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Novel technique reveals both gene number and protein expression simultaneously

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Researchers have discovered a method for simultaneously visualizing gene number and protein expression in individual cells. The fluorescence microscopy technique could permit a detailed analysis of the relationship between gene status and expression of the corresponding protein in cells and tissues, and bring a clearer understanding of cancer and other complex diseases, according to researchers who led the study.

The new technique is called the fluorescent in situ gene protein assay. It combines traditional fluorescent in situ hybridization (FISH) with the in situ proximity ligation assay, which is capable of resolving individual protein molecules.

"To my knowledge, this is the first technique that allows us to concurrently address gene activity and corresponding protein expression in the same cells," says co-principal investigator Dr. Arnab Chakravarti, chair and professor of radiation oncology and co-director of the Brain Tumor Program at the Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC - James).

"The ability to resolve gene and protein-expression changes across a tumor could help us understand what drives tumor behavior overall," Chakravarti says.

The new assay is described in the August issue of the journal *Neuro-Oncology*. For this study, principal investigator Dr. Markus Bredel, an

associate professor at the University of Alabama Birmingham, and an adjunct associate professor radiation oncology at the OSUCCC – James, along with Chakravarti and their collaborators first assayed fixed human glioblastoma tumor cells, then paraffin-embedded human glioblastoma tissue. In both cases, the researchers assayed for overexpression of a mutant form of the epidermal growth factor receptor gene, EGFRvIII, and for levels of its truncated protein in glioblastoma.

"This method has potential to perform a detailed analysis of the relationship between cancer gene status and corresponding protein expression in cells and tissues," Bredel says. "We demonstrate that the fluorescent in situ gene protein assay methodology is capable of resolving cancer gene and protein patterns simultaneously on a cell-by-cell basis, which is particularly important in heterogeneous diseases such cancers."

The implications of the assay include the following:

- It is particular relevant to cancer research due to the role of epigenetic and posttranscriptional regulation.
- The ability to correlate gene and protein information in the same cells might increase the reliability of biomarker screens.
- It might aid in therapeutic decision making when screening for only the gene or the protein yields indeterminate results.
- It can be applied to gene-transfection studies that use 'knock-in' models to study the effects of gene number on protein expression.

"We believe this assay is broadly applicable to disease-oriented and cell- and molecular-biology research," Chakravarti says.