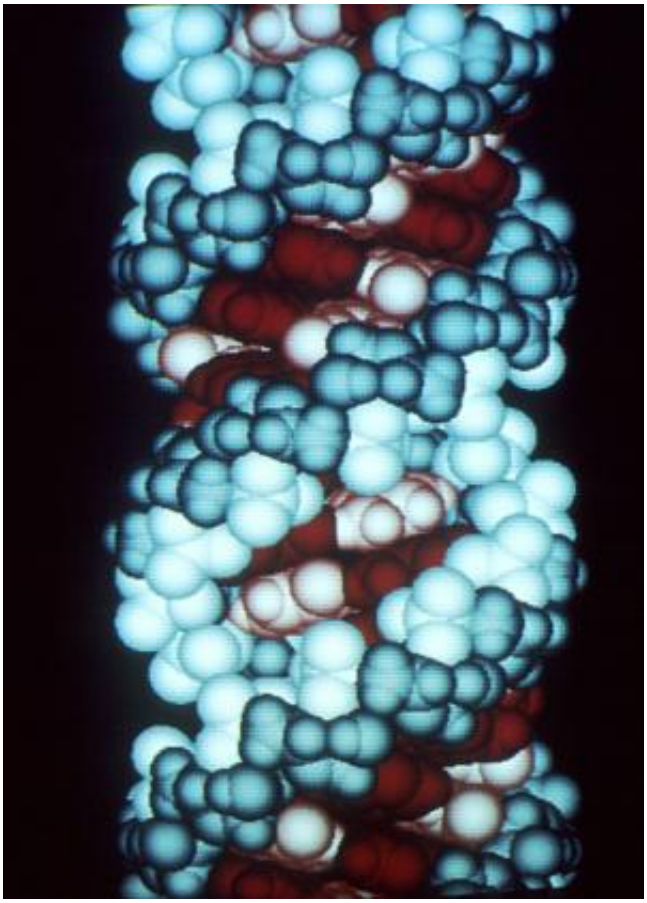
How cells master the art of reading life's recipes

July 20 2016



This is a computer graphic of an RNA molecule. Credit: Richard Feldmann/Wikipedia

A research project led by The Australian National University (ANU) has closed an important gap in the understanding of a fundamental process

of life - the creation of proteins based on recipes called RNA.

RNAs are short-lived copies of genetic information stored in DNA. They are read by cellular ribosomes, which translate the recipes into proteins to become the main building blocks of life.

Lead researcher Professor Thomas Preiss from The John Curtin School of Medical Research (JCSMR) at ANU, said the new understanding would open up avenues for treatment of a wide range of diseases including cancer, heart disease and a spectrum of rarer genetic diseases.

"We've captured a key process of life in action for the first time," Professor Preiss said. "This process of translation initiation has puzzled scientists globally for around 40 years."

The research team took snapshots of how ribosomes distribute along the RNA strings, paying particular attention to how ribosomes make sure they read the recipe from the correct starting point.

Cells throughout the body contain the same complete blueprint for life in their DNA.

"To create and maintain cells as diverse as those in the brain, bone or liver requires great precision in terms of which RNA recipes are made available, where and when," Professor Preiss said.

How efficiently and accurately ribosomes read and translate the recipes is also critical.

For example, ribosomes are known to become over-active in cancer.

"We are now applying our tools and insights to better understand what this means for their interaction with the RNA recipes during tumour

formation, with the prospect of developing new and better treatments," Professor Preiss said.

The research confirms a 40-year-old theory that explains how the ribosome correctly picks up the beginning of the code, even though the code usually only begins some distance inside the RNA string.

Research team member Dr Nikolay Shirokikh from ANU said the project examined where the two components of the ribosome started to attach to RNA strings.

"The theory was that the smaller half of the ribosome attaches itself to the very beginning of the RNA and then scans along the string until it finds the start signal of the recipe. There, the larger half joins and the whole ribosome begins to manufacture a protein," Dr Shirokikh said.

"Our ribosome snapshot approach has finally provided proof that the scanning model is correct. We also gained new insight into how fast the ribosome can complete the different tasks and how other cellular components come in to help it along."

Dr Stuart Archer, who initiated the project before moving to Monash University, said it took seven years for the researchers from ANU and Monash to develop the technique to answer a question that has puzzled scientists for 40 years.

"Many thought it couldn't be done," Dr Archer said. "It was extremely challenging, because of the transient nature of the interactions with RNA."

The ribosome snapshot data generated with the new technique was made available to scientists globally via an app for high-content data visualisation developed at the Monash Bioinformatics Platform.

The research was supported by a discovery grant from the Australian Research Council.

The research has been published in the journal *Nature*.

More information: Stuart K. Archer et al, Dynamics of ribosome scanning and recycling revealed by translation complex profiling, *Nature* (2016). DOI: 10.1038/nature18647

Provided by Australian National University