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NEWS RELEASE

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Gene discovered for Weaver syndrome

New genetic testing confirms diagnosis in children with rare genetic disorder

(Vancouver – December 15, 2011) – Scientists have found a gene that causes Weaver syndrome, a rare genetic disorder that typically causes large size at birth, tall stature, developmental delay during childhood, and intellectual disability. Published today in the *American Journal of Human Genetics*, the discovery means that testing the *EZH2* gene for mutations could help families who are seeking a diagnosis for their child.

“For the families among whom we identified the gene, this discovery definitively brings the diagnostic odyssey to a close – it’s DNA confirmation that their children have Weaver syndrome,” says Dr. William Gibson, the study’s lead investigator. Dr. Gibson is a clinician scientist at the Child & Family Research Institute at BC Children’s Hospital and an assistant professor in the Department of Medical Genetics at the University of British Columbia (UBC).

“Our discovery enables DNA-based diagnostic testing for this particular disease,” says Dr. Gibson. “For physicians who suspect Weaver syndrome in one of their patients, we can now confirm it if we find mutations in *EZH2*. There may still be other Weaver syndrome genes, and we need to study more families to be sure.”

Presently, doctors diagnose Weaver syndrome by assessing a child’s face, growth, skeleton and other clinical features. People with Weaver syndrome have an oversized head, typical facial features, problems with muscle tone and joints, and differences in the way their skeleton matures. Mutations in the *NSD1* gene, which normally causes a rare disease called Sotos syndrome, are also known to cause Weaver syndrome in some cases. There may be other genes involved in Weaver syndrome that are yet to be discovered.

“Now we have an answer for these families and we are also in a position to provide answers to other families affected by this rare and difficult disease,” says Dr. Gibson. He is available to see new patients clinically for diagnosis of Weaver syndrome. As a result of this discovery, Dr. Gibson’s team now offers sequencing of the *EZH2* gene on a research basis in partnership with the Ottawa Hospital Research Institute. Dr. Gibson’s team can be contacted by email at wtgibson@cfri.ubc.ca.

Traditionally, hunting for a disease-causing gene has relied on tracking a gene throughout a family’s history. However, Weaver syndrome usually occurs only once in a family, as it is thought to be caused by a new genetic mutation in the sperm or egg that conceived the child. For this study, the investigators sought patients with Weaver syndrome from Canada and the United States. They approached Dr. David Weaver, who discovered the syndrome in 1974 and is professor emeritus of Medical and Molecular Genetics at Indiana University School of Medicine in Indianapolis. In two families that Dr. Weaver had examined, the Canadian team looked for brand new genetic mutations by comparing the DNA of affected children to DNA from their unaffected parents. Once the investigators identified *EZH2* as a candidate gene, they sequenced it in DNA samples from a third Canadian family. They confirmed that an *EZH2* mutation was in this third family’s child but not in either of her healthy parents.

EZH2 is a cancer gene that is known to be mutated in leukemia, B-cell lymphomas and some other blood cancers. The gene helps control how DNA is packaged around specific proteins, which in turn helps to regulate which groups of genes are turned off and on.

“Our finding illuminates an emerging area of biology that links developmental syndromes and cancer,” says Dr. Gibson. “It appears that some mutations in *EZH2*, if these occur early in life, produce developmental syndromes such as Weaver syndrome, whereas mutations in the same gene that occur later in life can produce cancer.”

Dr. Steven Jones is the study’s senior author who led the DNA sequencing and bioinformatics. He is head of bioinformatics and associate director of the Michael Smith Genome Sciences Centre at BC Cancer Agency, professor in the UBC Department of Medical Genetics, and professor, Molecular Biology & Biochemistry at Simon Fraser University (SFU).

This research evolved out of a new consortium called FORGE Canada (Finding of Rare Disease Genes in Canada). It is funded by Genome Canada, Canadian Institutes of Health Research, Ontario Genomics Institute, Genome Québec and Genome British Columbia. Dr. Gibson is also supported by the Child & Family Research Institute (CFRI), and Dr. Steven Jones is supported by the Michael Smith Foundation for Health Research.

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 Hospital and Sunny Hill Health Centre for Children, BC Women’s Hospital & Health Centre, agencies of Provincial Health Services Authority (PHSA) and BC Children’s Hospital Foundation. CFRI has additional important relationships with the province’s five regional health authorities and with BC academic institutions SFU, the University of Victoria, the University of Northern British Columbia, and the British Columbia Institute of Technology. For more information, visit www.cfri.ca.

BC Children’s Hospital, an agency of PHSA, provides expert care for the province’s most seriously ill or injured children, including newborns and adolescents. BC Children’s is an academic health centre affiliated with UBC, SFU, and CFRI. For more information, please visit www.bcchildrens.ca.

BC Cancer Agency, an agency of PHSA, is committed to reducing the incidence of cancer, reducing the mortality from cancer, and improving the quality of life of those living with cancer. It provides a comprehensive cancer control program for the people of British Columbia by working with community partners to deliver a range of oncology services, including prevention, early detection, diagnosis and treatment, research, education, supportive care, rehabilitation and palliative care. For more information, visit www.bccancer.ca.

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