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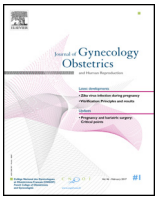

Letter to the editor

Luteal phase defects/insufficiency in the omics era: Challenges and opportunities ahead

Dear Editor

Corpus luteum (CL) is a transient endocrine gland that develops after rupture of the mature Graafian follicle to release ova. It synthesizes and secretes progesterone (P_4) which is necessary for the implantation of the blastocyst. In luteal phase defects, there is impairment in the secretion of P_4 and luteal function may be impaired in many other medical conditions such as the thyroid dysfunction, hyperprolactinemia, etc., apart from poor LH secretion. Although the association of luteal phase defects and as an independent entity causing infertility has not been proven, it is essential to understand luteal biology for fertility management [1,2]. Research involved in understanding of the primate CL is always challenging as there are many species differences in some fundamental aspects compared to luteal biology in non-primates. In the case of luteal phase defects or insufficiency, there has been a crying need to distinguish those luteal tissues/luteal phase that are likely to regress prematurely or secrete P_4 insufficiently. Attractive solution to address luteal phase defects can come from luteal tissue genomics and proteomics that regress prematurely or less functional in luteal phase defects. There are many unanswered questions which are still being explored and primary being the molecular cues for the regression at the end of non-fertile cycle. In cases of luteal phase defects, is there any intrinsic property of the CL itself or more susceptible to external cues that it undergoes premature luteal regression or less functional to cause luteal phase defects? Apart from biochemical markers, will the gene expression arrays employing luteal tissue from luteal phase defects reflect and allow researchers and clinicians to stratify luteal tissue of luteal phase defects from the normal having distinct biological properties and prognoses after suitable hormone supplementation? Can circulating non-coding RNAs act as an early biomarker to detect luteal phase defects soon after the ovulation induction in stimulated ovarian cycles? Several studies have indicated that ovulation induction is associated with luteal phase defect. The initial step to address these questions will be to develop non-human primate models to mimic human luteal phase defects. Earlier studies have documented the usefulness of non-human primate for investigation of luteal phase defects. As reviewed [3] multiple approaches and model systems exist and most luteal omics data has been generated by 1).Observation approach that compares the expression of genes and proteins in a fully functional CL to the regressing CL of the late luteal phase. 2. Manipulation of the master regulator of CL such as the LH/hCG prior to the CL removal, either by inducing luteolysis through administration of GnRH receptor antagonists or rescue of CL from luteolysis by re administeration of LH mimicking the hormonal change of early pregnancy. 3. *in vitro* culture of luteal cells by reductionist approach. Especially, the luteal tissue is complex with many distinct cell population, and the best way to arrive at solid and rigorous conclusions is to make the complex tissue into simpler components and study each separately. The use of currently available primate luteal gene expression arrays and bioinformatics will be only the beginning steps in a large–scale effort to analyze a variety of luteal phase defects. In addition to these gene expression analyses stands a generation of proteomic science, in which analysis of spectrum of proteins in a CL during different functional states, CL from induced and spontaneous luteolysis, CL in luteal phase defects will provide critical functional genomics and proteomics formation. We must somehow evaluate functional genomics and proteomic information into a larger scheme of how CL fingerprint will aid in the treatment and or diagnosis of luteal phase defects. So, the discovery of differential expression of primate luteal cellular genes using high throughput analysis during different physiological states and different experimental conditions is a very good beginning for further work required before a more complete understanding of short luteal phase pathology.

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