D. Neil Hayes & Katherine Hoadley Discuss Glioblastoma

New Hot Paper Commentary, March 2011

Article: Integrated Genomic Analysis Identifies Clinically Relevant Subtypes of Glioblastoma Characterized by Abnormalities in PDGFRA, IDH1, EGFR, and NF1

Left-right: Katherine Hoadley and D. Neil Hayes.

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D. Neil Hayes & Katherine Hoadley talk with ScienceWatch.com and answer a few questions about this month's New Hot Paper in the field of Biology & Biochemistry.

Why do you think your paper is highly cited? SW:

In current practice, glioblastoma (GBM) is diagnosed and treated as a single disease, yet it is widely suspected that patients with the disease have different underlying etiologies, and that some patients do worse than others. By reliably identifying four molecular subtypes of GBM, we offer a solid premise on which to build new models to understand the pathogenesis of the disease as well as suggest the means to stratify patients for different treatment regimens.

For example, it is widely known that some patients diagnosed with GBM may actually have a tumor which potentially arose from lower-grade tumors. In our work, there is a suggestion that the proneural subtype of GBM has features suggestive of such tumors. Strikingly, a fraction of these tumors also carry a mutation unique to this subtype in the gene IDH1.

While the full implications of this mutation remain to be elucidated, the opportunity to define a distinct subset of GBMs promises to open new avenues in understanding disease progression and treatment. Each of the subtypes tells a similar story.

Does it describe a new discovery, methodology, or synthesis of knowledge? SW:

This is a new synthesis of knowledge. We took individual genomic components and coordinated the

data to compile a comprehensive, integrated map of GBM. This emphasized that while key pathways were known to be disregulated in GBM, each of the subtypes disregulated the pathways in different, consistent manners.

Would you summarize the significance of your paper in layman's terms? SW:

"The roadmap of cancer the team is building will serve to guide a wide range of research extending well beyond the TCGA members, serving a global community of cancer researchers."

GBM is a deadly disease. We currently have few treatment options and changes to survival are only in units of months. Here, we identified four different types of GBM, each with a unique set of alterations. Many of the genes we found altered happen to be genes that are drug targets. This strongly suggests that we may be able to selectively target each of these types of GBM with a different subset of drugs in line with the idea of personalized medicine.

How did you become involved in this research, and how would you describe the particular challenges, setbacks, and successes that you've encountered along the way? SW:

UNC has had a long history of successful genomics research. This experience, in part, led to our part in The Cancer Genome Atlas (TCGA) project. TCGA's goal is to have a comprehensive genomic characterization of 20 different types. GBM was the first tumor type assessed by this Project. This was a large coordinated project among 13 different labs and many tissue source sites across the country to produce gene expression, microRNA expression, copy number, methylation, sequence data, pathology, and clinical data for each tumor.

It was a major success to pull together all these data types and groups to characterize GBM. In addition, these data are all publically available making this a fantastic resource for testing and/or validating GBM research.

Where do you see your research leading in the future? SW:

We expect to see similar integrated research on the other TCGA selected tumor types.

Do you foresee any social or political implications for your research? SW:

TCGA is one of the largest federally supported projects to study cancer, and as such, members of TCGA feel a deep responsibility to return benefits for the investment. This is big science, and we need to see big results if such work is to continue. We feel that this is exactly what is happening.

The roadmap of cancer the team is building will serve to guide a wide range of research extending well beyond the TCGA members, serving a global community of cancer researchers. The knowledge from these types of projects will help us make new decisions about cancer care and hopefully drive us into the world of real personalized medicine.

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