Mouse models of common Rett syndrome mutations recapitulate the severity seen in patients.

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Mutations in the X-linked MeCP2 gene are known to cause Rett Syndrome(RTT). MeCP2 is believed to act by binding methylated DNA via its methyl-binding domain (MBD) in addition to recruiting additional factors capable of transcriptional repression via the NCoR/SMRT interaction domain (NID). Mouse models also mimic the human disorder and have enabled us to gain a much greater understanding of the molecular mechanisms that underlie RTT. Here we present the characterisation of a GFP-tagged allelic series representing the three most common missense RTT mutations, which account for 25% of RTT cases; R133C, T158M and R306C. This series interrogates both the DNA binding and co-repressor complex recruitment capacity of the protein. The results of this study enable further annotation of MeCP2 relative to its function *in vivo* and the allelic series recapitulate the severities seen in patients.