may be associated with a variety of neuropsychiatric and motor syndromes. In addition, loss-of-function mutations in *TAHP1* are known to cause a variety of dystonia syndromes. Therefore, it is believed that brain calcinosis in this family is related to the deletion of *SLC20A2*, while the *TAHP1* deletion likely contributes to the early onset dystonia phenotype.

Conflicts of Interest:

None.

Abstract A4

Pathologic substrate, risk factors, and functional impact of delusions and hallucinations in neuropathologically diagnosed Alzheimer's disease

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Utilizing the National Alzheimer's Coordinating Center database we analyzed 728 patients with Alzheimer's disease (AD), neuropathologically confirmed based on the CERAD criteria, comparing those (n = 271) that at any moment in their evolution suffered delusions or hallucinations (P+) versus those (n = 457) that did not (P-). There was no difference in AD lesion load. P+ subjects had a higher prevalence of subcortical arteriosclerotic leukoencephalopathy (SAL) and, as expected, higher Lewy body stage. Hypertension was more common in P+ patients and diabetes in subjects with both delusions and hallucinations. P+ patients tended to quit smoking later in life. The functional associations diverged: patients with delusions only had better CDR, MMSE and FAQ than P-patients, whereas the opposite was true for patients with hallucinations, whether isolated or associated with delusions. In contrast, an overlapping sample of 890 subjects from the same database with a clinical diagnosis of AD and available neuropathological exam showed greater AD load in the P+ group, a result we interpret as due to clinical misdiagnosis, since the P- group was enriched in subjects with a Braak stage I and II. We conclude that SAL is, along with Lewy bodies, a substrate for psychotic symptoms in AD, and that vascular risk factors are likely to contribute to the development of this condition.

Conflicts of Interest:

None.

Abstract A5

Compared to normals, the cerebral expression of multiple inflammatory markers is reduced in Alzheimer's disease and Diffuse Lewy body disease

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The role of inflammation in the development of dementia is a controversial topic. However, inflammatory biomarkers could be used to differentiate different subtypes of dementia, and monitor responses to therapy. Here we describe the results of a multi-plexed ELISA study using Bio-Plex Pro™ premixed 40-plex human cytokine kits to obtain an overview of inflammatory biomarker expression in the left frontal pole frozen at autopsy in pathologically verified cases of Alzheimer degeneration (Braak stage ≤ 3), AD (Braak stage ≥ 4), AD-DLBD (Braak stage ≤ 3), 'pure' DLBD (without AD pathology) and normal controls.

Compared to normals, significant reductions were observed in levels of Interleukin (IL)-6, Tumor Necrosis Factor, IL-1β, and 5 CXCL (-2, -6, -11, -13, -16) and 4 CCL (-7, -15, -23, -26) chemokines in all cases. These reductions occurred in a stepwise fashion, with highest levels in cases of AD, followed by AD-DLBD, DLBD and Alzheimer degeneration. This suggests that inflammatory biomarkers reduce in the transition to AD, and undergo further profound reductions in cases of mixed AD-DLBD and particularly in cases of 'pure' DLBD. These results challenge the notion that dementia is characterized by increased brain inflammation, and suggest that biomarker reductions could be used to signal the onset of Alzheimer's disease, while sustained biomarkers during therapy could reflect neuroprotection.

Conflicts of Interest:

None.

Abstract A6

Understanding the role of surfen, a proteoglycan antagonist, in mouse models of multiple sclerosis: Applications for the development of novel therapeutics

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Connective tissue components such as proteoglycans are known inhibitors of remyelination in mouse models of demyelination and are found at the border of active demyelinating lesions in multiple sclerosis. Surfen (bis 2-methyl, 4-amino, 6-quinolyl amide) is a small molecule antagonist that preferentially binds heparan sulfate and related proteoglycans. We have previously reported that surfen reduces T cell proliferation *in vivo* and *in vitro*. Here we extend this work by characterizing surfen in mouse models of chronic neuroinflammation (experimental autoimmune encephalomyelitis; EAE) and demyelination (lysolecithin).

Female adult C57Bl/6 mice were immunized with myelin oligodendrocyte glycoprotein emulsified in a 1:1 ratio with complete Freund's adjuvant. Mice were scored daily and received either surfen (5mg/kg, i.p) or vehicle (DMSO, i.p.) every second day following the onset of clinical symptoms. In a separate cohort, lysolecithin was injected bilaterally into the corpus callosum of adult C57Bl/6 mice to induce demyelination.

Relative to vehicle treatment (0.1 % DMSO), stereotactic administration of surfen (100 μM) 48 hours following lysolecithin increased total lesion area seven days post-injection with concomitant increases in glial and macrophage activity. By contrast, surfen (5 mg/kg, i.p.) ameliorated EAE clinical severity compared to vehicle controls. Taken together, these results signify that while peripheral proteoglycan antagonism by

surfen reduces neuroinflammation and cellular infiltration in EAE, some families of proteoglycans such as heparan sulfate proteoglycans may serve to promote remyelination centrally where general antagonism should be avoided.

Conflicts of Interest:

None.

Abstract A7

EphrinB3 and EphrinB4 Receptors are potential therapeutic targets in glioblastoma

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Glioblastoma (GBM) is the most common malignant neoplasm of the central nervous system in adults. Despite advances in surgery, chemotherapy, and radiation technique, median overall survival remains dismal at 5 years after diagnosis. CD133 is a known putative cancer stem cell marker, and we aimed to identify markers in CD133 + GBM tumour initiating cell lines (TICs) with an infiltrative phenotype that could serve as therapeutic targets.

Expression (mRNA) microarray datasets including 22,278 probes for known cell-surface markers in three CD133 + TICs and 17 normal brain tissue lines were obtained. By expression profiling, we identified genes with uniformly high mRNA expression, filtered for known localization at the cell-surface, and for non- or low expression in normal brain; amongst the highly expressed were ephrin B3 receptor (EphB3), ephrin B4 receptor (EphB4) and fibroblast growth factor receptor (FGFR1). Protein expression was established by mass spectrometry using CD133 + cell line extracts. These were further evaluated in 27 patient GBM (IDH-wildtype) tumour samples by immunohistochemistry, both in the tumour and at the brain-tumor interface. Expression in >50% of tumour cells was enumerated as 7/27 for EphB3, 8/27 for EphB4, and 18/27 for FGFR1. Most tumours failed to exhibit a gradient of expression across the brain-tumor interface. Expression was occasionally noted in normal-appearing cells, particularly pyramidal neurons; most reactive-appearing astrocytes also strongly expressed FGFR1. Correlation with clinical parameters may disclose subsets of these tumours with varying infiltrative potential.

Conflicts of Interest:

None.

Abstract A8

Precision Care of Brain Tumour Patients via Personalized OncoGenomics – Promises and Challenges

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Cancerous behaviour is invariably governed by abnormalities within the genomes and epigenomes of tumour cells. These include mutations, copy number alterations such as amplifications, and structural variations that translate into aberrant transcripts and ultimately proteins. Examples of such changes in glioma include *IDH1* R132H mutation, *EGFR* amplification, and *FGFR3-TACC3* fusions. However, there are myriad other changes that could alter the biology of tumour with prognostic significance. Some, such as the mTOR pathway, maybe targeted by molecular therapeutic agents.

The BCCA Personalized OncoGenomics (POG) initiative utilizes whole genome, transcriptome, and panel sequencing of tumour to identify aberrant pathways for potential therapeutic intervention. POG aims to return informative and potentially actionable results within five to six weeks from time of biopsy. Over 250 patients have been sequenced in the past two years including 7 patients with CNS malignancies. In all cases, the data generated has served to confirm or re-align pathological diagnoses and also to identify aberrant genes, transcripts, and cellular pathways. In our hands, the integration of transcriptome and genome data has proven to be invaluable especially in comparing global gene expression profile against public cancer databases such as TCGA and ICGA. Moreover, we have incorporated analytic pipeline for measuring the expression of immune-related genes such as *PDL1*. Lastly, we are analyzing the mutational load and context to derive a "signature" which may inform on the molecular causation of the tumour. POG generates multilayer and granular genomic data that may provide clinical insight and treatment options for different tumour groups.

Conflicts of Interest:

None.

Abstract A9

Incomplete seizure reduction following resection of focal oligodendroglial hyperplasia

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The patient presented as a 39 year old right hand dominant female with medically refractory epilepsy. Pre-operative investigations, including MRI, electro- and magneto-encephalography, and fluorodeoxyglucose positron emission tomography (PET) were concordant with a lesion in the right inferomesial frontal lobe. Subdural electrode recordings demonstrated seizure onset in the right anterior inferior frontal lobe. The patient underwent surgical resection of the lesion.