

Figure 14.4 (=10th ed 17.32)

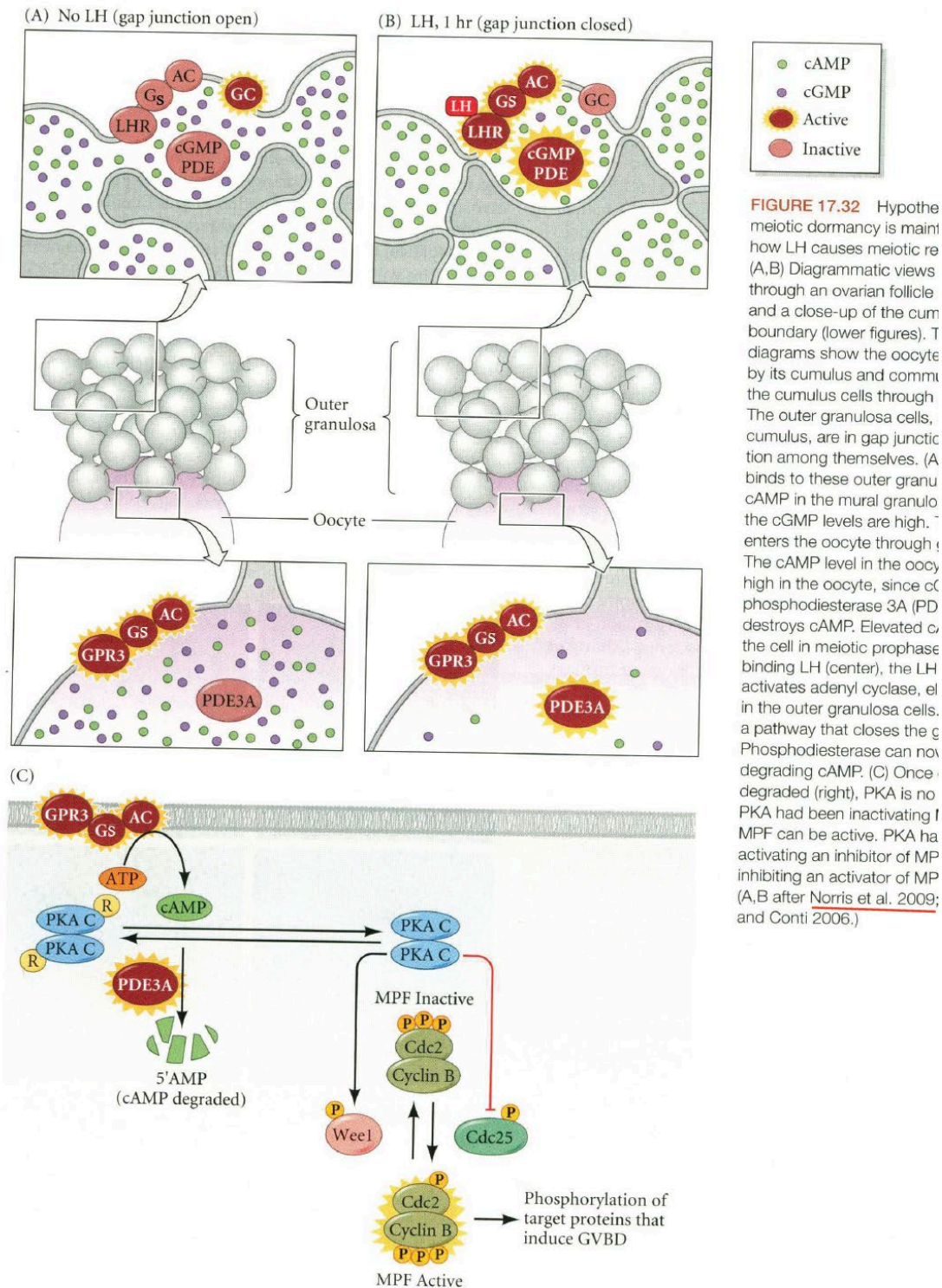


FIGURE 14.4@@ Intercellular communication mechanisms maintain meiotic dormancy and mediate LH-induced meiotic resumption. (A,B) Diagrammatic views of a segment through an ovarian follicle (upper panels) and a close-up of the cumulus-ovary boundary (lower panels). The middle panel shows the oocyte surrounded by its cumulus and communicating with the cumulus cells through gap junctions. The outer granulosa cells, above

the cumulus, are in gap junction communication among themselves. (A) Before LH binds to these outer granulosa cells, the cAMP in the mural granulosa is low and the cGMP level is high, due to an active guanylyl cyclase (GC). The cGMP enters the oocyte through gap junctions. The cAMP level in the oocyte is also high, since cGMP inhibits phosphodiesterase 3A (PDE3A), which destroys cAMP. Elevated cAMP keeps the cell in meiotic prophase. (B) Upon binding LH (upper right panel), the LH receptor activates adenylyl cyclase, elevating cAMP in the outer granulosa cells. This initiates complex pathways that inactivate the guanylyl cyclase and activate enzymes that degrade cGMP (cGMP PDE), thus lowering cGMP in the granulosa cells. Due to diffusion through gap junctions, cGMP also decreases in the oocyte. The cAMP phosphodiesterase in the oocyte can now function, degrading cAMP. (C) Once cAMP is degraded (right), PKA is no longer active. PKA had been inactivating MPF, but now MPF can be active. PKA had also been activating an inhibitor of MPF (Wee1) and inhibiting an activator of MPF (Cdc25B). (A,B after R. P. Norris et al. 2009. *Development* 136: 1869–1878, and L. A. Jaffe and J. R. Egbert, 2017. *Annu Rev Physiol* 79: 237–260; C after S. J. Han and M. Conti 2006. *Cell Cycle* 5: 227–231.)

Relabel (A) No LH (high cGMP) and (B) LH, 20 minutes (low cGMP)

— For the top panels of the figure, I would show the gap junctions open for both No LH and LH, as is the case until at least 10 minutes after LH

— For the middle panel, I would show just the version on the left, with open gap junctions, centered so that it applies to both of the upper panels.

— The lower panels are fine as is, but change G5 to Gs.

Norris R. P., Ratzan W. J., Freudzon M, Mehlmann L. M., Krall J, Movsesian M. A., Wang H, Ke H, Nikolaev V. O., Jaffe L. A. 2009. Cyclic G. M.P from the surrounding somatic cells regulates cyclic A. M.P and meiosis in the mouse oocyte. *Development* 136: 1869–1878.

Jaffe L. A., Egbert J. R. 2017. Regulation of mammalian oocyte meiosis by intercellular communication within the ovarian follicle. *Annu Rev Physiol* 79: 237–260.

Han S. J., Conti M. 2006. New pathways from P. K.A to the Cdc2/cyclin B complex in oocytes: Wee1B as a potential P. K.A substrate. *Cell Cycle* 5: 227–231.