systemic cancers. Recent research has provided insight into some important aspects of brain metastasis development, interaction of brain-metastatic tumor cells with resident cells of the CNS microenvironment and growth patterns within the brain parenchyma. Treatment choices have to consider clinical presentation, number, size and localization of brain metastases, status of extracranial tumor burden, prior therapies, co-morbidities and histological and molecular tumor characteristics. Recent advances show that targeted therapies against glioblastoma, Brain metastases and meningiomas drive clinical trial design and improvement of clinical management strategies for these common tumors.

**Key words:** brain metastasis, meningioma, targeted therapy, immunotherapy

### MS52

**CHALLENGES IN TREATMENT OF GLOBLASTOMA: CURRENT CONCEPTS AND THERAPEUTIC PERSPECTIVES**

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The natural disease course in glioblastoma is grim, in adults as well as in children. To date, there are no options for primary, secondary or tertiary prevention. However, unlike the fatalistic approach generally taken, there are subgroups of patients or individuals clearly benefitting over a variable time from current treatments, radiation and alkylating chemotherapy, as well as experimental precision or immune interventions. This heterogeneity in treatment response reflects the biological heterogeneity of the disease, which needs to be addressed in current preclinical and clinical investigations as well as this identifies primary and acquired treatment resistance as the key challenge in the field of glioblastoma. Importantly, even for most conventional treatments the basic molecular mechanisms for primary or secondary resistance are unknown or incompletely understood.

The present view is that progress will be made with a more precise classification and grouping of glioblastoma. The methylation subgroups clearly provide a first step, but further tumor bulk but potentially also subclonal or single-cell analyses might provide further insights and will be a prerequisite to meaningfully interpretable trials.

Novel preclinical and translational concepts of glioblastoma in adults reflecting the proposed network architecture of the glioma, but also the glioma-brain interface may for the first time separate options for trial interventions in glioblastoma form the usual mainstream in oncology.

Clinical trials of the past years have revealed the potential for further developments in glioblastoma, for example in O6-methylguanine-DNA-methyltransferase (MGMT) promoter hypermethylated glioblastomas and allow leaving out temozolomide for glioblastoma harboring an unmethylated MGMT promoter. The latter is not clinical standard, however we should at some point make sure we still understand, why temozolomide is provided in this particular situation and how we make a next step.

The field of immunoneurooncology is rapidly growing with preclinical work and trial concepts, but whereas patients with brain metastases seem to benefit from this development, success in glioblastoma is restricted to uncontrolled early-phase developments.

**Key words:** Brain tumor networks, Molecular targeted Therapy, Neoantigens

### MS5-1

**IMPLEMENTATION OF GENE PANEL TESTING USING NEXT-GENERATION SEQUENCING**

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The advance of next-generation sequencers (NGS) has dramatically improved the performance of genomic analysis of clinical samples in cancer precision medicine. The practical use of gene panel testing for clinical applications has begun in Japan. At present, “OncomineTM Dx Target Test” is listed as a companion diagnostic system using NGS, and “FoundationOne CDx Cancer Genomic Profile” and “OncoGuide™ NCC Oncopanel System” are listed as gene panel testing under insurance coverage. Formalin-fixed paraffin-embedded specimen have been routinely used for molecular diagnosis testing, therefore quality control such as formalin fixation time and tumor contents is important to ensure validity of diagnostic results. In this presentation, the issue to obtain evaluable results of gene panel testing using formalin-fixed paraffin-embedded specimen will be discussed.

Due to evolution of detection technologies, we can detect gene mutation with high sensitivity. Detection of gene mutation in circulating tumor DNA is feasible approach for diagnostic testing in cancer treatment. Liquid biopsy has been approved as a companion diagnostic testing to detect gene mutations in NSCLC. Examples of the clinical utility of plasma testing in cancer treatment will be presented.

### EL1

**BUILDING A CAREER IN NEURO-ONCOLOGY RESEARCH**

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A young neurosurgeon has several interesting and important possible career paths: clinical care, clinical/translational research and more fundamental research. Each of these has its own requirements for training, talent and commitment. A closer inspection of each of these, however, reveals that they are basically quite similar. From this, several general conclusions can be gleaned and recommendations for optimizing the chances of long-term career success. In this short talk, I will review the aspects of our training program that has allowed each of our Japanese trainees to have remarkable success both while with us in the US and upon their return to Japan. My goal is to explicitly describe and state these as a roadmap for success, particularly in the rapidly developing field involving the application of molecular and genetic technologies to translational and basic neuro-oncology research— but also as more generally applicable principles.

**Key words:** career, research, training

### S4-KL-1

**UPDATE OF WHO2016 CLASSIFICATION OF ADULT DIFFUSE GLIOMAS**

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The World Health Organization (WHO) central nervous system (CNS) tumor classification has represented the primary source of diagnosis and grading criteria of brain tumors. Nonetheless, recent advances of studies on their molecular alterations require more rapid update of recommendations for clinical practice. To accomplish this, dIMPACT-NOW (the Japan National Brain Tumor Clinical Trials Network to Inform Molecular and Practical Approaches to CNS Tumor Taxonomy) was established in 2016 and has published four updates. For adult gliomas, update 1 clarified the use of the term NOS (Not Otherwise Specified) and proposed a new entity NEC (Not Elsewhere Classified); update 2 revised EGFR mutations regarding diffuse astrocytoma/anaplastic astrocytoma, IDH-mutant; update 3 proposed molecular criteria for an IDH-wildtype diffuse or anaplastic astrocytic glioma without histological features of glioblastoma, which would have been previously classified to a grade IV glioblastoma. Nonetheless, no consensus on pathologic or molecular markers that could be incorporated into a more clinically relevant grading scheme for IDH-mutant gliomas has been reached. The molecular alterations previously studied using relatively large cohorts include CDKN2A/B homozygous deletion, CDK4 amplification, RBB1 mutation/homozygous deletion, PIK3CA or PIK3R1 mutations, PDRG1 amplification, NMYC amplification, global hypomethylation, genomic instability and chromosome 14 loss. The proliferative activity, based on the mitotic count or Ki67 indices, and other morphologic features typical of a high grade that