New Research Breakthroughs at UHN

Faulty Genes Can Cooperate in Breast Cancer

New research by Dr. Razq Hakem (OCI/PMH) and postdoctoral fellows John McPherson and Bénédicte Lemmers has provided new clues regarding how familial breast cancer develops.

Scientists have long known that defects in the BRCA1 gene can increase a women's risk of breast cancer. They also know that mutations in Chk2—a protein involved in the cellular response to damaged DNA—can also lead to breast cancer. But the question is, do they work together?

Dr. Hakem and his team compared breast cancer development in mice missing either of the genes, or missing both genes at the same time. Says Dr. Hakem, "Our results show that inactivation of both genes is cooperative—mice with mutations in both genes had more tumours and developed them at a faster rate than did mice with only one of the mutations."

These findings may lead to new ways of treating and preventing familial breast cancer.
Genes Dev. 2004. May 15;18(10):1144-53.
[PubMed abstract]

Institute: OCI/PMH
Division: Cell & Molecular Biology
Priority Platform: Genes, Proteins & People

Childhood Cancer Clue May Lead to New Treatments

Featured as the cover story in the June issue of Cancer Cell, new research by Dr. Rod Bremner (Krembil/TWH) and postdoctoral fellows Danian Chen, Izhar Livne-bar and Mahima Agochiya will lead to the development of new treatments for retinoblastoma, the most common eye cancer in children.

Using mice that have retinoblastoma, Dr. Bremner found that some retinal cells exhibit abnormal survival patterns—patterns that are the hallmark of cancer cells.

Says Dr. Bremner, "These cells may be partially cancer-like to begin with. They may explain why retinoblastoma, as well as other childhood cancers, develop in fewer steps than typical adult cancers. It may also help us develop drugs that interfere with the cellular development of cancers of many types."
Cancer Cell. 2004 Jun;5(6):539-551.
[PubMed abstract]

Institute: Krembil/TWH
Division: Cell & Molecular Biology
Priority Platform: Genes, Proteins & People

Targeting “Hidden” Cells Key for Ending Leukemia

New research by Dr. John Dick (TGRI/TGH), graduate student Kristin Hope, and research associate Liqing Jin may help explain why 60-90% of leukemia patients suffer a recurrence following treatment.

Using his pioneering method of studying human stem cells, Dr. Dick and his team learned that there are many different types of leukemia stem cells (LSC), just as there are different types of regular, healthy blood stem cells. Some of these LSCs are fast acting, while others can lay dormant for a long time before they become reactivated.

“Our research suggests that leukemia recurs so often because chemotherapy isn’t designed to target these dormant cells, which are essentially hiding from the treatment,” says Dr. Dick. “Now that we know they’re there, we need to figure out how to eliminate them.”

Dr. Dick predicts that similar cancer stem cells will be found for solid tumours, such as breast cancer.
Nat Immunol. 2004 May 30
[PubMed abstract]

Institute: TGRI/TGH
Division: Cell & Molecular Biology

Gene a Prospective Target for Treating Autoimmune Diseases

Recent research conducted at TGRI/TGH could lead to new therapies for diseases that result from excessive inflammation, such as sepsis and arthritis. Sepsis is a life-threatening condition caused when an immune response to infection spirals out of control and causes more harm than good.

Drs. John Marshall, Ori Rotstein, Andras Kapus, and Songhui Jia took blood samples from sepsis patients who had increased numbers of neutrophils. They found high levels of a gene called PBEF in these neutrophils, and showed that PBEF prevents neutrophils from self-destructing through a process called apoptosis.

Says Dr. Marshall, “Neutrophils attack indiscriminately, killing healthy tissue as well as destroying bacteria. They must be eliminated following infection, otherwise their prolonged attack may lead to sepsis, the leading cause of death in intensive care units.”

This research points to PBEF as a promising target for treating autoimmune diseases caused by excessive inflammation.
J Clin Invest. 2004 May;113(9):1318-27.
[PubMed abstract]

Institute: TGRI/TGH
Division: Clinical Investigation & Human Physiology and Cell & Molecular Biology
Priority Platform: Genes, Proteins & People

Gene Therapy Halts Hodgkin’s Disease in its Tracks

Exciting new research using a common cold virus to deliver gene therapy has identified a way to inhibit the growth of Hodgkin's disease (HD).

An earlier study by Drs. Tak Mak and Wen-Chen Yeh (AMDI/OCI/PMH) showed that the spread of HD was hastened in the presence of IL-13, a naturally occurring immune chemical. Building on this, Drs. Keith Stewart (OCI/PMH), Tak Mak, Andrea McCart, and Suzanne Trudel (TGRI/TGH) inserted a molecule designed to block IL-13 inside an inactive common cold virus. The virus was then injected into mice with the disease.

"In mice that received the treatment, both tumour onset and growth were delayed, and survival was increased," says Dr. Stewart. "Of equal note, when the virus was injected directly into established tumours, they shrank."

This study proves that blocking the IL-13 signaling pathway may be effective in treating HD, and further studies in humans will determine whether this treatment should be given in combination with other therapies.
Cancer Res. 2004 May 1;64(9):3271-5.
[PubMed abstract]

Institute: OCI/PMH, AMDI/OCI/PMH and TGRI/TGH
Division: Experimental Therapeutics and Cell & Molecular Biology
Priority Platform: Genes, Proteins & People

Tick-Tock of the Body Clock Under Tight Control

Research by neuroscientist Dr. Qi Wan (Krembil/TWH) provides new clues regarding how our body's internal clock keeps such good time.

Our internal clock is made up of numerous "clock cells" that all work together to control the timing of rhythmic functions such as sleeping, waking, and digestion, to name a few.

Dr. Wan's research shows that proteins called GABA-A receptors—long believed to be the principal clock regulators—are actually controlled by another protein called CKI epsilon-CKI delta.

"Our research provides evidence of an intracellular mechanism for regulating synchronization of our body's clock," explains Dr. Wan. "It is relevant for the future development of treatments for people with health problems associated with insomnia, shift work, and jet lag."
Nat Neurosci. 2004 May;7(5):489-90.
[PubMed abstract]

Institute: Krembil/TWH
Division: Cell & Molecular Biology
Priority Platform: Genes, Proteins & People

Breaking News from UHN Research

UHN Researcher Named a "Top 40 Under 40"

Congratulations to Dr. David Jaffray (OCI/PMH), who was selected as one of Canada's Top 40 Under 40 for 2003, for his leadership in the development of image guided radiation therapy. This prestigious award honours people who have reached a significant level of success

but have not yet reached the age of 40.

OCI/PMH Scientist Wins Cancer Research Award

UHN Research extends its congratulations to Dr. Frances Shepherd, recipient of the 2004 Jacqueline Seroussi Memorial Foundation for Cancer Research Award (US$150,000) for her research on malignant disease.

Also, congratulations to Dr. Shepherd who was the leader of an international study that boasts important medical advances in the treatment of advanced lung cancer. The study showed that patients who took the drug Tarceva lived an average of 42% longer than patients who did not receive the drug. Despite numerous Tarceva studies, this study is the first to demonstrate a survival advantage.

Updates

UHN Launches Global Ventures

UHN Research is pleased to announce that Dr. Brian Barber has been recruited to helm Global Ventures, a new strategic initiative that has two mandates. The first is to pursue new sources of revenue, and the second is to facilitate new collaborations with institutions around the world. Dr. Barber will work closely with the Research Business Development Office to achieve these goals.

Institute for Breast Cancer Research a Canadian First

The new IBCR located at OCI/PMH and announced on June 2, 2004 will focus on three principal areas of breast cancer research: the identification of new targets for treatment, the development of new therapies and drugs, and the expansion of clinical trials.

The centre will ultimately raise $125M in funding and has already received generous support from the Weekend to End Breast Cancer, the PMH Foundation and the Canada Foundation for Innovation. The institute, directed by Dr. Tak Mak (AMDI/OCI/PMH), is the only one in Canada solely devoted to fighting breast cancer.

<Research Fact

Dr. David Kelvin (TGRI/TGH) has identified a key immune molecule associated with SARS. The molecule, called IP-10, was found in the blood of SARS patients from the 2003 outbreak. It remained high in people who were unable to recover and who ultimately succumbed to the disease.

The findings were reported in April at the World Vaccine Congress held in Montreal.

(News Release)

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