LOGAN GODFREY AND BRUCE ANTHONY Ph.D., Department of Chemistry and Biochemistry, West Virginia Wesleyan College, Buckhannon, WV 26201. Effects of alcohol on Chk2 expression and cellular localization in a model of FASD and adult alcoholism.

Fetal alcohol Spectrum Disorders (FASD) are associated with reduced proliferation and loss of large numbers of neural crest stem cells. Previous studies suggest that alcohol increases oxidative stress inducing DNA damage and increasing apoptosis in a p53 independent manor. p53 independent cell losses are often associated with ATM and Chk-2 activation and points to a possible mechanism of cell loss in FASD. In addition, increased phosphorylation activity of Chk-2 effects cell cycle progression, in part, through phosphorylation of the Fox-1 transcription factor. This suggests a possible mechanism effecting proliferation and apoptosis in FASD. Both Chk-1 and Chk2 proteins may play a critical role in the cellular response following DNA damage, altering cell proliferation and increasing cell loss. This study examined the possible effect of alcohol exposure of neuronal stem cells and the effect on expression and localization of Chk-2. Immuno-cytochemistry and Western blot analysis were conducted in order to determine cellular localization and expressional changes of Chk-2 associated with alcohol exposure. We demonstrate a significant different in expression levels and nuclear localization between alcohol-treated and control cells. We suggest strong support for the role of the Chk-2 and Fox-1 in cell loss and proliferative changes in FASD phenotypes.