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Research provides new insights into deadly brain cancer

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New findings by researchers at UNC Lineberger Comprehensive Cancer Center suggest that the most common form of malignant brain cancer in adults, glioblastoma multiforme (GBM), is probably not a single disease but a set of diseases, each with a distinct underlying molecular disease process. The study, published by Cell Press in the January issue of the journal *Cancer Cell,* provides a solid framework for investigation of future targeted therapies that may improve the near uniformly fatal prognosis of this devastating cancer.

"Previous work has established that gene expression profiling can be used to identify distinct subgroups of GBM," says senior study author, Dr. D. Neil Hayes from the Division of Hematology/Oncology at the University of North Carolina at Chapel Hill. "However, the exact number and clinical significance of these was unclear." Dr. Hayes and colleagues at UNC Lineberger expanded on previous GBM classification studies and used expression profiling techniques to comprehensively analyze hundreds of GBM patient samples. The group was able to reliably identify four distinct molecular subtypes of GBM tumors.

The researchers then went on to perform a unique integrative analyses across multiple platforms to look for defining characteristics associated with each subtype. Their findings were quite striking, implying that there are distinct types of GBM and that each one is associated with a specific molecular process. "We discovered a bundle of events that unequivocally occur almost exclusively within a subtype," explains Dr. Hayes.

The researchers also report that the nature of these events indicate that the underlying disease process for each subtype may involve distinct cells of origin at a specific stage of differentiation. This is finding has potential clinical significance as determining the cells of origin of GBM is critical for establishing effective treatment regimens. Clearly, given this new information, it makes sense that some drug classes would be expected to work for some tumor subtypes and not other. In support of this conclusion, Dr. Hayes's group found that response to aggressive chemotherapy and radiation differed by subtype.

Taken together, the findings represent an important step towards more rational therapies for GBM. "It appears that the simple classification into these four subtypes carries a rich set of associations for which there is no existing diagnostic test," says Dr. Hayes "This comprehensive genomic and genetic-based classification of GBM should lay the groundwork from an improved molecular understanding of GBM pathway signaling that could ultimately result in personalized therapies for groups of patients with GBM."

Provided by University of North Carolina School of Medicine