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INSIGHT INTO OOCYTES: THE OVARIES OF FRAGILE X PREMUTATION MICE

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FMR1 alleles with 55-199 CGG•CCG-repeats in the 5' UTR are referred to as Fragile X premutation alleles. Female carriers of such alleles are at increased risk of Fragile X primary ovarian insufficiency (FXPOI). This disorder is associated with early ovarian decline leading to menstrual cycle irregularities, hormonal fluctuations and decreased fertility. However, the relationship between the increased number of CGG•CCG-repeats and ovarian pathology is unknown. We have generated a knockin (KI) mouse model in which the endogenous murine *Fmr1* gene was retrofitted with ~130 CGG•CCG-repeats. We have been studying the ovaries of these mice as well as the progeny of these mice with larger repeat numbers. Our investigations have included the characterization of *Fmr1* mRNA and protein levels, follicle number and inclusion formation. The KI mice differ from wild-type animals in a number of interesting ways. Some of these differences are reminiscent of what is seen in women with FXPOI and suggest possible mechanisms by which repeat expansion in human premutation carriers could lead to ovarian insufficiency.