

## OOGENESIS IN MAMMALS

- i) Mammalian oogenesis (egg production) differs greatly from spermatogenesis. The eggs mature through an intricate (জটিল) coordination of hormones, paracrine factors, and tissue anatomy.
- ii) In the human embryo, the thousand or so oogonia reaching the developing ovary divide rapidly from the second to the seventh month of gestation. They generate roughly 7 million oogonia (**Figure 1**). Most of these oogonia die soon afterward, but the surviving oogonia initiate meiosis, become primary oocytes, and remain in the diplotene stage meiotic prophase (Pinkerton et al. 1961).
- iii) This **prolonged diplotene stage** is sometimes referred to as the **dictyate resting stage**. With the onset of puberty, groups of oocytes periodically resume meiosis. At that time, **luteneizing hormone (LH)** from the pituitary gland releases this block and permits these oocytes to resume meiotic division (Lomniczi et al. 2012).
- iv) They complete first meiotic division and proceed to second meiotic metaphase, when the secondary oocyte is **ovulated**. After the secondary oocyte is released from the Ovary, meiosis will resume if fertilization occurs (At fertilization, calcium ions are released in the egg, and (as in the frog) these calcium ions release the inhibitory block and allow the haploid nucleus to form .
- v) The biochemistry of this meiotic regulation is intimately connected to ovarian anatomy. Each oocyte is enveloped by a primordial follicle consisting of a single layer of epithelial granulosa cells and a less organized layer of mesenchymal thecal cells. Periodically, a group of primordial follicles enters a stage of follicular growth. During this time, the oocyte undergoes a 500-fold increase in volume (corresponding to an increase in oocyte diameter from 10  $\mu\text{m}$  in a primordial follicle to 80  $\mu\text{m}$  in a fully developed follicle). FSH encourages the growth of the follicle and also induces receptors for LH on the outer follicle cells (Peng et al. 1991; Eppig et al. 1997).
- vi) Concomitant (*a phenomenon that naturally accompanies or follows something*) with oocyte growth is an increase in the number of granulosa cells, which form concentric layers around the oocyte. This proliferation of granulosa cells is mediated by a paracrine factor, **GDF9** (*Growth differentiation factor 9 (GDF9) is an oocyte derived growth factor in the transforming growth factor  $\beta$  (TGF- $\beta$ ) superfamily. It is highly expressed in the oocyte and has a pivotal influence on the surrounding somatic cells, particularly granulosa, cumulus and theca cells*), a member of the TGF  $\beta$  family (Dong et al. 1996).
- vii) Interestingly, **mutations of GDF9** produce a variety of phenotypes from premature ovarian failure to a propensity to have fraternal twins (i.e., to ovulate two instead of one oocyte) (Palmer et al. 2006; Otsuka 2011). Throughout this growth period, the oocyte remains in the dictyate stage. The fully grown follicle thus contains a large oocyte surrounded by several layers of granulosa cells. The innermost of these cells will stay with the ovulated egg forming the cumulus, which surrounds the egg in the oviduct. In addition, during the growth of the follicle, an **antrum** (cavity) forms and becomes filled with a complex mixture of proteins, hormones, and other molecules.
- viii) Oocytes are maintained in the **dictyate stage** (*The dictyate or dictyotene is a prolonged resting phase in oogenesis. It occurs in the stage of meiotic prophase in ootidogenesis. It starts late in fetal life and is terminated shortly before ovulation by the LH surge. Thus, although the majority of oocytes are produced in female fetuses before birth, these pre-eggs remain arrested in the dictyate stage until puberty commences and the cells complete ootidogenesis*) by the outer layer of ovarian follicle cells.
- ix) The inhibitory signal from the outer granulosa cells to the oocyte is cyclic GMP (cGMP). This **cGMP** is made by the outer granulosa cells of the follicle, transported through **gap junctions** between the follicle cells, and delivered by the follicle cells closest to the egg (the cumulus cells) by gap junctions to the oocyte (**Figure 2**).
- x) Once in the oocyte, cGMP **blocks phosphodiesterase enzymes** from degrading cyclic AMP (cAMP). The cAMP blocks meiotic progression by maintaining **protein kinase A (PKA)** in an active state. PKA **phosphorylates** the Cdc25 (*Cdc25 is a dual-specificity phosphatase first isolated from the yeast Schizosaccharomyces pombe as a cell cycle defective mutant. As with other cell cycle proteins or genes such as Cdc2 and Cdc4, the "cdc" in its name refers to "cell division cycle"*) protein, thus inactivating the activator of **MPF**, which induces cell division. PKA also phosphorylates Wee 1 (*Wee1 is a nuclear kinase belonging to the Ser/Thr family of protein kinases in the fission yeast Schizosaccharomyces pombe (S. pombe). Wee1 has a molecular mass of 96 kDa and is a key regulator of cell cycle progression. It influences cell size by inhibiting the entry into mitosis,*