

## **NEWS RELEASE**

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### **Variants in two genes predict deafness from chemotherapy, shows new research**

(**Vancouver – November 8, 2009**) – Researchers have identified variations in two genes that predict with high specificity which children will likely become deaf as an adverse effect of cisplatin, a lifesaving anti-cancer drug that's used to treat over one-million patients worldwide each year. It's frequently used in children to treat different types of cancer including brain, bone and liver cancers. Cisplatin is also used in adults for ovarian, lung, bladder, head and neck cancers.

The study is published online November 8<sup>th</sup>, 2009 in the journal *Nature Genetics*.

“These results are very promising because we will be able to identify a very serious adverse drug reaction using these DNA markers. This is really what personalized medicine is all about,” says Dr. Michael Hayden, the study's principal investigator.

“We need to treat disease without creating additional disability,” says co-principal investigator Dr. Bruce Carleton. “This study is an important first step in accomplishing that for cisplatin.”

“Some people may be more susceptible to an adverse reaction because they metabolize a medication differently. This may be caused by normal variations in their DNA,” says Dr. Colin Ross, the study's first author.

For this study, researchers analyzed more than 1800 genetic variations in 220 key genes involved in the absorption, distribution, metabolism, and elimination of medications and their metabolites. The researchers first studied the genes of 54 patients from BC Children's Hospital, an agency of the Provincial Health Services Authority (PHSA), who had received cisplatin. Of these children, 33 (61 per cent) suffered serious hearing loss requiring hearing aids or cochlear implants. Children with variations in the TPMT (thiopurine methyltransferase) gene and the COMT (catechol-O-methyltransferase) gene had close to 100 per cent chance of becoming deaf from cisplatin. The researchers then replicated the findings in 112 patients from children's hospitals across Canada.

Underpinning this research is the Canadian Pharmacogenomics Network for Drug Safety. The \$20.1-million national network is set up in all the major children's hospitals across Canada. Network surveillers in each hospital collect patient DNA samples and clinical data on reactions to different medications. The network's initial priority is to find the genes behind reactions to three widely used drugs: the analgesic codeine and the anticancer drugs cisplatin and anthracyclines. Network researchers are also beginning to work on adult psychiatric and cardiac medications.

“These are promising research results and we're following up with the required studies to determine the cost and benefit of screening for these DNA variants. When appropriate these findings would be incorporated into the health care system for the benefit of patients,” says Dr. Hayden. “The next step is to validate these findings in different populations, including adult patients.”

The researchers aim to develop a saliva test that would allow doctors to know with high specificity which patients are vulnerable to deafness. Presently, all children are monitored for hearing loss during cisplatin treatment.

“We’re very excited to be developing new paradigms to improve drug safety in the patients we serve,” says Dr. Carleton.

Dr. Michael Hayden is director of the Centre for Molecular Medicine and Therapeutics (CMMT) at the Child & Family Research Institute (CFRI) in Vancouver. He is University Killam professor in the department of Medical Genetics at the University of British Columbia (UBC). He is a Canada Research Chair in Human Genetics and Molecular Medicine.

Dr. Bruce Carleton is a CFRI senior clinician scientist, UBC professor of Pediatrics, and director of the Pharmaceutical Outcomes Programme (POPi) at BC Children’s Hospital and BC Women’s Hospital & Health Centre, agencies of PHSA.

Dr. Colin Ross is a research associate at the CMMT and in the UBC department of Medical Genetics.

The study was funded by Genome Canada, Genome British Columbia, CFRI, BC Children’s Hospital Foundation, UBC Faculty of Pharmaceutical Sciences, the Canadian Institutes of Health Research, Canada Foundation for Innovation, Canada Gene Cure Foundation, Canadian Society of Clinical Pharmacology, BC Clinical Genomics Network, C17 Research Network and Childhood Cancer Foundation – Candlelighters Canada, Michael Smith Foundation for Health Research, Health Canada, Pfizer Canada, Eli Lilly Canada, Merck Frosst Canada, and Janssen-Ortho.

The Canadian Pharmacogenomics Network for Drug Safety’s research hub is moving into 750 square metres of new lab space in the BC Mental Health & Addiction Research Institute co-located with CFRI in Vancouver.

CFRI conducts discovery, clinical and applied research to benefit the health of children and families. It is the largest institute of its kind in Western Canada. CFRI works in close partnership with UBC, BC Children’s and Sunny Hill Health Centre for Children, BC Women’s, PHSA, and BC Children’s Hospital Foundation. CFRI has additional important relationships with BC’s five regional health authorities and with BC academic institutions Simon Fraser University, the University of Victoria, the University of Northern British Columbia, and the British Columbia Institute of Technology. For more information, visit [www.cfri.ca](http://www.cfri.ca).

CMMT is a synergistic group of scientists and researchers who share a strong sense of commitment to solve the many genetic questions surrounding human illness and well being. Affiliated with UBC and CFRI, CMMT conducts discovery research and translates that research into effective clinical and therapeutic strategies to promote health. For more information, visit: [www.cmmt.ubc.ca](http://www.cmmt.ubc.ca).

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