Methylmercury (MeHg) is a harmful and ubiquitous toxicant that provokes neurological defects in the developing fetal nervous system. MeHg mercury has been shown to target the Notch pathway, a highly-conserved intercellular signalling mechanism responsible for normal development and neurogenesis. We have previously shown in a *Drosophila* model system that MeHg significantly upregulates anumber of the conventional Notch target genes of the Enhancer of Split (E(spl)) complex. Our most recent studies using the *Drosophila* neural-derived C6 cell line demonstrate E(spl) upregulation by MeHg can occur independent of the Notch receptor itself, pointing to potentially unique mechanisms for MeHg to regulate transcription. We have explored the unique properties of MeHg by comparison to inorganic mercury chloride ($HgCl_2$) in transcriptional activation of E(spl) targets. The E(spl)Mγ and E(spl)Mδ genes were upregulated by MeHg twelve-fold and seven-fold respectively, while treatment with $HgCl_2$ produced only a two-fold activation in both. In contrast, the E(spl)M3 and E(spl)M7 genes were more significantly upregulated by $HgCl_2$ than by MeHg. These data point to potentially specific regulatory actions of the two mercury species at the chromatin level. Preliminary data show that treatment with the histone deacetylase inhibitor, sodium butyrate, exacerbates the MeHg response supporting the notion that MeHg acts via alteration of chromatin state. Overall, these data confirm the ability of mercurials to augment signaling in the Notch pathway and suggest that the contrasting developmental effects of organic versus inorganic mercury may result from distinct mechanisms of transcriptional regulation.