



מכון ויצמן למדע

WEIZMANN INSTITUTE OF SCIENCE

Science Tips

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Positive Results

Even when the results of the basic research at the Weizmann Institute are translated directly to medical application, it may take years to reach patients. But, once in a while, a finding can change lives almost immediately.

In 2006, Prof. Nava Dekel of the Institute's Biological Regulation Department, together with doctors in the IVF unit of Kaplan Medical Center, made the surprising discovery that performing a uterine biopsy – causing a slight injury to the lining of the uterus – just before a woman undergoes *in vitro* fertilization (IVF) doubles the chances of a successful pregnancy. Although the mechanism was not

completely clear, Dekel and her team assumed that the injury provokes a response in the uterus that makes it more receptive to the embryo's implantation.

The next year, Dekel was in Toronto, Canada, giving a lecture in the framework of the Weizmann Women and Science series, organized by Weizmann Canada. That lecture was reported in detail in a local Jewish newspaper, where it caught the attention of Howard and Roslyn Kaman. After many years of undergoing unsuccessful fertility treatments, failed IVF and miscarriages, the article gave the couple new hope. They contacted Dekel by e-mail, and she referred them to Drs.

Amichai Barash and Irit Granot, who had participated in the original research along with Drs. Yael Kalma and Yulia Gnainsky of the Weizmann Institute.

The doctors in Rehovot sent, as requested, a detailed description of the procedure, which was then performed in a fertility clinic in Toronto. The result: A healthy baby girl, Hannah Esther Angel Kaman, was born this past October. ■

Prof. Nava Dekel's research is supported by the Kirk Center for Childhood Cancer and Immunological Disorders. Prof. Dekel is the incumbent of the Philip M. Klutznick Professorial Chair of Developmental Biology.

Weizmann Institute Scientists Create

Working Artificial Nerve Networks

Scientists have already hooked brains directly to computers by means of metal electrodes, in the hope of both measuring what goes on inside the brain and eventually healing conditions such as blindness or epilepsy. In the future, the interface between brain and artificial system might be based on nerve cells grown for that purpose. In research that was recently featured on the cover of *Nature Physics*, Prof. Elisha Moses of the Physics of Complex Systems Department and his former research students Drs. Ofer

Feinerman and Assaf Rotem have taken the first step in this direction by creating circuits and logic gates made of live nerves grown in the lab.

When neurons – brain nerve cells – are grown in culture, they don't form complex "thinking" networks. Moses, Feinerman and Rotem wondered whether the physical structure of the nerve network could be designed to be more brain-like. To simplify things, they grew a model nerve network in one dimension only – by getting the neurons to grow

along a groove etched in a glass plate. The scientists found they could stimulate these nerve cells using a magnetic field (as opposed to other systems of lab-grown neurons that only react to electricity).

Experimenting further with the linear set-up, the group found that varying the width of the neuron stripe affected how well it would send signals. Nerve cells in the brain are connected to great numbers of other cells through their axons (long, thin extensions), and they must receive

a minimum number of incoming signals before they fire one off in response. The researchers identified a threshold thickness, one that allowed the development of around 100 axons. Below this number, the chance of a response was iffy, while just a few over this number greatly raised the chance a signal would be passed on.

The scientists then took two thin stripes of around 100 axons each and created a logic gate similar to one in an electronic computer. Both of these “wires” were connected to a small

number of nerve cells. When the cells received a signal along just one of the “wires,” the outcome was uncertain; but a signal sent along both “wires” simultaneously was assured of a response. This type of structure is known as an AND gate. The next structure the team created was slightly more complex: Triangles fashioned from the neuron stripes were lined up in a row, point to rib, in a way that forced the axons to develop and send signals in one direction only. Several of these segmented shapes were then

attached together in a loop to create a closed circuit. The regular relay of nerve signals around the circuit turned it into a sort of biological clock or pacemaker.

Moses: “We have been able to enforce simplicity on an inherently complicated system. Now we can ask, ‘What do nerve cells grown in culture require in order to be able to carry out complex calculations?’ As we find answers, we get closer to understanding the conditions needed for creating a synthetic, many-neuron ‘thinking’ apparatus.” **I**

For the scientific paper, please see: <http://www.nature.com/nphys/journal/v4/n12/pdf/nphys1099.pdf>

Weizmann Institute Scientists Discover **How Cancer Cells Survive a Chemotherapy Drug**

What separates the few cancer cells that survive chemotherapy – leaving the door open to recurrence – from those that don’t? Weizmann Institute scientists developed an original method for imaging and analyzing many thousands of living cells to reveal exactly how a chemotherapy drug affects each one.

For research student Ariel Cohen, together with Naama Geva-Zatorsky and Eran Eden in the lab of Prof. Uri Alon of the Institute’s Molecular Cell Biology Department, the question posed an interesting challenge. To approach it, they needed a method that would allow them to cast a wide net on the one hand – to sift through the numerous cellular proteins that could conceivably affect survival – but that would let them zoom in on the activities of individual cells in detail, on the other. Letting the computer take over the painstaking work of searching for anomalies enabled the team to look at the behavior of over 1000 different proteins. Even so, it took several years to complete the project, which entailed tagging the specific proteins in each group of cancer cells with a fluorescent gene and capturing a series of time-lapse images over 72 hours. A second, fainter fluorescent marker was added to outline the cells, so the computer could identify them. A chemotherapy drug was

introduced 24 hours into this period, after which the cells began the process of either dying or defending themselves against the drug.

The team’s efforts have produced a comprehensive library of tagged cells, images and data on cancer cell proteins – a virtual goldmine of ready material

A small subset of the proteins could act unpredictably, even when the cells and drug exposure were identical

for further cancer research. And they succeeded in pinpointing two proteins that seem to play a role in cancer cell survival.

Although most of the proteins behaved similarly in all the cells, the researchers found that a small subset of them – around five percent – could

act unpredictably, even when the cells and drug exposure were identical. The scientists called these proteins bimodal, as they acted in one of two ways.

The team then asked whether any of the bimodal proteins they had identified were those that occasionally promote cell survival. They found two molecules that seem to fit the bill. One of them, known by the letters DDX5, is a multi-tasking protein that, among other things, plays a role in initiating the production of other proteins. The other, RFC1, also plays varied roles, including directing the repair of damaged DNA. When the researchers blocked the production of these proteins in the cancer cells, the drug became much more efficient at wiping out the growth.

Cohen: “This method gave us tremendous insight into how a cell responds to a drug. By conducting an unbiased study – we started with no preconceived notions of which proteins were involved – we were able to pinpoint possible new drug targets and to see how certain activities might boost the effectiveness of current drugs.” **I**

Prof. Uri Alon’s research is supported by the Kahn Family Foundation for Humanitarian Support and Keren Isra - Pa’amei Tikva.

For the scientific paper, please see: <http://www.sciencemag.org/cgi/reprint/322/5907/1511.pdf>