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Everests, polar bears, unpaved roads, antibiotics and the evolving ribosome

The way to elucidating the high resolution structures of ribosomes, the cellular machines that translate the genetic code into proteins, was far from being paved. It turned to be a sequence of Everest climbing, just to find out that there are taller Everests still to be climbed. Hibernating polar bears, in which ribosomes are packed orderly inspired the intimation of these studies, which were widely considered formidable. Once determined, the ribosomal structures revealed the decoding mechanism, detected the mRNA path, identified the tRNA sites, elucidated the position and the nature of the nascent proteins exit tunnel, illuminated the interactions of the ribosome with non-ribosomal factors, such as the initiation, release, recycling factors and the first chaperone encountered by the nascent chains. Furthermore, these structures proved that the ribosome is a ribozyme whose active site is situated within a highly conserved symmetrical region within the otherwise asymmetric ribosome structure, which seems to be the remnant of the proto-ribosome, an apparatus that functioned in the prebiotic era and formed peptide bonds and non-coded polypeptide chains. Structures of complexes of ribosomes with antibiotics revealed the principles allowing antibiotics clinical use, identified resistance mechanisms and showed the structural bases for discriminating pathogenic bacteria from hosts, hence providing valuable structural information for antibiotics improvement and the design of novel compound that can serve as antibiotics.

Ada Yonath was born in Jerusalem (Israel). After completing her PhD studies at the Massachusetts Institute of Technology and Carnegie Mellon University in the United States, she established the first protein-crystallography laboratory in Israel. She is currently director of the Helen and Milton A. Kimmelman Center for Biomolecular Structure and Assembly at the Weizmann Institute of Science in Rehovot (Israel). Prof. Yonath is a renowned crystallographer known for her pioneering work with the structure of ribosomes. She successfully established the use of cryo-bio-crystallography, a new technique for crystallographic studies of biological structures. Her research focussed on the mechanisms underlying protein biosynthesis which led to the discovery of the ribosomal tunnel and revealed the dynamics involved at the different steps of protein synthesis. In parallel with her colleagues Venkatraman Ramakrishnan and Thomas A. Steitz, she applied x-ray crystallography to decipher the structural basis for antibiotic selectivity, showing how it plays a fundamental role in both clinical usefulness and therapeutical effectiveness, thus paving the way for future structure-based drug design. She shared the 2009 Nobel Prize in Chemistry with Venkatraman Ramakrishnan and Thomas A. Steitz for her studies on ribosome structure and functions. She is the first Israeli woman to become a Nobel laureate and the only woman to obtain the Nobel Prize for Chemistry in the last 45 years.

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