מכון ויצמן למדע
WEIZMANN INSTITUTE OF SCIENCE

Science Tips

Publications and Media Relations Department, Rehovot, Israel 76100 Tel: 972-8-934-3852 / 56 Fax: 972-8-934-4132
http://wis-wander.weizmann.ac.il news@weizmann.ac.il December 2006

A Transplant in Time

Weizmann Institute Scientists demonstrate how tissues transplanted from pig embryos might, in the future, present a solution to genetic diseases

In hemophilia, a mutated gene prevents the production of a critical blood-clotting protein. Treatments for hemophilia and other such genetic diseases, when they exist, may consist of risky blood transfusions or expensive enzyme replacement therapy. But what if the body could be induced to begin producing these proteins, say by transplanting healthy tissue with the abilities that are lacking?

Prof. Yair Reisner and Ph.D. student Anna Aronovich of the Weizmann Institute's Immunology Department, together with colleagues, showed, in research recently published in the *Proceedings of the National Academy of Sciences* (PNAS), how such a transplant might, in the future, be made feasible.

Previous attempts to treat genetic disease by transplanting (mother to daughter) a spleen, an organ that can manufacture a number of the missing proteins in some such diseases, had made little headway due to the fact that the spleen is home to the immune system's T cells – cells responsible for the severe immune responses against the recipient known as graft-versus-host disease (GVHD).

Reisner and his team revived the idea, with a twist. Over the past several years, he and members of his lab have been experimenting with tissue transplanted from pig embryos – a possible substitute for human donor organs. From this, they have learned that for each type of tissue, there is a window of opportunity during which cells taken from the developing embryo can be most successfully transplanted. Tissues taken too early, when they are still fairly undifferentiated, may form tumors, while those taken too late can be identified as foreign, causing the host to reject them.

What if the body could be induced to begin producing these proteins, say by transplanting healthy tissue with the abilities that are lacking?

By taking spleen tissue from embryonic pigs over the course of gestation, they found that the harmful T cells are not present in the tissue prior to day 42 of gestation. The scientists also found that tissue of this age exhibits optimal growth potential as well as secreting factor VIII, the blood-clotting protein missing in hemophilic patients. Thus, the scientists fixed the ideal time for spleen transplantation at 42 days. Hemophiliac mice with spleen tissue transplanted from pig embryos at this time experienced completely normal blood clotting within a month or two of implantation.

Although a number of problems would need to be surmounted before researchers could begin to think of applying the technique to humans, the Institute team's experiment is "proof of principal" – evidence that transplanted embryonic tissue, whether human or pig, could one day help the body to overcome genetic diseases. ❙

Prof. Reisner's research receives major funding from Tissera Inc. His work is also supported by the J & R Center for Scientific Research; the Belle S. and Irving E. Meller Center for the Biology of Aging; the Gabrielle Rich Center for Transplantation Biology Research; the Abisch Frenkel Foundation for the Promotion of Life Sciences; the Loreen Arbus Foundation; the Crown Endowment Fund for Immunological Research; the Mario Negri Institute for Pharmacological Research – Weizmann Institute of Science Exchange Program; the Charles and David Wolfson Charitable Trust; Dr. and Mrs. Leslie Bernstein, Sacramento, CA; and Mr. and Mrs. Barry Reznik, Brooklyn, NY. Prof. Reisner is the incumbent of the Henry H. Drake Professorial Chair in Immunology.

Joining Forces

The "resistance movement" founded by bacteria to combat antibiotics may be losing ground. By combining key properties of two different types of weapons used by the innate defense systems of organisms, a team of scientists at the Weizmann Institute of Science has managed to design a more powerful weapon, hoping that this will provide a basis for novel and more effective antibiotics.

The first is a "magnetic" weapon – a natural antibiotic produced by all organisms. Because these antimicrobial peptides (AMPs) are positively charged, they are attracted to the bacteria's negatively charged surface like a magnet, where they can then exert their antibacterial effects. The second, "detergent-like" weapon – called a lipopeptide – is produced only by bacteria and fungi which, due to a negative charge, target mainly fungi. This weapon contains a fatty acid chain that, like similar chains in soap which dissolve dirt and oils, breaks down the fatty membranes of the fungi.

As reported in the *Proceedings of the National Academy of Sciences* (PNAS), Prof. Yechiel Shai and Ph.D. students Arik Makovitzki and Dorit Avrahami of the Biological Chemistry Department have succeeded in combining the properties of AMPs with lipopeptides – resulting in a synthetic lipopeptide that has both a positive charge and the soap-like ability to dissolve oils.

They are attracted to the bacteria's surface like a magnet, where they can then exert their antibacterial effects

By altering the length of the fatty acid chains and the sequence of positively charged amino acids, they were able to create an array of weapons. Some are active against both bacteria and fungi, while others target just one or the other. And, as if this was not enough, they managed to design these new synthetic peptides (protein fragments) to contain only four amino acids, as opposed to the 12 – 50 found in their natural forms.

These findings will hopefully open up a whole range of potential applications. The short length of the synthetic peptide makes it attractive for drug design as it would be both easier and economically cheaper to synthesize, less prone to resistance, and potentially modified to target a large range of bacterial and fungal infections.

Prof. Yechiel Shai's research is supported by the Robert Koch Minerva Center for Research in Autoimmune Disease; the Prostate Cancer Research Fund; the estate of Julius and Hanna Rosen; and the Eugene and Delores Zemsky Charitable Foundation Inc. Prof. Shai is the incumbent of the Harold S. and Harriet B. Brady Professorial Chair in Cancer Research.

Dust to Gust

The health of the Brazilian rain forest depends on dust from one valley in Africa

More than half of the dust needed for fertilizing the Brazilian rainforest is supplied by a valley in northern Chad, according to an international research team headed by Dr. Ilan Koren of the Institute's Environmental Sciences and Energy Research Department. In a study published recently in *Environmental Research Letters*, the scientists have explained how the Bodélé valley's unique features might be responsible for making it such a major dust provider.

It has been known for more than a decade that the Amazon rainforest depends for its existence on a supply of minerals washed off by rain from the soil in the Sahara and blown across the Atlantic by dust. By combining various types of satellite data, Dr. Koren and colleagues from Israel, the United Kingdom, the United States and Brazil have now for the first time managed to obtain quantitative information about the weight of this dust. Analyses of dust quantities were performed near the Bodélé valley itself, on the shore of the Atlantic and at an additional spot above the ocean.

The data revealed that some 56 percent of the dust reaching the Amazon forest originates in the Bodélé valley. They also showed that a total of some 50 million tons of dust make their way from Africa to the Amazon region every year, a much higher figure than the previous estimates of 13 million tons. The new estimate matches the calculations on the quantity of dust needed to supply the vital minerals for the continued existence of the Amazon rainforest.

The researchers suggest that the Bodélé valley is such an important source of dust due to its shape and geographic features: it is flanked on both sides by enormous basalt mountain ridges, which create a cone-shaped crater with a narrow opening in the north-east. Winds that "drain" into the valley focus on this funnel-like opening similarly to the way light is focused by an optical lens, creating a large wind tunnel of sorts. As a result, gusts of surface wind that are accelerated and focused in the tunnel lift the dust from the ground and blow it toward the ocean, allowing the Bodélé valley to export the vast amount of dust that makes a life-sustaining contribution to the Amazon rainforest.

Some 50 million tons of dust make their way from Africa to the Amazon region every year

Dr. Ilan Koren's research is supported by the Samuel M. Soref and Helene K. Soref Foundation; and the Sussman Family Center for the Study of Environmental Sciences.