3 Win Nobel for Ribosome Research

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From left, Venkatraman Ramakrishnan of the MRC Laboratory of Molecular Biology in Cambridge, England; Thomas A. Steitz of Yale University; and Ada E. Yonath of the Weizmann Institute of Science in Rehovot, Israel, will share the 2009 Nobel Prize in Chemistry. (Reuters)

Three scientists who showed how the information encoded on strands of DNA is translated into the thousands of proteins that make up living matter will share the 2009 Nobel Prize for Chemistry, the Swedish Academy of Sciences said Wednesday.

The trio are Venkatraman Ramakrishnan of the M.R.C. Laboratory of Molecular Biology in Cambridge, England; Thomas A. Steitz of Yale University; and Ada E. Yonath of the Weizmann Institute of Science in Rehovot, Israel. Each will get a third of the prize, worth 10 million Swedish kronors total, or $1.4 million, in a Dec. 10 ceremony in Stockholm.

Working independently and using, among other things, the X-rays generated by powerful particle accelerators and prodigious computer calculations, the three winners and their colleagues succeeded in mapping the locations of the hundreds of thousands of atoms in the giant molecular complexes inside cells known as ribosomes. In a news release, the Swedish academy said the three were being honored "for having showed what the ribosome looks like and how it functions at the atomic level."

The work, scientists said, has had important medical implications. Some antibiotics work by gumming up the ribosomes of bacteria, allowing those bacteria to be stopped at no danger to their host. The ribosome research, the academy said, is being used to develop new antibiotics.

Dr. Ramakrishnan was born in Chidambaram, India, in 1952 and obtained his Ph.D. at Ohio University. He holds United States citizenship. Dr. Steitz was born in Milwaukee in 1940 and got his Ph.D. from Harvard.

Dr. Yonath was born in Jerusalem in 1939, earned her Ph.D. at the Weizmann Institute of Science and has worked in Israel her whole life. She said on Wednesday that she was both surprised and not surprised at being awarded a Nobel Prize.

Speaking by telephone, Dr. Yonath said people had long been telling her that her project was a potential winner. But at the same time, she said, there were "many, many people with fantastic work standing in line."

She said she was working and watching over her 13-year-old granddaughter when she received the news. One of the first people who

called to congratulate her was the president of Israel, Shimon Peres, who shared a Nobel Peace Prize with the late leaders Yitzhak Rabin and Yasir Arafat in 1994.

Dr. Yonath is the fourth woman to win the chemistry prize and the first since 1964, said Thomas Lane, president of the American Chemical Society. Mr. Lane said it reflected "a tremendous change in the demographics of the field." More than 50 percent of chemistry degrees are now earned by women, he said.

In a telephone interview, Dr. Ramakrishnan said that when he was first told of the prize he thought it was a joke. "It was a bit overwhelming," he said.

Asked what he would do with the money, he laughed and said he did not even own a car, but that he might buy a new cello for his son who is a cellist in New York.

If the sequence of letters in the DNA forms the blueprint for life, ribosomes are the factory floor.

It starts in the nucleus of a cell with the master hereditary molecule DNA, which spells out the recipe for life and in particular the proteins that do all the work in the body using a four-letter alphabet of chemical bases, or nucleotides, designated by A, G, C and T.

When a gene, a stretch of DNA that contains the instructions for making a protein, is copied to make a similar stretch of single-stranded RNA, something like a mirror image of DNA, that bit of RNA floats from the nucleus over to a ribosome (there are many ribosomes, but they all have the same basic structure), where another RNA molecule reads the first one and assembles amino acids in the proper order to construct a protein.

That much biologists knew by the 1960s, but they could not go any farther without understanding the detailed structure of the ribosome, a forbidding task since it contains hundreds of thousands of atoms.

Enter Dr. Yonath. "She's the one who is really the trailblazer," said Jeremy M. Berg, director of the National Institute of General Medical Sciences.

In the late 1970s, Dr. Yonath set out to solve this problem by growing crystals of the ribosome material from a desert bacteria known as Geobacillus stearothemophilus and then irradiating it with X-rays. Passing through the layers in a crystal, X-rays are diffracted into a pattern of dots and blobs that can be read by a computer to reconstruct the internal structure of the ribosome, a technique known as X-ray crystallography that had helped decipher the double helix of DNA itself.

A trio's work has important medical implications.

But getting several hundred thousand atoms to sit for such a portrait was no easy task. It took 25,000 tries before the first ribosome crystals were created in 1980 and 20 years before the crystals were good enough to produce the X-ray patterns: millions of black dots pregnant with meaning about the arrangement of atoms in the so-called large sub unit, which makes up one of two parts of the ribosome.

Dr. Yonath's success, meanwhile, had drawn others into the field, including Dr. Steitz, who solved a key problem on how to interpret the dots on the diagram of the large sub unit, aided

by electron microscope images of the ribosome obtained by Joachim Frank, then at the Wadsworth Center in Albany and now at Columbia. Meanwhile, Dr. Ramakrishnan, who got his start in ribosomes working as a postdoctoral fellow at Yale with Dr. Steitz's colleague Peter Moore, decoded the structure of the other half of the ribosome, the so-called small sub unit.

Both Dr. Steitz and Dr. Ramakrishnan did their X-ray work at the Brookhaven National Laboratory's National Synchrotron Light Source, where intense radiation lost from whirling beams of electrons can be used for probing the properties of matter. They published their results in 2000, the same year that Dr. Yonath published her own analysis of both parts of the ribosome.

Dr. Steitz is the co-founder of the company Rib-X Pharmaceuticals of New Haven, formed to apply the ribosome research to develop and commercialize drugs for the treatment of multi-antibiotic resistant infections.

Besides the implications for biomedical research, another consequence of the ribosome work was to resolve an old "classic chicken and egg problem" about evolution, Dr. Berg of the National Institute of General Medical Sciences explained. If ribosomes are needed to make proteins but they are also made of proteins, which came first?

The answer, Dr. Berg said, is that the active core of the ribosome is made of RNA. The protein seems to have been added later, which means the ribosome is "an RNA-based machine that evolved the ability to make proteins."

If ribosomes depended on proteins to function, that would have been a paradox.

"This is a key point in evolution," Dr. Berg said, "when RNA learned to make proteins." ■