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## **Israeli scientists identify:**

## Genes that Affect Responses of Multiple Sclerosis Patients to Copaxone®

A group of Israeli scientists from the Technion – Israel Institute of Technology, the Weizmann Institute of Science and Teva Pharmaceutical Industries have recently identified genes responsible for the positive response of many multiple sclerosis patients to the drug Copaxone<sup>®</sup>. These findings may contribute to the development of personalized medicine for multiple sclerosis sufferers.

Copaxone<sup>®</sup> was the first original Israeli drug to be approved by the U.S. Food and Drug Administration (FDA), and is today marketed in over 40 countries worldwide, including the U.S.A., Europe, Australia, Latin America and Israel.

The drug molecule was the fruit of research by Prof. Michael Sela, Prof. Ruth Arnon and Dr. Dvora Teitelbaum of the Weizmann Institute's Immunology Department. It was developed for the treatment of multiple sclerosis (MS) by Teva, which produces and markets Copaxone® today.

"Until now, medical treatments for all kinds of diseases have relied on trial and error methods to determine dosage and treatment protocols," says Prof. Ariel Miller of the Ruth and Bruce Rappaport Faculty of Medicine at the Technion, and Head of the Multiple Sclerosis and Brain Research Center, Carmel Medical Center, Haifa. "But the process of fixing the correct dosage affects the efficacy of the treatment and can lead to complications in some cases." In the past few years, it has been shown that many drugs are not equally effective for every patient, and this variability is due, at least in part, to genetic differences. Finding medications and doses to suit the genetic make-up of each individual patient is likely to be more successful and to cause fewer side effects.

The new research, which deals with the genetic components of the response to Copaxone<sup>®</sup>, was recently published in the journal *Pharmacogenetics and Genomics*. It represents a significant step toward realizing this medical vision. In the collaborative study, Teva supplied DNA samples from drug-treated patients, and the genetic tests were performed at the Crown Human Genome Center of the Weizmann Institute, headed by Prof. Doron Lancet of the Institute's Department of Molecular Genetics. The scientists used state-of-the-art equipment – the first of its kind in Israel –which allows for the rapid and accurate scanning of variations in the human genome. The scientists then examined the links between the genetic markers they found and the response of MS patients to Copaxone<sup>®</sup>. They identified several genes that are tied to a positive response to the drug. "We analyzed the DNA sequences in 27 candidate genes from each patient participating in the trial," said Lancet, "and we identified two genes with a high potential for determining the response to Copaxone<sup>®</sup>. In the future, it may be possible to use this method to scan the genome of MS sufferers, to predict the response levels in advance, and to optimize the dosage and treatment protocol to suit each patient personally."





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Also participating in the research were Prof. Jacques Beckmann (formerly at the Weizmann Institute); Drs. Liat Hayardeny and Dan Goldstaub of Teva; and Iris Grossman, a joint research student at the Technion and the Weizmann Institute.

## **Copaxone® – Interface between Past and Future**

In the 1950's, Prof. Efraim Katzir of the Weizmann Institute of Science, later fourth president of the State of Israel, commenced research on the properties of proteins – the building blocks of all biological systems. This research led to the design of simple synthetic models of proteins, called "polyamino acids." His research student at the time, Prof. Michael Sela (who later became President of the Weizmann Institute and was the recipient of, among many honors, the Israel Prize), decided to test the influence of these synthetic molecules on the immune system. This research led him to the conclusion that it might be possible to use these synthetic substances to curb symptoms of multiple sclerosis – an autoimmune disease in which the body's immune system attacks proteins in the fatty layer surrounding nerve fibers, preventing the conductance of electrical signals through them. Sela, together with his student at the time, Prof. Ruth Arnon (recipient of the Israel Prize and past Vice President of the Weizmann Institute and Vice President of the Association of Academies of Sciences in Asia), and Dr. Dvora Teitelbaum, conducted a long series of experiments. These experiments eventually led to the development of Copaxone®, and clinical trials carried out by Teva showed its efficacy in treating MS. At the end of the process, in 1996, Copaxone® became the first original Israeli drug to be approved by the FDA. Today, following ten years of active sales in the U.S. and 40 countries around the world, Copaxone® has made a significant contribution to the Israeli economy.

Prof. Doron Lancet's research is supported by the Nella and Leon Benoziyo Center for Neurological Diseases; the Crown Human Genome Center; and the Laub Fund for Oncogene Research. Prof. Lancet is the incumbent of the Ralph and Lois Silver Professorial Chair in Human Genomics.

The Weizmann Institute of Science in Rehovot, Israel, is one of the world's top-ranking multidisciplinary research institutions. Noted for its wide-ranging exploration of the natural and exact sciences, the Institute is home to 2,600 scientists, students, technicians and supporting staff. Institute research efforts include the search for new ways of fighting disease and hunger, examining leading questions in mathematics and computer science, probing the physics of matter and the universe, creating novel materials and developing new strategies for protecting the environment.

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