CHARACTERIZATION OF THE MOLECULAR PROFILE OF THE FOLLICULAR MILIEU IN POOR AND NORMO-RESPONDERS

Raquel Garrido-Casserras[2], **Nuria Pellicer**[2], Mercedes Monterde[1], Alicia Marzal Escrivá[1,3], Antonio Pellicer[1,2,4,5], César Díaz-García[1,2,4]

[1]*Grupo Acreditado de investigación en Medicina Reproductiva, IIS La Fe, Spain*
[2]*Área de Salud de la Mujer, Hospital Universitario y Politécnico La Fe, Spain*
[3]*IVI-Valencia, IVI-Valencia, Spain*
[4]*Departamento de Pediatría Obstetricia y Ginecología., Universidad de Valencia, Spain*
[5]*IVI-Roma, IVI-Roma, Spain*

Introduction: The molecular mechanisms underlying the poor ovarian response (POR) are poorly understood and there are still discrepancies regarding the characterization of the molecular features of POR. Aim: To compare the hormonal levels and the expression of the primary receptors and enzymes involved in the late stages of the follicular development and steroidogenesis between confirmed POR and normo-responders (NR). Study design: Sub-study of the FOLLPRIM study (NCT01310647). 99 potential PORs were included and subsequently underwent controlled ovarian stimulation (COS) in an antagonist protocol. Confirmed POR was defined as less than 5 MII oocytes retrieved during pick-up. Material and Methods: FSH-receptor (FSHR) and androgen-receptor (AR) were quantified in luteinized granulosa cells (LGC) by flow cytometry. Genetic expression of FSHR, LHR, AR, Star, CYP11A1 and CYP19A1 from Cumulus cells (CC) was quantified by RT-PCR. Hormonal determinations in follicular fluids were conducted using ELISA. Results: 81 POR patients were confirmed after COS. When compared POR and NR, the former had less MII oocytes retrieved (1,7±1,3 vs 6,7±2,0;p0,001), lower follicular levels of androstenedione (4,37 [0,53-29,65] vs 8,41 [3,99-12,82];p=0,010), testosterone (11,20 [2,91-31,92] vs 13,45 [9,47-53,88];p=0,021) and E2 (803,14 [63,70-2.089,76] vs 2.753,46 [772,70-7.392,75];p0,001). These changes were accompanied by a significant overexpression of the AR gene in POR patients, but such change wasn't followed by a parallel increase in FSHR on the membranes of LGCs. Conclusions: Molecular features of POR are characterized by an overexpression of AR in CC and a deprived intra-follicular androgenic environment.