65		Date 30/04/2015 Hour 11:24 AM

2nd International Conference on FMR1 Premutation: Basic Mechanisms and Clinical Involvement

First author's data

First name	Montserrat
Last name	Mila
Center	Hospital Clínic. Barcelona
City (Center)	Barcelona. Spain
E-mail	mmila@clinic.cat

Sumary information

Title	Deregulation of key signaling pathways involved in oocyte maturation in *FMR1* premutation carriers with Fragile X-associated primary ovarian insufficiency
Topics	FXPOI clinical issues
Authors	Montserrat Mila [(1)], M Isabel Alvarez-Mora [(2)], Francisco Garcia-Garcia [(3)], Magda Duran [(1)], Joaquin Dopazo [(3)], Irene Madrigal [(1)], Laia Rodriguez-Revenga [(1)]
Centers	[(1)]Hospital Clínic. Barcelona, [(2)]CIBERER, [(3)]Centro de Investigación Príncipe Felipe

Summary

Background: *FMR1* premutation female carriers are at risk for Fragile X-associated primary ovarian insufficiency (FXPOI). Insights in the knock-in mouse model have demonstrated that FXPOI is due to an increased rate of follicle depletion or impaired development of the growing follicles. We report the first investigation involving transcription profiling of total blood from *FMR1* premutation females carriers with and without FXPOI.
Methods: A total of 16 unrelated females (6 *FMR1* premutated with FXPOI; 6 *FMR1* premutated without FXPOI; and 4 no-FXPOI females) were analyzed by whole human genome oligonucleotide microarray (Agilent Technologies).
Results: Fold-change analysis did not show any genes with significant differential gene expression. However, functional profiling by gene set analysis showed a large number of statistically significant deregulated GO annotations as well as numerous KEGG pathways in FXPOI females. Conclusion: These results suggest that the impairment of fertility in these females might be due to a generalized deregulation of key signaling pathways involved in oocyte maturation. In particular, vasoendothelial growth factor signaling, inositol phosphate metabolism, cell cycle, and the MAPK signaling pathways were found to be down-regulated in FXPOI females. Furthermore, a high statistical enrichment of biological processes involved in cell death and survival were found to be deregulated among FXPOI females.
Conclusions: Our results provide new strategic approaches to further investigate the molecular mechanisms of FXPOI not focused on a single gene but rather on the set of genes involved in these pathways.