those of parental tumors. The organoids exhibited consistent histological features and molecular profiles with those of the parental tumors. Using a public database of meningioma, we identified that upregulated *forkhead box M1* (*FOXM1*) was correlated with increased tumor proliferation. Overexpression of *FOXM1* in benign meningioma organoids increased organoid proliferation; depletion of *FOXM1* in malignant organoids decreased proliferation. Additionally, thiostrepton, a FOXM1 inhibitor combined with radiation therapy, significantly inhibited proliferation of malignant meningioma organoid models ($P<0.01$).

An organoid model for meningioma enabled us to elucidate the tumor biology of meningioma along with potent treatment targets for meningioma.

Key words: Meningioma | Organoid | *FOXM1*

TB-3

MIR-33A DEPLETION ACCELERATE MEDULLOBLASTOMA GENERATION AND INVASION

Yohei Mineharu[1,2], Yasuzumi Matsui[1], Yuki Oichi[1], Takahiko Kamata[1], Takaaki Morimoto[3], Tetsushi Nakao[4], Takahiro Horie[4], Koh Ono[4], Yokinori Terada[1], Masahiro Tanji[1], Yoshiki Arakawa[1], Susumu Miyamoto[1]; [1]Department of Neurosurgery, Kyoto University, Kyoto Japan [2]Department of Artificial Intelligence in Healthcare and Medicine, Kyoto University Graduate School of Medicine, Kyoto, Japan [3]Hyogo Prefectural Amagasaki General Medical Center, Amagasaki, Japan [4]Department of Cardiology, Kyoto University, Kyoto, Japan

Background and purposes: Lipid metabolism have been shown to be associated with tumorigenicity in various malignancies. The purpose of this study was to investigate the association of miR-33, a key regulator of lipid metabolism, in tumorigenicity and progression of medulloblastoma. Methods: Incidence of medulloblastoma and histopathological findings were compared between ptch1+/- mice and ptch1+/- miR-33a-/- mice. Tumors extracted from these mice were transplanted subcutaneously in nude mice (n=14 for ptch1+/-, n=19 for ptch1+/- miR-33a-/-) and in C57BL/6 mice (n=12 for each). Gene expression profile was compared between tumors from ptch1+/- mice and those from ptch1+/- miR-33a-/- mice. Results: Knockout of miR-33a in ptch1+/- transgenic mouse model increased the incidence of spontaneous generation of medulloblastoma from 34.5% to 84.0% ($p< 0.001$) at 12 months. Histopathological analysis showed infiltrative tumor borders in ptch1+/- miR-33a-/- tumors as compared with ptch1+/- ones. Tumor formation was observed in 21.4% for ptch1+/- tumors and 68.4% for ptch1+/- miR-33a-/- tumors in nude mice ($p= 0.008$). It was observed in 0% and 16.7% in immune competent mice. RNA sequencing detected that SCD1 and SREBF1 was upregulated in tumors from miR-33a knockout mice. Discussion: Our results demonstrated that depletion of miR-33a accelerated medulloblastoma generation and invasion. miR-33a may also be important for immune evasion. SCD1, which is reported to play a role in tumor stem cell maintenance and metastasis, can be a potential therapeutic target for medulloblastoma.

Key words: medulloblastoma | lipid metabolism | transcriptome

TB-4

ANTITUMOR EFFECTS OF A NOVEL CURCUMIN DERIVATIVE CURCUMIN MONOGLUCURONIDE ON GLIOBLASTOMA CELLS IN VITRO AND IN VIVO

Takashi Fujii[1,2], Shun Yamamuro[3], Masamichi Takahashi[4], Akihide Kondo[5], Yoshitaka Narita[4], Atsuo Yoshino[3], Kojiro Wada[1], Koichi Ichimura[2], Arata Tomiyama[1,2]; [1]Department of Neurosurgery, National Defense Medical College, Saitama, Japan [2]Department of Brain Disease Translational Research, Juntendo University Faculty of Medicine, Tokyo, Japan [3]Department of Neurological Surgery, Nihon University School of Medicine, Tokyo, Japan [4]Department of Neurosurgery and Neuro-Oncology, National Cancer Center Hospital, Tokyo, Japan [5]Department of Neurosurgery, Juntendo University Faculty of Medicine, Tokyo, Japan

The therapeutic outcome of glioblastomas (GBMs) is still very poor. Therefore, invention of novel therapeutic methods against GBM cases is considered urgent. The antitumor effects of naturally-derived compounds are attracting attention recently, and therapeutic efficacy of curcumin, a plant-derived compound previously used for multiple purpose, has been indicated in many cancer systems; however, clinical application of curcumin is considered difficult because of its poor bioavailability (under 1 %). Curcumin monoglucuronide (CMG), a water-soluble prodrug of curcumin recently developed for overcoming this weakness, has been demonstrated excellent antitumor effects for several malignancies in vitro and in vivo; therefore, we investigated the effects of CMG against GBM cells. CMG induced cell death of human GBM cells lines (T98G, U251MG, and U87MG) by dose dependent manner by triggering multiple forms of cell death such as apoptosis and perthanatos. Immunoblotting of CMG-treated GBM cell lysates demonstrated activation of multiple cell death signaling. Furthermore, immunodeficiency mice harboring intracerebral U87MG cell xenografts systemically treated by CMG showed significantly prolonged survival compared with control mice. These results suggest CMG would be a novel therapeutic agent against GBM cases.

Key words: Glioblastoma | Curcumin monoglucuronide | Therapeutic model

TB-6

EXPERIMENTAL EVALUATION OF THE THERAPEUTIC POTENTIAL OF BORON NEUTRON CAPTURE THERAPY IN PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA

Kohei Yoshimura[1], Hideki Kashiwagi[1], Shinji Kawabata[1], Yusuke Fukuo[1], Koji Takeuchi[1], Ryo Hiramatsu[1], Naonori Hu[2], Hiroki Tanaka[3], Minoru Suzuki[3], Shin-Ichi Miyatake[2], Masahiko Wanibuchi[1]; [1]Osaka Medical and Pharmaceutical University, Osaka, Japan [2]Kansai BNCT Medical Center [3]Institute for Integrated Radiation and Nuclear Science, Kyoto University

Background: High-dose methotrexate and whole brain radiation therapy (WBRT) is the recommended treatment for primary central nervous system lymphoma (PCNSL). Although the initial treatment is successful, the recurrence rate is high and the prognosis is poor. Boron neutron capture therapy (BNCT) is a nuclear reaction-based tumor cell-selective particle irradiation that occurs when non-radioactive boron-10 is irradiated with neutrons to produce α particles (10B [n, α] 7Li). In this study, we conducted a basic research to explore the possibility of BNCT as a treatment option for PCNSL. Methods: Cellular uptake of boron using human lymphoma cell-lines after exposure to boronophenylalanine (BPA) were evaluated. The cytotoxicity of lymphoma cells by photon irradiation or neutron irradiation with BPA were also evaluated. The lymphoma cells were implanted into the mouse brain and the bio-distribution of boron after administration of BPA were measured. In neutron irradiation studies, the therapeutic effect of BNCT on mouse CNSL models were evaluated in terms of survival time. Results: The boron concentration in lymphoma cells after BPA exposure was sufficiently high, and lymphoma cells showed cytotoxicity by photon irradiation, and also by BNCT. In in vivo bio-distribution study, lymphoma cells showed enough uptake of BPA with well contrasted to the brain. In the neutron irradiation experiment, the BNCT group showed a significant prolongation in their survival time compared to the control group. Conclusions: In our study, BNCT showed its effectiveness for PCNSL in a mouse brain tumor model. PCNSL is a radio-sensitive tumor with a extremely good response rate, but it also has a high recurrence rate / a high rate of adverse events, so there is no effective treatment for recurrence after treatment. Our translational study showed that BNCT is possibly have an important role against PCNSL during the therapy lines as a new treatment option for PCNSL patients.

Key words: boron neutron capture therapy (BNCT) | primary central nervous system lymphoma (PCNSL) | radiation therapy

TB-8

GENETIC AND MOLECULAR PROPERTIES OF LONG-TERM PROLIFERATING TUMORSPHERE -FORMING GLIOMA DERIVED CELLS

Noriyuki Kijima[1], Daisuke Kanematsu[3], Tomoko Shofuda[4], Ema Yoshioka[5], Atsuyo Yamamoto[4], Yukako Handa[3], Hayato Fukusumi[4], Asako Katsuma[3], Miho Sumida[3], Shusuke Moriuchi[2,6], Masahiro Nonaka[2,7], Yoshiko Okita[1,2], Naohiro Tsuyuguchi[8,9], Takehiro Uda[8], Toshiyuki Kawashima[8], Junya Fukai[10], Yoshinori Kodama[11,12], Masayuki Mano[11] Yuichiro Higuchi[13], Hiroshi Suemizu[13], Yonehiro Kanemura[2,3,5]; [1]Department of Neurosurgery, Osaka University Graduate School of Medicine [2]Department of Neurosurgery, National Hospital Organization Osaka National Hospital [3]Division of Regenerative Medicine, Department of Biomedical Research and Innovation, Institute for Clinical Research, National Hospital Organization Osaka National Hospital [4]Division of Stem Cell Research, Department of Biomedical Research and Innovation, Institute for Clinical Research, National Hospital Organization Osaka National Hospital [5]Division of Molecular Medicine, Department of Biomedical Research and Innovation, Institute for Clinical Research, National Hospital Organization Osaka National Hospital [6]Moriuchi Clinic of Neurosurgery [7]Department of Neurosurgery, Kansai Medical University [8]Department of Neurosurgery, Osaka City University Graduate School of Medicine [9]Department of Neurosurgery, Kindai University, Faculty of Medicine [10]Department of Neurosurgery, Wakayama Medical University [11]Department of Central Laboratory and Surgical Pathology, National Hospital Organization Osaka National Hospital [12]Department of Diagnostic Pathology, Kobe University Graduate School of Medicine [13]Laboratory Animal Research Department, Central Institute for Experimental Animals

Long-term proliferating tumorsphere-forming glioma derived cells (LTP-TS-GDCs) and patient derived xenografts (PDXs) are essential tools for translational research for glioma. However, only small subsets of glioma