

ABSTRACT:

## **Linking the FMR1 Alleles with Small CGG Expansions with Neurodevelopmental Disorders: Preliminary Data suggest an involvement of Epigenetic Mechanisms**

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The major aim of this study was to get a better insight into the mechanisms involved in the FMR1 mRNA 'toxicity' in GZ carriers identified in the Tasmanian study, by relating the levels of mRNA transcript to the expression of a prominent epigenetic marker, DNA-methyltransferase 1 (DNMT1). This marker is known to regulate FMR1 transcription in full mutation subjects and to play a major role in regulation of global methylation coupled to DNA replication. We have also investigated the relationship between levels of these two transcripts and Cytochrome C1 (CYC1), a nuclear oxidative-phosphorylation gene expressed during Grey zone FMR1 alleles and neurodevelopment 4 periods of mitochondrial expansion [Li et al., 1996]. This was to explore the possibility that epigenetic mechanisms are associated in the FMR1 mRNA toxicity of GZ alleles, leading to CYC1 over expression associated with mitochondrial dysfunction. Here we validated the assays for FMR1mRNA levels using a relative standard curve method, and found that the results closely corresponded to those earlier estimates in a larger sample, which included the present participants.

Keywords: FMR1, grey zone alleles, DNMT1, apoptosis, mRNA, neurodevelopment, autism, gene regulation

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