NANYANG TECHNOLOGICAL UNIVERSITY

School of Biological Sciences

# Seminar Announcement

## Targeting brain tumors: Improving lives through Precision Medicine

## Building resources that enable biological validation of large patient dataset analyses

Date: 05 October 2015 Monday

Time: 2:30pm to 3:30pm

Venue: SBS Classroom 4 (SBS-01n-24)

Host: A/Prof Andrew Tan Nguan Soon

**Speaker**: **Dr Carol Tang**
Senior Principal Investigator,
Neuro-Oncology Research Laboratory
National Neuroscience Institute



## Abstract

Brain tumors are highly infiltrative and recurrent. Among the reasons for the poor prognosis of patients lies in the cellular and molecular heterogeneity of tumor cells. This means that the composition of tumors is a mixed population. Furthermore, studies have shown that the various cell types constituting this mixed population display differential responses to chemotherapeutic drugs, complicating the specificity and therefore efficacy of therapeutic targeting. Large US-led public efforts such as The Cancer Genome Atlas recently showed that histologically identical grade IV glioblastoma multiforme (GBM) tumors can be divided into four subclasses based on gene expression, each subclass being characterized by unique genomic aberrations and clinical outcome. These findings are significant because they highlight the limitation of relying solely on morphological approaches such as histology to diagnose and subsequently treat patients. Consistent with research advances in brain tumors, the World Health Organization recently formulated a blueprint for the inclusion of such molecular parameters in the new brain tumor classification scheme. Moreover, imaging methodologies are being established to discriminate such molecular subclasses, with the goal of improving non-invasive methods of stratifying patients to inform targeted therapy and personalized treatment of GBM. This forms the basis of Precision Medicine. *Precision Medicine does not mean the creation of new drugs or medical devices; instead, it focuses on understanding individual patient tumor profiles so as to identify those most likely to receive treatment benefit from targeted therapy. This in turn spares non-responders of financial costs and side effects*.

In this research forum, we will present the role of a carbohydrate-patterning enzyme, ST3Gal1 in brain tumor disease progression and clinical outcome (JNCI, accepted). This study demonstrates the application of large clinical dataset analyses to drive hypotheses that are validated using patient-derived glioma cells and an orthotopic mouse xenograft model. Specifically, we define the role of ST3Gal1 in the mesenchymal patient cohort typified by up-regulated TGFb signaling. We identify FoxM1 as a mediator of ST3Gal1 signaling in self-renewing tumor cells. Active *ST3GAL1*-associated transcriptomic program enriches for tumors of higher grade and larger T2 volume, a surrogate for tumor infiltration. Collectively, these findings suggest that ST3Gal1 has a prognostic role in brain tumors, and is a potential therapeutic target.