Polycystic ovary syndrome (PCOS) is the most common endocrine disease, affecting around 6 – 20% of reproductive-age women. PCOS is characterized by hypothalamic–pituitary–gonadal disruption, often leading to infertility. The symptoms of PCOS consist of oligo/amenorrhoea, clinical and/or biochemical hyperandrogenism, and polycystic ovarian morphology manifesting with the accumulation of prematurely arrested small antral follicles. It has been suggested that the key dysfunction in most women with PCOS is functional ovarian hyperandrogenism due to unexplained steroidogenic hyperactivity disturbing the intraovarian processes that control ovarian androgen and estrogen secretion. Granulosa and theca cells are essential components of follicle development known to cooperate through complex interactions to maintain normal ovarian function and the biosynthesis of ovarian steroid hormones. The theca cells of PCOS ovaries have been shown to produce increased levels of androgens, but the molecular mechanism of steroidogenesis dysregulation and cell-to-cell interactions in the PCOS ovary are not well understood.

Thus, this present planned basic research study would try to precisely characterize the novel co-activators/co-inhibitors of signaling pathways involved in the pathobiology of PCOS ovary. Specific goals of this project, are to: 1) characterize different distinct cell populations and cell-to-cell interactions in PCOS ovary; 2) analyze functional implications of the LH, FSH, and steroid hormones in different cells populations of PCOS ovary; 3) investigate the cross-talk between theca/GCs and immune system cells. This basic research project will be carried out in a research laboratory setting using ovarian samples from women with severe PCOS phenotype I (n=20) and control healthy (n=20) women. The functional studies will be done using immortalized ovarian theca and granulosa cells, as well as immune cells for co-culture studies.

This project will enable a comprehensive characterization of different cell populations in the PCOS ovary to better understand the factors and cell interactions that regulate PCOS pathobiology. These findings may indicate novel regulators of steroidogenesis disruption in PCOS. Understanding the whole molecular mechanisms behind hormone production and secretion, intraovarian cell interactions, as well as paracrine factors that may regulate steroidogenesis in the ovary, could bring an effective treatment strategy for PCOS in the future. Moreover, we will obtain novel, unique stable PCOS ovarian cell lines, which are mandatory for any future drug discovery study.