

CHRISTOPHER GUM AND BRUCE ANTHONY Ph.D., Department of Chemistry and Biochemistry, West Virginia Wesleyan College, Buckhannon, WV, 26201. Effects of Alcohol on CHK-1 and Phospho-CHK-1 in Neuronal Stem Cell losses in FASD.

Fetal Alcohol Spectrum Disorders (FASD) are associated with changes in proliferation and induced cell losses of neuronal stem cells during development. Alcohol induced oxidative stress has been noted in previous studies to cause chronic genomic instability and DNA damage. This damage results in the halting of S-Phase cell cycle progress and, in many cases, either induces DNA repair or apoptosis of the cell. However, alcohol induced apoptosis has been shown to work in a p53 independent fashion. Typically, proteins CDC25a and c as well as CHK-1 and 2 monitor DNA damage and help to determine cellular fate in p53 independent apoptosis. A study utilizing alcohol treated neuronal stem cells resulted in approximately 40% of the population maintaining DNA damage without inducing p53 dependent apoptotic mechanisms. The goal of this study was to elucidate the role, expression and localization of checkpoint kinase-1 (CHK-1) during the G1-S phase transition and to determine any major difference in phosphorylated, CHK-1 between control and alcohol treated neuronal stem cells. A Western Blot was run to determine quantitative presence of Phosphorylated CHK-1 and Immuno-fluorescent staining was used to quantitatively measure the abundance of Phosphorylated CHK-1 in groups. Image analysis determined that there was a significant difference in Phosphorylated Chk-1 in alcohol treated cells. The increased level of Phospho-CHK-1 indicates recognition of DNA damage, initiation of signaling G1/S phase transition and possible induction of apoptosis. Understanding the mechanistic changes in alcohol induced proliferation and cell losses may help in defining treatment paradigms effective in treating FASD.