

SBS Seminar Announcement

Neuro-Oncology: Connecting Cancer Stem Cells To Their Primary Tumor

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Abstract

Brain tumors are among cancers with the poorest prognosis despite surgery and adjuvant chemo-radiation. The Cancer Genome Atlas effort recently showed that gene expression drives brain tumor disease progression and clinical outcome, independently of current clinical indicators. These findings highlight the limitation of relying solely on histology to diagnose and subsequently treat patients. Glioma-propagating cells (GPCs) are stem-like cells that have extensive self-renewal and tumor-propagating characteristics, making them plausible candidates for the highly infiltrative and recurrent nature of the disease (Chong et al, *Stem Cells*, 2009). Using genome-wide gene expression programs, we recently showed that GPCs contain transcriptomic information that dictates primary tumor behavior and phenotype (Ng et al, *Clin Cancer Res*, 2012). Moving further, we studied the nature of drug resistance by focusing on reactive oxygen species, specifically the superoxide and hydrogen peroxide molecules; *in press* (Koh et al, *Antioxid Redox Signal*, 2013). We formulated the ROS Index as a quantitative measure of O_2^- : H_2O_2 ratio, and showed its ability to predict the propensity for drug-induced apoptosis, an advance in a previously qualitative redox biology field. Furthermore, depletion of this Index sensitized GPCs to apoptotic triggers, and prolonged tumor latency and extended survival in mouse orthotopic models. Strikingly, patients with gene expression programs associated with reduced ROS Index tended to have a more favorable prognosis, providing firm evidence that tilting the balance between O_2^- and H_2O_2 can constitute a viable treatment strategy. In addition to the orthotopic xenograft models used in our lab, we are also exploring lineage-tracing mouse models to evaluate the role of Parkin as a tumor suppressor in glioma (Yeo et al, *Cancer Res*, 2012). This talk will highlight the relevance of GPCs as a clinically relevant platform to work with, and the importance of representative mouse models for investigation.

Friday, 12 Apr 2013 3.00pm to 4.00pm SBS Classroom 2 (SBS-01n-22)

Host: Assistant Prof Andrew Tan Nguan Soon