Author's response to reviews

Title: DNA methylation analysis reveals distinct methylation signatures in pediatric germ cell tumors

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Version: 3 Date: 1 November 2012

Author's response to reviews: see over
October 31, 2012

Editorial Board

BMC Cancer

Dear Dr. Storey:

I am submitting a manuscript entitled “DNA methylation analysis reveals distinct methylation signatures in pediatric germ cell tumors” by JF Amatruda et al. for consideration for publication in BMC Cancer. Germ cell tumors (GCTs) are among the most common cancers of adolescents and young adults, however very little is known about the molecular origins of GCT. The tumors display features of primitive, embryonic germ cells, and it has been suspected that developmental signaling pathways may play a role in germ cell tumorigenesis.

To understand the mechanisms behind the development of GCTs, we performed a cancer-focused DNA methylation study of 53 pediatric GCTs, the largest such study to date. We validated our findings with pyrosequencing. We found striking differences in methylation patterns among different histologic types of GCTs, defining distinct methylation classes for these tumors. Pathway analysis highlighted potential roles of several novel pathways in GCTs, including embryonic stem cell signalling. Significantly, we found significant demethylation of genes involved in stem cell/pluripotency and cancer-relevant isignaling pathways in immature teratomas, a GCT subtype that has been little-studied and for which there are currently no targeted therapies. Finally, we explored the methylation pattern of imprinted genes, defining specific imprinting patterns for different tumor histologies and anatomic locations. Taken together, these results suggest that differential methylation may represent a mechanism of tumorigenesis in GCTs, and further suggest possibilities for novel therapeutic approaches for GCTs. For these reasons, we believe our work would be of interest to readers of BMC Cancer. I certify that all authors have read and approved the manuscript, and this manuscript is not under consideration elsewhere, and that the authors have declared no competing interests. Thank you for your consideration.

Sincerely,

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