第25回

若手研究者交流会

2014年
日時：**7月 31 日（木）**
18:00～19:00

場所：**臨床小講堂**

脳神経外科学講座　　宮嵜 健史　先生

Department of Neurosurgery
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『グリオーマ幹細胞標的療法としてのG-quadruplex安定化剤・Telomestatinの可能性
～グリオーマ幹細胞仮説の概略と共に～』
Therapeutic potential of G-quadruplex, Telomestatin as a GBM stem cells Targeted Therapy
~ with Over view of GBM stem cells hypothesis ~

教員（助教～准教授）、職員、大学院生、
学部学生等、どなたでもご参加いただけます。

連絡先：若手交流会世話人　原伸正・日吉峰麗　（代謝生化学），山崎雅之（環境予防医学）

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Therapeutic potential of G-quadruplex, Telomestatin as a GBM stem cells Targeted Therapy　~ with Over view of GBM stem cells hypothesis ~

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【Abstract】

The development of effective therapies for glioblastoma multiforme (GBM) is a challenging endeavor due to the aggressive proliferation and the high migratory potential of this form of cancer. Recent studies have suggested the existence of a hierarchical organization of multiple heterogeneous cell populations in GBMs having distinct tumor-driving capacities. Among heterogeneous tumor cells, GBM stem cells (GSC) are defined as a subpopulation that is capable of self-renewal and differentiation into multilineaged tumor cells with distinct tumorigenic potentials *in vivo*. Identification of novel therapeutic strategies for GSCs in GBMs remains a major hurdle to effectively attack this highly malignant tumor. GSCs exhibit phenotypic and genetic similarities to their somatic counterparts, neural stem cells (NSC). Targeting shared pathways that regulate the survival of both GSCs and NSCs, therefore, may eradicate both types of stem cells.

Here, we show that telomestatin triggers the preferential apoptosis of GSCs with less of an effect on normal precursors or non-GSCs in GBMs. Immunofluorescence *in situ* hybridization (iFISH) detected the presence of damage in both telomeric and non-telomeric DNA regions in GSCs but not in non-GSCs. Analysis of a cDNA microarray identified a reduction in the proto-oncogene, *c-Myb*, following telomestatin treatment of GSCs. Decreased *c-Myb* expression was also observed in pharmacodynamic analyses of telomestatin-treated xenografted tumors. Moreover, treatment of tumor-bearing mice showed a statistically significant reduction in tumor sizes *in vivo*.

Finally, we will overview and update GSC hypothesis potentials along with some recent advances in the role of GCS in GBM.