(small and large RNAs) isolated from AGO2-miRISC (microRNA-induced silencing complex) of GSCs and normal human neural stem cells (hNSCs). Additionally, we have also established this interactome after exposure of GSCs and normal hNSCs to hypoxia, a key tumor micro-environmental factor that is known to be pivotal in generating GBM heterogeneity. The rank order list of miRNA-mRNA interaction nodes generated from RNA sequence reads reveals that enrichment of specific RNAs in functional AGO2-miRISC is not a direct function of their relative abundance in cells, thus this biochemically generated interactome is distinct from that generated by bioinformatics tools. We demonstrate that scope and influence of GSC specific miRNA-mRNA network and specific nodes of this interactome varies with hypoxia and tumor region in GBMs.

SP9

doi:10.1017/cjn.2014.77

Nilotinib inhibits pediatric high-grade glioma cell growth by blocking PDGFR

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Solid tumours arising from malignant transformation of glial cells are one of the leading causes of central nervous system tumor related death in children. Tumor recurrence in spite of rigorous surgical and chemoradiation therapies remains a major hurdle in management of these tumors. Here, we have investigated the efficacy of second-generation receptor tyrosine kinase (RTK) inhibitor nilotinib as therapeutic option for management of pediatric gliomas. We have utilized two independent pediatric high glioma cell lines with either high platelet-derived growth factor alpha (PDGFRα) or high PDGFRα expression in our in vitro assays to investigate the specific downstream effects of Nilotinib treatment of these cells. Using in vitro cell based assays we show that nilotinib inhibits PDGF-BB dependent activation of PDGFR. We further show that nilotinib is able to block cell proliferation and anchorage dependent growth via blockade of AKT and ERK1/2 signaling pathways. Our results suggest that nilotinib may be effective for management of PDGFRα dependent group of pediatric gliomas.

SP10

doi:10.1017/cjn.2014.78

Neurodevelopmental implications of DLX2 homeobox gene expression in human gangliogliomas

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Introduction: Gangliogliomas are low-grade, well differentiated neuroepithelial tumours of the central nervous system (CNS) comprised of neoplastic glial and neuronal cells. From microarray data, gangliogliomas overexpress the homeobox gene DLX2 required for differentiation and migration of inhibitory interneurons in the embryonic forebrain. We are interested in the role DLX2 plays in specifying neural progenitor fate. We hypothesize that in CNS progenitors, DLX2 promotes neural cell fate while simultaneously repressing glial fate. Methods: DLX2 expression was examined in a cohort of ganglioglioma FFPE sections using immunohistochemistry and immunofluorescence labelling. To examine co-localization of DLX2 with a glial specific marker, double immunofluorescence staining of DLX2 with glial fibrillary acidic protein (GFAP) was carried out. Results: Out of 30 patient samples examined, 10 samples expressed DLX2. Double immunofluorescence studies with GFAP determined that DLX2 co-localizes with GFAP expressing cells. Conclusions: Although DLX2 was not expected to co-localize with GFAP, as we hypothesized that DLX2 represses glial cell fate, GFAP may also be expressed in CNS progenitors specified to become neurons. To verify GFAP expressing cells are indeed from a neuronal lineage, co-expression studies with DLX2 and established markers for neurons, including synaptophysin and NeuN, will be carried out. In addition, co-expression of DLX2 with nestin and OLIG2, a marker for oligodendroglia, will be examined.

SP11

doi:10.1017/cjn.2014.79

Glia maturation factor (GMFb) promotes glial and neuronal tumor cell differentiation

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Introduction: GMFb was identified as a factor promoting glial cell process outgrowth in vitro and is predicted to be a member of the actin depolymerization factor (ADF) family. GMFb is highly expressed in the nervous system, with cytoplasmic expression in neurons and glia. We sought to understand the role of GMFb in CNS development and in gliomas. Methods: Anti-peptide antibodies to GMFb were generated. Co-immunoprecipitations (co-IP) were performed with actin antibodies. Glioma cells were treated with cytochalasin D to depolymerize actin or with colchicine to disrupt microtubules. Cis-retinoic acid (RA) was used to promote neurite outgrowth. Phosphorylation status of GMFb was ascertained using Western blots. Results: Co-IP experiments