

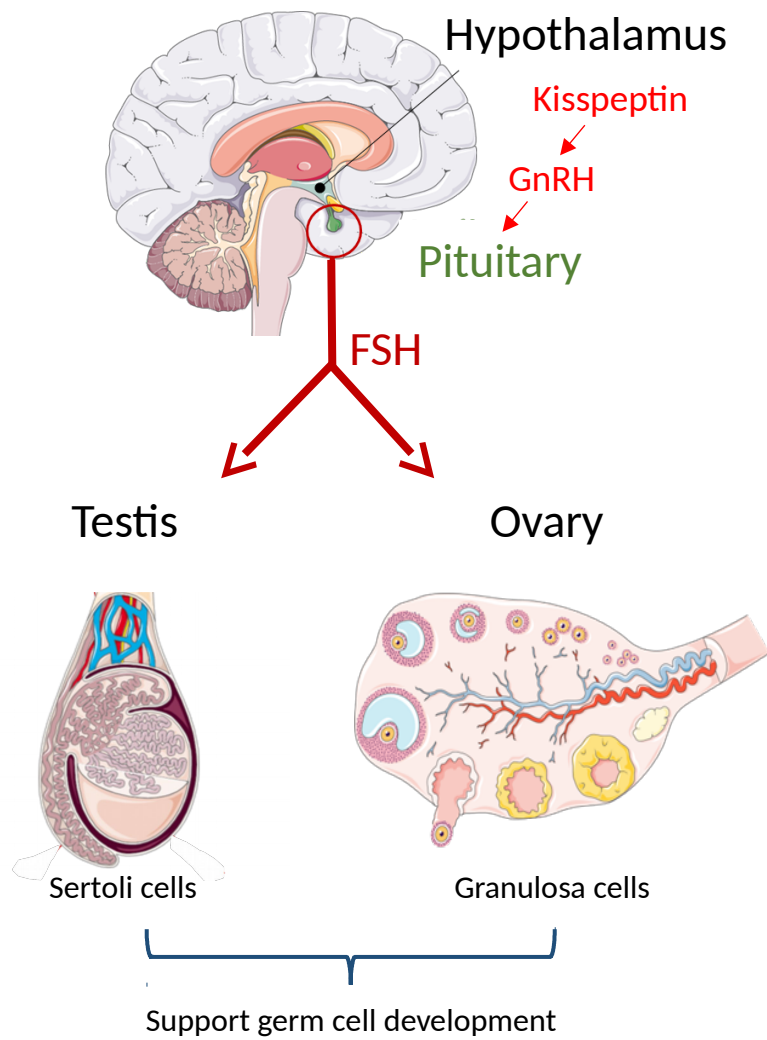


Figure 1

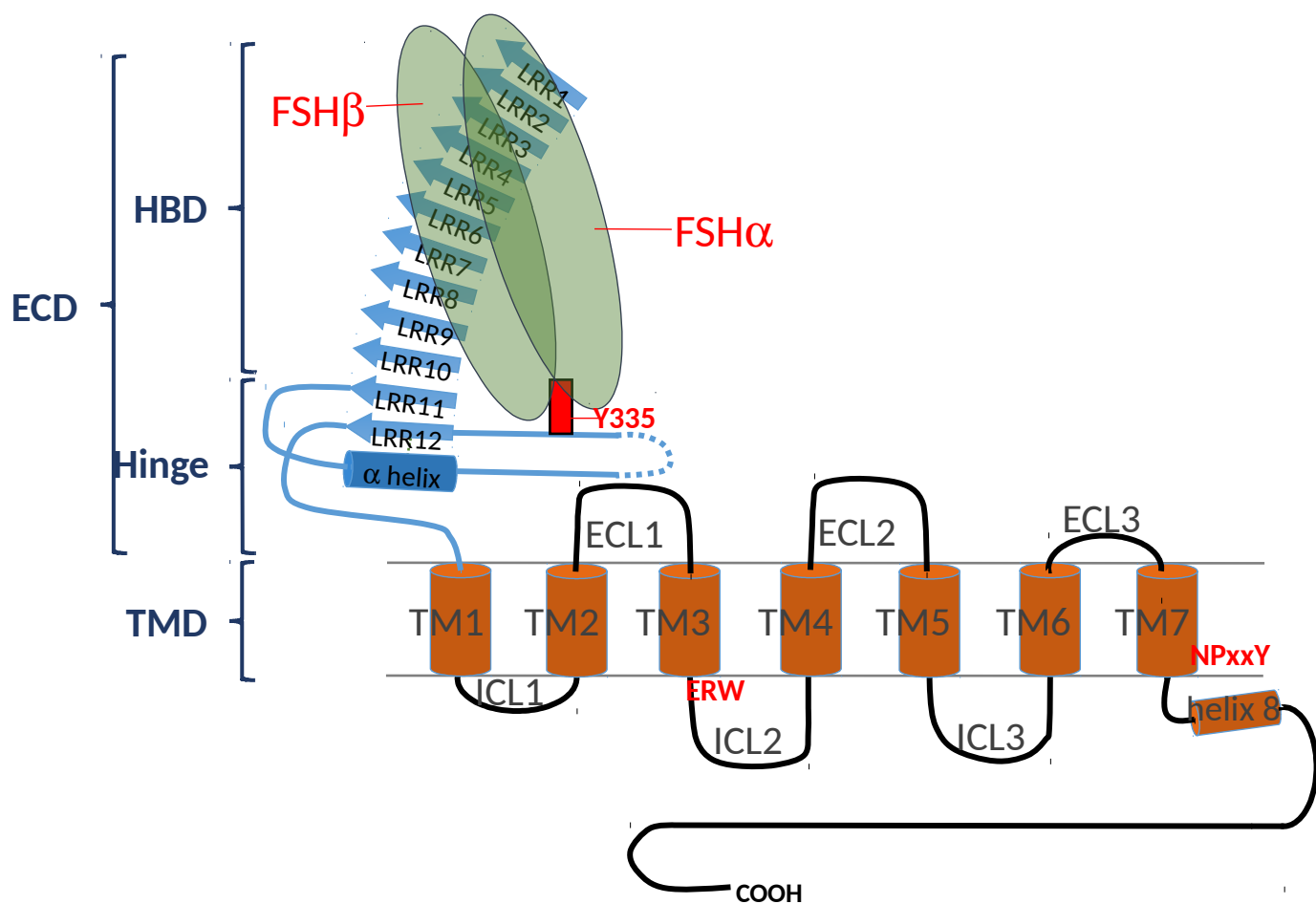


Figure 2

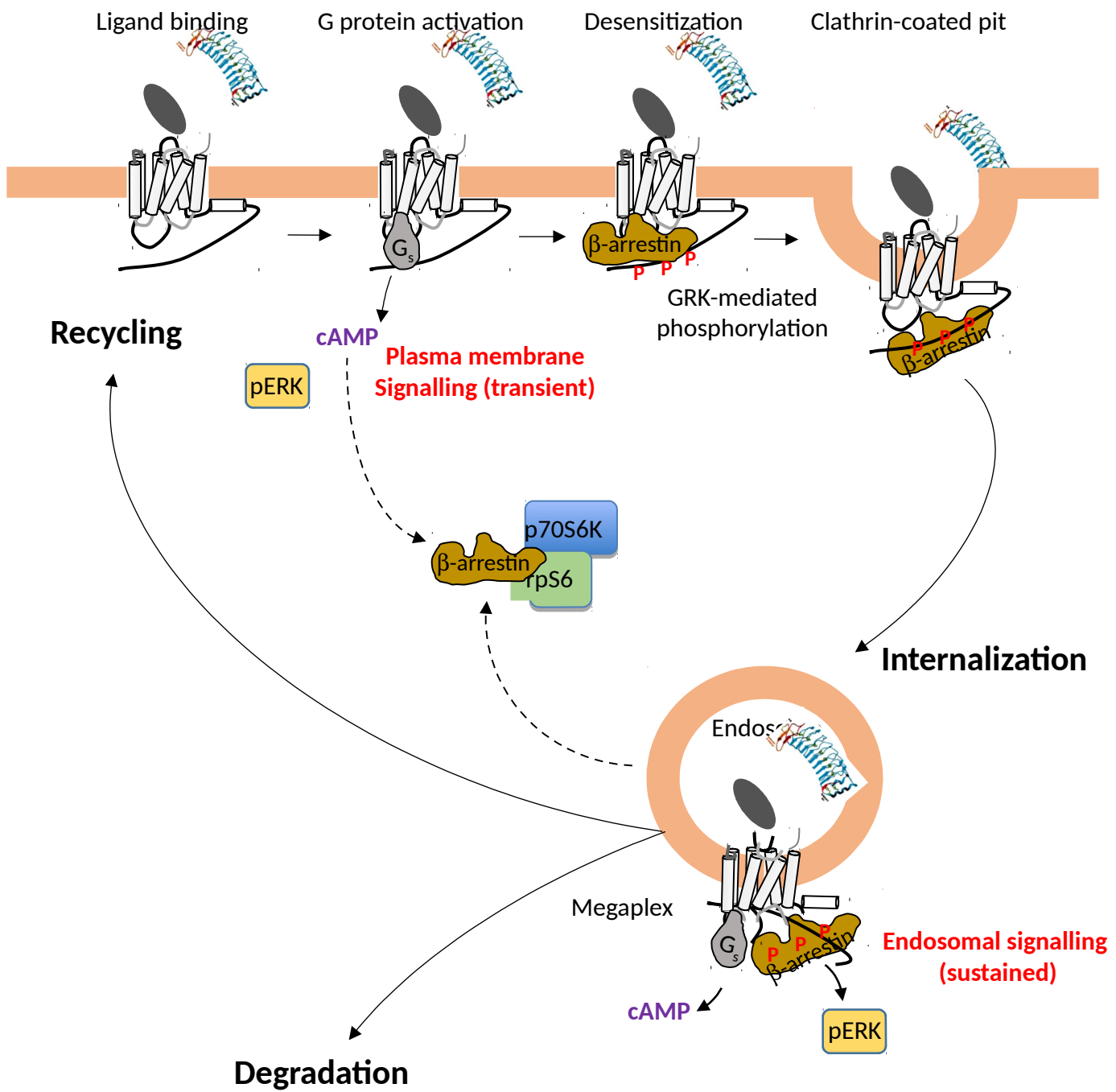
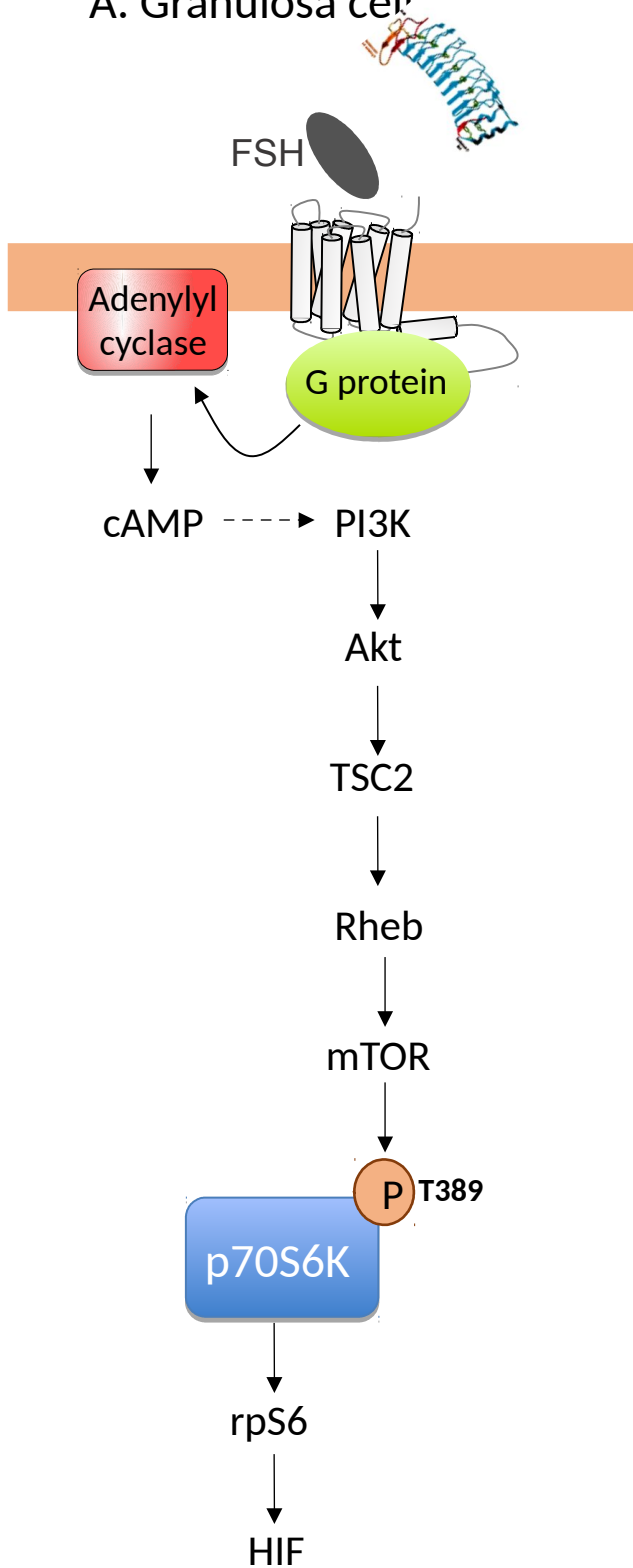


Figure 3





## A. Granulosa cell



## B. Sertoli cell

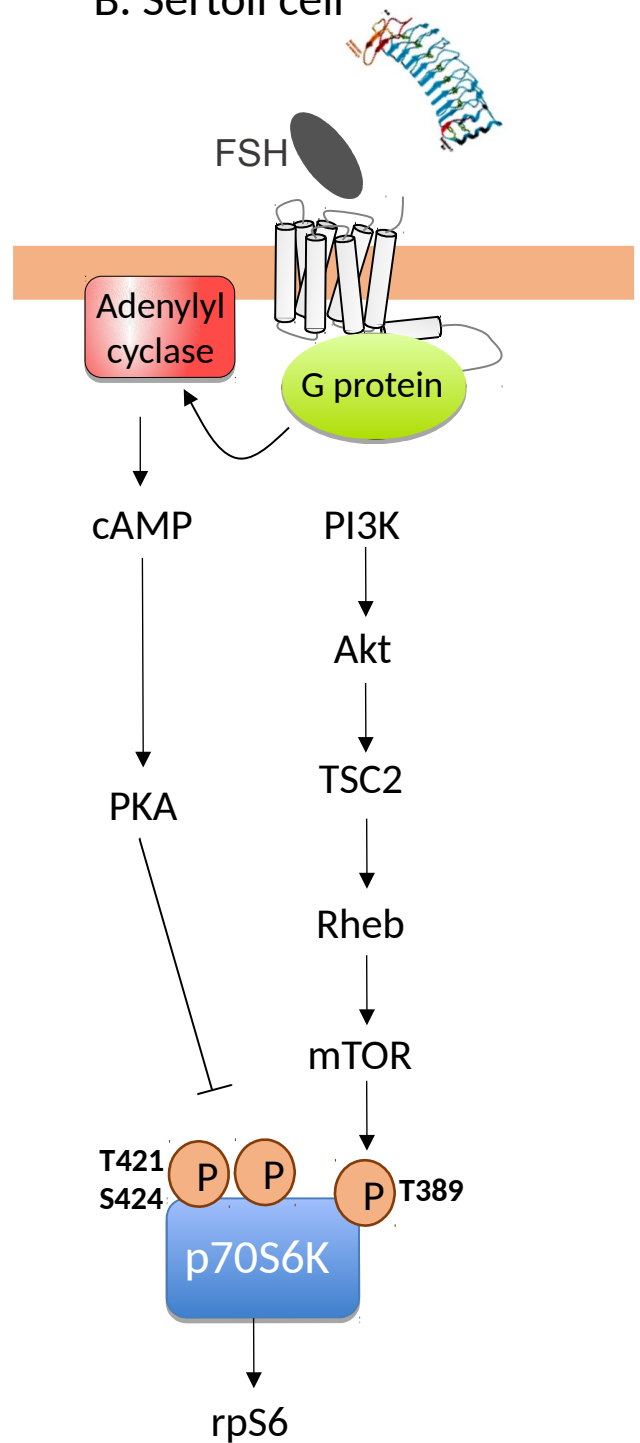


Figure 5

**Table 1: high throughput studies assessing FSH impact on gene transcription.**

| Stimulus                                                 | Cell/ Tissue                                                  | Model organism                                                     | Method                                                       | Nbr of DEG                                   | Main conclusions                                                                                                                                                     | Reference             |
|----------------------------------------------------------|---------------------------------------------------------------|--------------------------------------------------------------------|--------------------------------------------------------------|----------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| 0, 2, 4, 8, 24 h oFSH (NIH, 25 ng/ml)                    | in vitro SC                                                   | 20d rat                                                            | Affymetrix U34A $\mu$ array (9000 probes)- n=2               | 100-300                                      | New FSH-responsive genes identified i                                                                                                                                | McLean, 2002          |
| 2h $\beta$ -folliotropin (Organon) or FSH1208, 500 ng/ml | in vitro GrC                                                  | healthy women (18-35y)                                             | Affymetrix Human Focus Chip (8795 probes)-n=5                | 74                                           | No difference between the two FSH isoforms. Importance of the number of GATA-regulated genes                                                                         | Perlman, 2006         |
| oFSH injection (10IU), 4, 8, 12, 24h                     | Whole testes                                                  | hpg mice                                                           | Affymetrix GeneChip U74A (12488 probes)- n = 2               | 316 at 4h, 124 at 8h, 193 at 12h, 101 at 24h | Confirms and extends previous in vitro data                                                                                                                          | Sadate-Ngatchou, 2004 |
| FSH suppression 2d and 4d prior collection               | 3, 9, 18d rat testis                                          | rat treated with anti-FSH Abs and with the flutamide AR antagonist | Affymetrix RG_ U34A $\mu$ array (8799 probes)- n=2           | 60 at 18 d                                   | FSH differentially affects SC and GC cells in an age-dependent manner in vivo, promoting Sertoli cell mitosis at day 9, and supporting germ cell viability at day 18 | Meachem, 2005         |
| FSH and T suppression 4d prior collection                | Stage VII and VIII seminiferous tubules                       | adult rat treated with anti-FSH Abs                                | Affymetrix GeneChip Rat Genome 230 2.0 (31099 probes)- n=5-6 | 185 in SC                                    | Hormone-responsive global transcriptional repressors in SC, spermatogonia, and spermatids                                                                            | O'Donnell, 2009       |
| hFSH injection (8IU, Serono) 12, 24, 72h                 | Whole testes                                                  | 10 weeks hpg mice                                                  | Affymetrix MOE430A $\mu$ array (14000 probes)- n=3-4         | 400                                          | FSH directly and indirectly induces rapid changes in SC and LC transcript levels , but the effect on GC occurs within longer time-span                               | Abel, 2009            |
| FSH (0.5 ng/ml, NHPP), 6d                                | GC from F1 and F2 follicles                                   | Cow                                                                | Illumina Hi-Seq sequencing-n=4                               | n.d.                                         | A potential role for WNT signaling in potentiating FSH action during selection of the dominant follicle                                                              | Gupta, 2014           |
| FSH (0.5 $\mu$ g/ml, Gonal-f, Merck-Serono) 6h in vitro  | Cumulus cells before and after IVM                            | Cow                                                                | EmbryoGENE bovine $\mu$ array n=3                            | 1469 (IVM + FSH)                             | DEG involved in cumulus expansion, steroidogenesis, cell metabolism, oocyte competence                                                                               | Khan, 2015            |
| zFSH (100 ng/ml), 48h                                    | Whole testes, in vitro                                        | Adult zebrafish                                                    | Illumina Hi-Seq sequencing- n=6                              | 206                                          | Marked impact on metabolic genes and on BTB components                                                                                                               | Crespo, 2016          |
| FSH (NIDDKD), 24h                                        | Granulosa cells transduced with Foxo1-expressing adenoviruses | Oestradiol-treated immature rat                                    | Ion Torrent RNAseq                                           | 3772                                         | Foxo1 regulates most FSH target genes in granulosa cells                                                                                                             | Herndon, 2016         |