INTRODUCTION: Medulloblastomas (MBs) are the most common type of solid, malignant childhood brain tumour. Recently, integrated genomics has identified four distinct sub-groups of which display different demographics, and clinical outcomes. Approximately 30% of MB patients present with metastatic spread at the time of diagnosis. Group 3 are considered the most metastatic, carry the worst prognosis and characteristically overexpress c-Myc.

C-Myc, is involved in the initiation of several genes responsible for tumour growth and metabolism. Lactate dehydrogenase A (LDHA), a downstream target of c-Myc is often de-regulated in metastatic and invasive tumours. We have begun to investigate the role of LDHA and lactate on MB metabolism.

METHOD: LDHA protein was examined in three medulloblastoma cell lines using Immunocytochemistry (ICC) and western blot analysis (WB). To investigate the role of LDHA in MB cell lines, LDHA was inhibited either by shRNA or with sodium oxamate. Metabolic assays and analysis include lactate and pyruvate assays.

RESULTS: The three MB cell lines demonstrated varying levels of LDHA protein however ICC analysis showed consistency in localisation of LDHA in cytoplasmic and nuclear areas. Successful knockdown of LDHA protein using shRNA was confirmed with WB analysis. Knockdown of LDHA resulted in decreased lactate levels. LDHA inhibition by sodium oxamate also caused a decrease in lactate levels in a time and concentration dependent manner. Interestingly, pyruvate levels also decreased when LDHA was inhibited.

CONCLUSION: Targeting medulloblastoma metabolism, such as LDHA, warrants further investigation to determine if this approach will affect not only metabolism but also cancer cell spread.