Tumor microvesicles reveal detailed genetic information

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The Massachusetts General Hospital (MGH) research team that first discovered tumor-associated RNA in tiny membrane-enclosed sacs released into the bloodstream by cancer cells has now found that these microvesicles also contain segments of tumor DNA, including retrotransposons – also called "jumping genes" – that copy and insert themselves into other areas of the genome. The investigators' report, which has been published in *Nature Communications*, is the first to show that microvesicles are involved in transferring retrotransposons between cells.

"Retrotransposons' action of self-copying and reinserting themselves into the genome leads to genetic instability," says Johan Skog, PhD, who led the current study while an investigator in the MGH Neurology Service. "Many researchers have proposed this as a mechanism for genetic diversity and for evolution. Retrotransposons are known to be upregulated in cancer, and discovering them in microvesicles that can be found in all body fluids suggests they could be useful biomarkers to help understand tumor progression and monitor treatment response."

Skog was lead author of a 2008 study that first identified tumor-associated RNA in microvesicles, also called exosomes, released by the deadly adult brain tumor glioblastoma. To further investigate the ability of microvesicles to reflect the genetic status of tumors, in the current study the MGH team analyzed the nucleic acid contents of microvesicles from glioblastomas, from two types of pediatric brain tumors, and from malignant melanomas.

They found that the microvesicles contained tumor DNA as well as RNA and that microvesicles from one of the pediatric tumors studied had elevated levels of both DNA and RNA from the oncogene c-Myc, which correlated with the gene's expression in that tumor. "We showed that amplification of c-Myc was present in microvesicles whenever it was present in the donor cell and that microvesicle analysis can reveal oncogene expression in the original tumor," explains Leonora Balaj of MGH Neurology, the first author of the study.

High levels of retrotransposon-associated RNA sequences were also detected in tumor microvesicles, and the investigators found those microvesicles could transfer their contents into normal cells. "One of the most important functions of tumor-derived microvesicles may be modification of normal cells in the microenvironment to make them more supportive of tumor growth," says study co-author Xandra Breakefield, PhD, MGH Neurology and a professor of Neurology at Harvard Medical School.

Provided by Massachusetts General Hospital

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