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ESTABLISHING SYSTEMS FOR EVALUATING TREATMENT EFFECTS ON THE NEURONAL AND BEHAVIOURAL PHENOTYPE OF FRAGILE X SYNDROME

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Fragile X Syndrome (FXS) is a monogenetic disorder that is the most common form of inherited mental retardation. Our principle aim is to develop systems to determine the effect of treatments targeted at post-translational mechanisms of neuronal development on neuronal morphology and the behavioural phenotype of FXS. The Habenular Complex (HbC) is a neural circuit consisting of the habenular nuclei and the interpenduncular nucleus, and is implicated in a wide range of cerebral functions including modulating motor behaviours, learning conditional avoidance responses, spatial learning and attention, circadian rhythms, sleep and several psychological disorders. Interestingly, these functions have many commonalities with the clinical phenotype of FXS. Here we present the early expression of FMRP in the HbC in the embryonic human, mouse and zebrafish, and further show the atypical neuronal phenotype in knock-out mouse and knock-down zebrafish models of FXS. The zebrafish model provides the ideal means by which to genetically manipulate with morpholino antisense technology, to administer various pharmacological compounds, to conduct *in vivo* imaging of neuronal development, and to capture the effects on behavioural phenotype. We present a behavioural phenotyping assay for larvae and adult zebrafish targeting specific HbC-related behaviours including hyperactivity, circadian rhythms, and learning and memory. It is our intention to establish both fish and mouse models of FXS with genetic and pharmacological rescue protocols which, used in combination, will enhance our ability to identify new treatments for FXS.