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Singapore: Researchers at Dana-Farber/Children's Hospital Cancer Center (DF/CHCC) and several collaborating institutions have linked mutations in specific genes to each of the four recognized subtypes of medulloblastoma, the most common malignant brain tumor of children. The discovery, published in the Nature, provides doctors with potential biomarkers for guiding and individualizing treatment and reveals prospective therapeutic opportunities for countering this devastating malignancy.

The study was conducted by a research team led by Dr Scott Pomeroy, a neuro-oncologist at DF/CHCC; Dr Yoon-Jae Cho of the Stanford University School of Medicine; and Dr Matthew Meyerson of DF/CHCC.

Although overall survival in medulloblastomas hovers around 70 percent, most survivors are unable to live independently due to the lasting effects of both tumor and treatment. Over the last two years, studies by researchers including Dr Pomeroy and his colleagues have bolstered this view by dividing medulloblastoma into four molecular subtypes based on gene expression profiles and copy number variations. Each subtype has a distinct survival rate, ranging from 20-to-90 percent.

Dr Pomeroy said that, "Not only do we now know how to stratify medulloblastomas genomically, we have a firm grasp of what gene mutations drive each molecular subtype. For the first time, we'll be able to classify and treat medulloblastoma based on molecular typing, providing the best therapy with the fewest long-term consequences."

In this new study, Pomeroy and his team used next generation sequencing technologies to read the full complement of protein-coding genes (also called the exome) of tumors from 92 patients. Within these tumors the team discovered that somatic (that is, non-heritable) mutations occur at very low frequency, one-tenth to one-hundredth of that seen in cancers of adults.

Specific gene mutations clustered neatly into the four molecular subtypes, although the majority of genes (88 percent) were mutated only once in the entire tumor collection. Only 12 genes were mutated in more than one tumor, illustrating

medulloblastoma's genetic heterogeneity.

Dr Pomeroy also highlighted that, "The results reflect two emerging genetic themes seen throughout childhood tumors. First, very low mutation rates, much lower than those seen in adult tumors, and second, the importance of mutations in genes that regulate the function of the cell's growth pathways but which aren't direct components of those pathways."

The study was supported by grants from the National Human Genome Research Institute , the National Cancer Institute, the National Institute of Neurological Disorders and Stroke, the Eunice Kennedy Shriver National Institute of Child Health and Human Development, the Canadian Institutes of Health, German Cancer Aid, St Baldrick's Foundation, the Mullarkey Research Fund, the Pediatric Brain Tumor Foundation and the Howard Hughes Medical Institute.