### Similar, Yet Different

The results of the 2010 U.S. Census are not yet available, but the results of a widescale population census taken in Israel in 2008 have recently been released. Although Israel is a much smaller country than the U.S., there appear to be many similarities, yet also distinct differences between the two. Below is a sampling of the findings:

- The average Israeli has 2.1 mobile phones; personal computers are found in 71.1% of Israeli households, and 90.8% of those homes have an internet connection.
- Some 61.8% of households own at least one car, and 18.8% have two or more.
- Homeowners account for 65.8% of the population, and 26.4% rent.
- The median age is 28 for males and 30 for females. The largest age group is comprised of those under 5 years of age, and the smallest age group is comprised of those 85 and above.
- 32.7% of families in Israel have one child, 31.4% have two, 19.7% have three, 8.6% have four, and 7.6% of families in Israel have five or more children.

### Radiation and Brain Tumors

Dr. Sigal Sadetzki, Director of the Cancer and Radiation Epidemiology Unit at Chaim Sheba Medical Center, received an ICRF Project Grant to study the long-term health effects of radiation, with particular emphasis on the brain.

Dr. Sadetzki has found that the development of brain tumors following irradiation does not happen by chance. Rather, it may be attributed to a genetic susceptibility. She suspects that mutations in a particular gene, termed BRIP1, may be the culprit, and will attempt to better identify which mutations are most significant for radiation sensitivity.

Considering the increase in exposure to relatively-high doses of radiation due to the increasing number of diagnostic procedures being routinely performed today (such as CT scan), particularly in children, identification of genetic markers for radiation sensitivity should have great significance for public health. Dr. Sadetzki’s findings should have practical implications for the development of radiation protection guidelines for the total population, and may suggest that some people should avoid exposure to ionizing radiation at all costs.

Dr. Sadetzki is also involved in several national and international epidemiological studies. She led the Israeli part of the international study that sought to assess the possible association between mobile phone use and cancer risk. Dr. Sadetzki and her husband, Eli, live in Shoham with their two daughters.

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**Also of note:** Two Israeli institutions have been named among the top 10 best international places to work for scientific researchers in the world by The Scientist, a U.S.-published magazine. The rankings of the two Israeli universities (where many ICRF-funded scientists work) placed the Weizmann Institute in the second spot and Hebrew University in the fifth. Kudos to both of these fine institutions for validating ICRF’s investment in Israeli science and kudos to our donors as well. Your continued, generous support of the work of the Israel Cancer Research Fund makes you a partner in the research work of Israel’s exceptional scientists — research that will benefit all mankind.

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**Radiation and Pancreatic Cancer**

The ICRF sponsors the most promising projects in all areas of cancer research, and while many of our scientists appear to be investigating similar avenues, they are each actually approaching their target from differing angles.

As you read through this issue of ICRF Insights, you will learn about several Israeli scientists working in areas that seem closely related, but are also very different — opposite sides of the same coin, you might say. Your continued friendship and support will help these scientists and others like them to better understand cancer’s complexities and to ultimately lead us down the path towards its cure.
RADIATION AND PANCREATIC CANCER

While Dr. Sadetzki’s research involves the study of cancer caused by radiation, Dr. Elkin’s research involves radiation for cancer treatment, with a particular emphasis on pancreatic cancer.

Metastasis, the spread of cancer cells to distant sites within the body, is what makes pancreatic cancer so lethal. This process occurs when tumor cells acquire the ability to invade blood vessel walls and tissue barriers, due to the presence of certain enzymes. Dr. Elkin has observed that increased levels of a particular enzyme, known as heparanase, may promote pancreatic tumor aggressiveness.

Since radiation therapy is often a major component of cancer treatment, used to control tumor progression and metastasis, Dr. Elkin performed a series of experiments to evaluate the biological effects of radiation on pancreatic carcinoma cells. He was quite surprised to discover that rather than killing the cancer cells, clinically-relevant doses of radiation caused the cells to invade more effectively. He also found that the radiation caused an increase in heparanase levels, and he believes that this increase is partly responsible for augmenting tumor aggressiveness after irradiation.

With the help of his ICRF Project Grant, Dr. Elkin is now investigating the molecular mechanisms underlying this phenomenon. He hopes that by using heparanase-inhibiting molecules that were developed in his laboratory at Hadassah University Hospital, he will be able to block this undesired effect, thus rendering radiation therapy beneficial for growth arrest and cell killing of pancreatic tumors.

Born in Moscow, in the former USSR, Dr. Elkin now lives in Jerusalem with his wife and four children.

GENETICS AND PANCREATIC CANCER

Despite significant advances in our understanding of the molecular mechanisms that contribute to the development of pancreatic cancer, current therapies have largely remained ineffective. In order to win the war on cancer, Dr. Katzav-Shapira believes that the identification of new and better molecular targets is absolutely essential. Using a mouse model of PDA that accurately mimics the disease’s development in humans, she will employ new experimental approaches in order to gain a better understanding of the onset and progression of PDA. The knowledge gained could ultimately lead to the design of novel targeted therapies for this type of cancer.

Born in Tel-Aviv, Israel, Dr. Katzav-Shapira has held positions at the U.S. National Cancer Institute, St. Jude’s Children’s Research Hospital in Tennessee, and McGill University in Montreal, Canada, before returning to Israel to set up her own lab. She is currently the Chairman of the Department of Experimental Medicine and Cancer Research at Hebrew University/Hadassah Medical School.

Dr. Shulamit Katzav-Shapira is also working in the pancreatic cancer research area, but she is taking a much different approach than that of Dr. Elkin - one involving genes. She is studying how two transforming genes, named K-Ras and Vav, cooperate in the development of pancreatic ductal adenocarcinoma (or PDA).

The gene, Vav, was originally identified by Dr. Katzav-Shapira during her postdoctoral studies, and was named after the sixth letter of the Hebrew alphabet because it was the sixth transforming gene detected in the laboratory. Transforming genes, also known as oncogenes, help turn normal cells into tumor cells.

GENETICS AND BREAST AND OVARIAN CANCER

Epigenetics is the study of changes in how a gene behaves that may change the behavior or appearance of cells without changing their DNA. In his project, Dr. Cohen will investigate the role of germ-line epigenetic changes as cancer risk modifiers in BRCA1/2 mutation carriers. The discovery of BRCA-related risk modifiers should ultimately lead to improved individualized cancer risk prediction and assist in the optimized timing and targeting of preventive strategies. Dr. Cohen firmly believes that by gaining insight into the epigenetic mechanisms involved in cancer formation, the door will be opened to novel approaches, to the discovery of early detection markers, and to improved clinical treatment of BRCA1 and BRCA2 mutation carriers.

Dr. Cohen and his wife, Dr. Nitza Goldenberg-Cohen, a physician-scientist at Schneider Children’s Medical Center, live in Shoham. They have two daughters in high school and one son in elementary school.

DIET, GENETICS AND BREAST CANCER

Dr. Yaron Cohen, a physician-scientist and Head of the Gynecologic Research Laboratory at Chaim Sheba Medical Center, is also studying cancer genetics, but his work involves the BRCA1 and BRCA2 genes that contribute to breast and ovarian cancers.

Carriers of a mutated BRCA1 and/or BRCA2 gene are at an increased risk for developing breast and ovarian cancers, but the fact that a sizable proportion of these carriers live to an advanced age without developing either disease suggests that other genes or lifestyle attributes may modify their cancer risk. The goal of Dr. Cohen’s ICRF Project Grant is to gain a better understanding of the role of epigenetic alterations in gynecologic malignancies.

Dr. Cohen will examine the specific mechanisms by which Vitamin D, a known inhibitor of breast cancer proliferation, can augment the tumor suppressor activity of the BRCA1 gene. Dr. Cohen and his wife, Dr. Nitza Goldenberg-Cohen, a physician-scientist at Schneider Children’s Medical Center, live in Shoham. They have two daughters in high school and one son in elementary school.

Dr. Yarden will examine the specific mechanisms by which Vitamin D and BRCA1 work in concert to regulate cell proliferation. Her studies are designed to address not only whether Vitamin D has an effect on breast cancer cells, but also on breast stem cells, which may be the precursor cells of tumors. She hopes that her work will advance the current knowledge on the tumor suppression mechanisms of BRCA1 and will eventually lead to better treatment or prevention of breast cancer.

Dr. Cohen has a long-term interest in breast cancer initiation and progression. She and her husband, Shahr, live in Hod-Hasharon. They have two daughters and two sons.
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Despite significant advances in our understanding of the molecular mechanisms that contribute to the development of pancreatic cancer, current therapies have largely remained ineffective. In order to win the war on cancer, Dr. Katzav-Shapira believes that the identification of new and better molecular targets is absolutely essential. Using a mouse model of PDA that accurately mimics the disease’s development in humans, she will employ new experimental approaches in order to gain a better understanding of the onset and progression of PDA. The knowledge gained could ultimately lead to the design of novel targeted therapies for this type of cancer.

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**GENETICS AND BREAST AND OVARIAN CANCER**

Dr. Ronit Yarden is also studying the genes that cause breast and ovarian cancers, but in a slightly different context. As Head of the Laboratory of Genomic Applications at Chaim Sheba Medical Center, Dr. Yarden is studying the interaction between diet and genetics in cancer formation.

Today, more than a decade after the discovery of the tumor suppressor gene, BRCA1, it is known that not all mutation carriers will be affected at the same age or with the same disease (ovarian vs. breast cancer). Dr. Yarden believes that there could be a window of opportunity for BRCA1 mutation carriers to decrease their chances of being diagnosed with cancer early in life by maintaining adequate nutrition. In particular, the goal of her current ICRF Project Grant is to uncover whether vitamin D, a known inhibitor of breast cancer proliferation, can augment the tumor suppressor activity of the BRCA1 gene.

Dr. Yarden has had a long-term interest in breast cancer initiation and progression. She and her husband, Shahar, live in Hod-Hasharon. They have two daughters and two sons.
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OPPOSITE SIDES OF THE COIN

More and more, scientists in Israel and all over the world are coming to the realization that cancer is not a single disease or even a single disease within each location in the body – such as the brain, breast, or pancreas. Rather, the more scientists learn about the genes, proteins, and molecular pathways that drive cancer, the more complicated a disease it becomes.

Dr. Siegal Sadetzki, Director of the Cancer and Radiation Epidemiology Unit at Chaim Sheba Medical Center, received an ICRF Project Grant to study the long-term health effects of ionizing radiation, with particular emphasis on the brain.

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