integrity and reaction to oxidative stress. Further studies are needed to examine those proteins/genes as biomarkers for PIH.

C.4

Epigenetic drivers of malignant transformation in diffuse gliomas

MR Voisin (Toronto)* *V Patil* (Toronto) *F Nassiri* (Toronto), *G Zadeh* (Toronto)

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Background: Despite treatment, gliomas often exhibit disease progression, leading to recurrent glioblastoma (GBM) or malignant transformation of low-grade gliomas (LGG) associated with treatment resistance and poor prognosis. To date, the molecular factors driving glioma recurrence are poorly understood. **Methods:** We analyzed a cohort of 324 glioma samples from our institution including a unique cohort of 81 patients with matched primary and recurrent tumour pairs. We performed a paired, integrated multi-platform analysis consisting of DNA methylation profiling on all 324 samples, gene expression on 87 samples, and matched plasma cell-free DNA methylome analysis on 82 samples. **Results:** LGG that undergo malignant transformation are associated with DNA hypomethylation at recurrence, including decreased tumour purity and increased copy number variation. Integrated pathway analyses identified *IL-6*, associated with multiple pro-oncogenic pathways, and *CCR2*, associated with the recruitment of tumour-associated macrophages, as top genes involved in malignant transformation. Matched plasma methylation demonstrated a shift in the methylation signature at recurrence that can prove valuable as a non-invasive biomarker for early detection of malignant progression. **Conclusions:** We provide the first detailed description of the epigenetic evolution of gliomas and identify epigenetic drivers of malignant transformation including non-invasive biomarkers for early detection of malignant progression.

C.5

Musashi-1 is a master regulator of aberrant translation in MYC-amplified Group 3 medulloblastoma

MM Kameda-Smith (Hamilton)* *H Zhu* (Toronto) *E Luo* (San Diego) *C Venugopal* (Hamilton) *K Brown* (Toronto) *BA Yee* (San Diego) *S Xing* (Hamilton) *F Tan* (San Diego) *D Bakhshinyan* (Hamilton) *AA Adile* (Hamilton) *M Subapanditha* (Hamilton) *D Picard* (Dusseldorf) *J Moffat* (Toronto) *A Fleming* (Hamilton) *K Hope* (Hamilton) *J Provias* (Hamilton) *M Remke* (Dusseldorf) *Y Lu* (Hamilton) *J Reimand* (Toronto) *R Wechsler-Reya* (La Jolla) *G Yeo* (San Diego), *SK Singh* (Hamilton)

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Background: Medulloblastoma (MB) is the most common solid malignant pediatric brain neoplasm. Group 3 (G3) MB, particularly MYC amplified G3 MB, is the most aggressive subgroup with the highest frequency of children presenting with metastatic disease, and is associated with a poor prognosis. To further our understanding of the role of MSI1 in MYC amplified G3 MB, we performed an unbiased integrative analysis of eCLIP binding sites, with changes observed at the transcriptome, the translatome, and the proteome after sh*MSI1* inhibition. **Methods:** Primary human pediatric MBs, SU_MB002 and HD-MB03 were kind gifts from Dr. Yoon-Jae Cho (Harvard, MS) and Dr. Till Milde (Heidelberg) and cultured for in vitro and in vivo experiments. eCLIP, RNA-seq, Polysome-seq, and TMT-MS were completed as previously described. **Results:** *MSI1* is overexpressed in G3 MB. shRNA Msi1 interference resulted in a reduction in tumour burden conferring a survival advantage to mice injected with sh*MSI1* G3MB cells. Robust ranked multiomic analysis (RRA) identified an unconventional gene set directly perturbed by MSI1 in G3 MB. **Conclusions:** Our robust unbiased integrative analysis revealed a distinct role for MSI1 in the maintenance of the stem cell state in G3 MB through post-transcriptional modification of multiple pathways including identification of unconventional targets such as HIPK1.

C.6

Action-Related Fixation in Microsuturing, a New Gaze Behavior Metric to Differentiate the Level of Expertise

J Chainey (Edmonton)* *B Zheng* (Edmonton) *M Kim* (Edmonton) *A Elomaa* (Kuopio) *R Bednarik* (Kuopio), *C O'Kelly* (Edmonton)

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Background: Gaze behavior differences between expert and novice surgeons have been established in previous studies mainly from the general surgery field.Limited information is available about surgeon's visual attention during microsurgery procedures where surgical microscope is used. **Methods:** 4 experts and 3 novices performed 37 independent sutures under the surgical microscope.Eye movements of surgeons and scene video of the surgical performance were recorded.Total suturing time and subtask times were compared between level of expertise.We defined three discrete surgical actions and examined eye gaze (fixation) directly related to each of these actions.Fixation duration (measured by total,pre-action,and post-action duration) were compared between expert and novice, over 3 subtasks (piercing, exiting and cutting) and between pre- and post-action phases. **Results:** Expert surgeons completed the suture with shorter total time than novices.On average,expert displayed longer fixation time than novice.Experts also maintained their visual engagement constantly over the 3 level of subtask in comparison to novices who required a longer fixation time for the challenging subtask (piercing).Experts use longer pre- than post-action fixation, and this pattern is distributed over all three subtasks.This gaze engagement strategy was not shown in novices. **Conclusions:** The action-related fixation can be used to evaluate microsurgeons' level of expertise and in surgical education for gaze training.