

## Abstract 79

### DISTRIBUTION OF FMRP TO GRANULES IN HUMAN GRANULOSA CELLS UPON STRESS

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About 1% of women experience menopause before 40 years of age, a condition known as premature ovarian failure (POF). The *FMR1* premutation is the most frequent genetic factor associated with POF that is present in about a quarter of premutation carriers. *FMR1* is normally expressed in germ cells of human female fetuses. *Fmr1* mRNA is highly concentrated in mouse ovaries at the stage of oogonia cell proliferation, during development and, in adult female mice, *Fmrp* levels are higher in growing follicles. The size of the premutation, X-chromosome inactivation pattern, transcription and translation alterations, and RNA toxic gain-of-function are factors that may be involved in the etiology of *FMR1*-associated POF. To investigate the *FMR1* gene functioning in the human ovary and mechanisms by which ovarian cells can be affected by the premutation, we isolated and cultured human granulosa cells (HGC) from follicular fluid aspirates obtained during *in vitro* fertilization procedures. FMRP was expressed in follicular fluid cells as a major isoform of roughly 90 kDa. Immunofluorescence of cells cultured for six days revealed a diffuse, dotted, cytoplasmic distribution of FMRP. After induction of oxidative stress by treating cell cultures with sodium arsenite, FMRP was shifted to coarse perinuclear granules, colocalizing with TIA1, a stress granule marker. These data indicate that, similarly to the rat central nervous system submitted to stress, human FMRP function should be regulating translation in ovarian granulosa cells, shifting between polysomes and stress granules, in specific physiological conditions. Biochemical fractionation experiments will help to validate the morphological data reported here.