of patient before, comments Anders Virtanen. They are rare, and there is no uniform clinical picture. But it is possible to find them today, thanks to the development of new large-scale genetic screening techniques that use DNA sequencing to look blindly for mutations among hundreds of thousands of patients.

Anders Virtanen’s research team has also been able to show that other types of RNA molecules, small non-coding RNAs, have poly(A) tails. The synthesis of these poly(A) tails is an important step in the maturation of small non-coding RNA molecules. The synthesized poly(A) tails exist only briefly on the immature non-coding RNA molecules before they are removed. That is why you cannot find them in healthy cells. You have to look in cells with defective poly(A)-specific ribonuclease to find these poly(A) tails, explains Anders Virtanen.

The results from the group’s work are improving our understanding of the mechanisms that regulate the critical synthesis and turnover of RNA molecules. The results are important too in the development of new drugs, such as new antibiotics. Anders mentions his company, Bioimics AB, which he started together with his colleague Leif Kirsêborn. The company develops new antibiotics that target RNA molecules as a new approach to overcoming the problem of multidrug-resistant bacteria.

Anders Virtanen enjoys being both researcher and businessman. However, he believes it is important to keep the two roles, with their very different objectives, separate. His role of researcher at the university also includes some teaching. He mentions the students’ involvement in the International Genetically Engineered Machine (iGEM), a student competition in synthetic biology, for which he is the team coach. He says it is an amazing success story, a “pure joy”, and he is proud to be a part of it. He is fascinated by the students’ commitment and drive. He almost has to put the brakes on, sometimes.

“It is a privilege to teach students. A fresh intake of 22-year-olds arrives each year. They are always 22 years old, and they keep you young yourself – at heart, at any rate. Students are a tonic for your telomeres,” laughs Anders Virtanen.

He mentions another role that he is very proud of: Inspektor, the prestigious chairmanship of Gästrike-Hälssinge Nation, one of Uppsala University’s student societies. He comments that it is probably the most enjoyable role he has ever had.