

TRISTAN QUINONES and BRUCE ANTHONY, Department of Chemistry/Biochemistry, West Virginia Wesleyan College, Buckhannon WV, 26201. The Role of FOX-1 in FASD.

It is well-known that abusive alcohol exposure in humans induces a wide range of defects including changes to the heart, liver renal function and central nervous system (CNS). In the CNS, repetitive exposure reduces stem cell and neuron numbers and function, in turn reducing the potential for neuroplasticity and altering limbic system signaling. Alcohol-exposed neuronal stem cells, show reduced proliferation and survival through cell cycle mis-regulation and induced cell death. Both the G1-S and the G2-M checkpoints are disrupted through variations in cyclin/cyclin dependent kinase activities. Our lab has demonstrated increased expression of transcription factor E2F1, CDK4/6, and retinoblastoma (Rb) which accelerates G1-S phase transition and inducing premature DNA synthesis. This acceleration into replication can induce apoptosis or hinder the success of the G2-M phase transition. FOXM1 has been demonstrated to regulate a set of genes that are mainly involved in regulating progression of G2-M phase. However, its mechanism and interaction with other proteins is unclear. Therefore, it was hypothesized that FOX-1 is notably upregulated in alcohol induced cells. This upregulation could potentially affect interactions with key regulatory protein that monitor DNA integrity and induce cell death. We examine FOXM1 expression through western blot and immunohistochemistry to determine the extent of mis-regulation. Our results indicate expressional and possible functional changes in FOX1 and potential regulation changes by RB that may induce apoptosis in alcohol induced neuronal stem cells.