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Research Breakthroughs at UHN

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Combined Drug-Radiation Therapy Dramatically Cuts Risk of Breast Cancer Recurrence

In a ground-breaking new multi-centre study that garnered extensive media coverage, Drs. Anthony Fyles, David McCready, and Lee Manchul (OCI/PMH) have found that the use of the drug tamoxifen combined with radiation therapy to treat breast cancer following surgery reduced the likelihood of cancer relapse to virtually zero at five years.

In this study, the researchers compared the rate of breast cancer recurrence after surgery in 769 women. Half received the combined treatment, and half received tamoxifen alone. Less than 1% of the women who received the combined treatment suffered a relapse five years after surgery, compared to almost 8% of the women who received tamoxifen alone. Those women who benefited the least from radiation treatment were patients aged 60 or older, with very small tumours. Their rate of relapse (without radiation) was 1.2%.

Says Dr. Fyles, "We didn't expect to see such a dramatic difference, but the results definitely show that post-surgery radiation therapy offers a significant benefit. Women should continue to discuss the risks and benefits of treatment with their doctors, and make decisions based on what will best work for them."

The study also involved researchers from Toronto Sunnybrook Cancer Centre (Sunnybrook and Women's College Health Sciences Centre), University of Toronto, and the British Columbia Cancer Agency.
N Engl J Med. 2004 Sep 2;351(10):963-70
[PubMed abstract]

Institute: OCI/PMH
Division: Clinical Studies Resource Centre

Inflammatory Switch May Turn Off Disease

In a paper called a landmark in the inflammation field, UHN researchers have identified a switch important in controlling the body's inflammatory response. The switch—actually a gene called Timp3—was identified by Drs. Rama Khokha (OCI/PMH) and Wen Chen Yeh (AMDI/OCI/PMH), and graduate student Dr. Fazilat Mohammed.

Reported in *Nature Genetics*, the researchers found that mice missing the Timp3 gene were unable to turn off their

OCI/PMH Joins US-Based Consortium

Research Fact

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inflammatory response following tissue injury.

"Inflammation is the way in which the body defends itself against injury and infection, but if it is not switched off when the job is done, it can cause more harm than good," explains Dr. Khokha. "Our research has identified the gene we need to target to gain control of an excessive inflammatory response. Also, it points to Timp3 as a potential treatment for inflammatory conditions. At least one arthritis drug has been shown to increase Timp3 in the body, and this finding has important implications for treating a multitude of diseases including rheumatoid arthritis, diabetes, hepatitis, and cancer, to name just a few."
Nat Genet. 2004 Sep;36(9):969-77
[PubMed abstract]

Institutes: OCI/PMH and AMDI/OCI/PMH
Divisions: Experimental Therapeutics and Cell & Molecular Biology
Priority Platform: Genes, Proteins & People

Parkinson's Lessons Applied in New Huntington's Treatment

In yet another first for UHN, Drs. Elena Moro, Andres Lozano, Anthony Lang, and William Hutchison (Krembil/TWH) used deep brain stimulation—a treatment normally reserved for treating people with Parkinson's disease—to alleviate the symptoms of a person with Huntington's disease (HD).

HD is a progressively fatal hereditary brain disorder that causes brain cells to die. As a result, people with HD lose the ability to control their movements, which can become unpredictable, stiff, and jerky in nature.

"Our results showed that deep brain stimulation effectively alleviated the movement-disorder symptoms that are associated with HD," says Dr. Lozano. "The treatment noticeably improved the patient's quality of life, and the benefit is still evident 19 months after treatment, indicating that it is long lasting."

In the future, the group plans to investigate whether varying frequencies of stimulation can be used to treat other neurological disorders.
Ann Neurol 2004. Aug 56(2):290-4
[PubMed abstract]

Institute: Krembil/TWH
Division: Applied & Interventional Research
Priority Platforms: Regenerative Medicine and Medical Technology Innovation

Regulation of Appetite a Complex Mechanism—Ask Any Dieter!

New research from Dr. Daniel Drucker's lab (TGRI/TGH) reveals that the way in which the digestive system tells the brain that it's had enough to eat is more

complicated than once thought.

It has long been known that proteins in the digestive system play an important role in communicating hunger and the feeling of "fullness" to our brain after we eat. What was not known though, is that two of these proteins —called GLP-1 and OXM—actually transfer different messages via the same receptor.

Says Dr. Drucker, "Despite the fact that GLP-1 and OXM are structurally different, they both act through the same pathway to regulate satiety, providing further evidence that the pathways regulating feeding behaviour are actually quite complex."
Gastroenterology. 2004 Aug;127(2):546-58
[PubMed abstract]

Institute: TGRI/TGH
Division: Cell & Molecular Biology
Priority Platform: Genes, Proteins & People

Infection-Fighting Cells Protected by Immune Molecule

Recent research by Dr. Tak Mak (AMDI/OCI/PMH) provides new insight into how the immune system regulates its population of CD4 cells, a special population of T cells that sit on the front lines of the body's disease-fighting army.

Dr. Mak's research shows that an immune molecule called IRF4, which their lab discovered and found to be essential for immune functions, is important for preventing these important cells from dying too soon.

Says Dr. Mak, "Seven weeks after infection, mice lacking IRF4 had virtually no CD4 cells left. Mice with IRF4 showed normal levels of these cells. This tells us that IRF4 is very important for protecting the body's disease-fighting cells from programmed cell death."

This finding has implications for an entire host of diseases including cancer and HIV, and also for patients undergoing organ transplant.
J Exp Med. 2004 Jul 19;200(2):247-53
[PubMed abstract]

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

Breaking News from UHN Research

Walkers Raise $14.7M in Second WEBC

In what's been described as the most successful fundraising event in Canadian history, 4565 walkers raised an astounding $14.7M in the second annual *Weekend to End Breast Cancer* benefiting breast cancer research at PMH.

The proceeds will support PMH's new Breast Cancer Research Institute, announced June 2, 2004, and other initiatives.

Cancer Research Awards Top $1.8M

UHN Research extends its congratulations to Drs. Alejandro Jadad, Ian McGilvray (TGRI/TGH), Ming-Sound Tsao, and Mark Minden (OCI/PMH) who together won over $1.8M from the Ontario Cancer Research Network for their projects designed to improve treatments for cancer.

TGRI/TGH Researcher Elected Into Royal Society

Congratulations to Dr. John Dick (TGRI/TGH), newly elected Fellow of the Royal Society of Canada. Dr. Dick was elected for his development of the first human xenotransplant assay for normal and leukemic stem cells. He will be inducted into the society in Ottawa on November 20, 2004.

Updates

OCI/PMH Joins US-Based Research Consortium

On August 17, 2004, OCI/PMH became part of the US-based Multiple Myeloma Research Consortium, which also includes the Mayo Clinic (Rochester), the Dana-Farber Cancer Institute (Boston) and the H. Lee Moffitt Cancer Center & Research Institute (Tampa).

The consortium will share customized tissue and data banks, as well as expertise and data to accelerate the development of new therapies for multiple myeloma.

"The benefit to Canadians is that they will have access to newer drugs to treat myeloma faster," says Dr. Keith Stewart (TGRI/TGH), a member of the consortium's leadership team.

Research Fact

The base building for the Toronto Medical Discovery Tower (TMDT) is expected to be complete by the end of 2004, and it will be ready for full occupancy in August, 2005.

When construction is completed, the 140 workers on site each day will have poured 20,000m^3 of concrete, erected 2,770,000 kg of reinforcing steel, and installed 2,500 window frames!

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Insert images adapted from archives of UHN RSS (Diane Bransch), UHN Public Affairs, Drs Rama Khokha and Anthony Fyles, NCIC.