

Japan-German Symposium in Ulm

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Yamaguchi University

Tokyo

Kyoto

Historic architectures



Yamaguchi University



Rich nature



Obstetricians / Gynecologists in University Hospital in Japan

— Physician —



— Scientist —



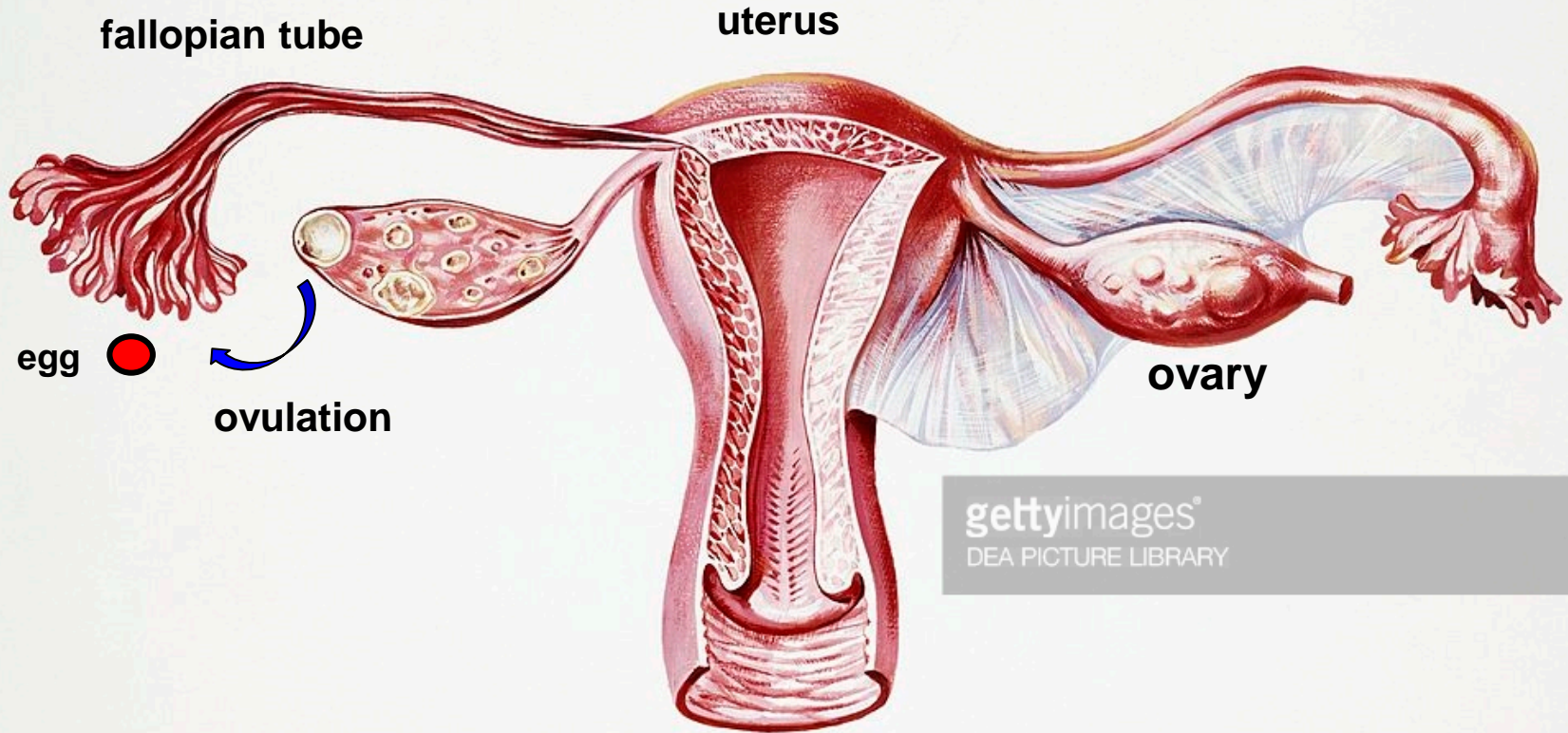


Molecular mechanisms of ovulation

Department of Obstetrics and Gynecology
Yamaguchi University Graduate School of Medicine

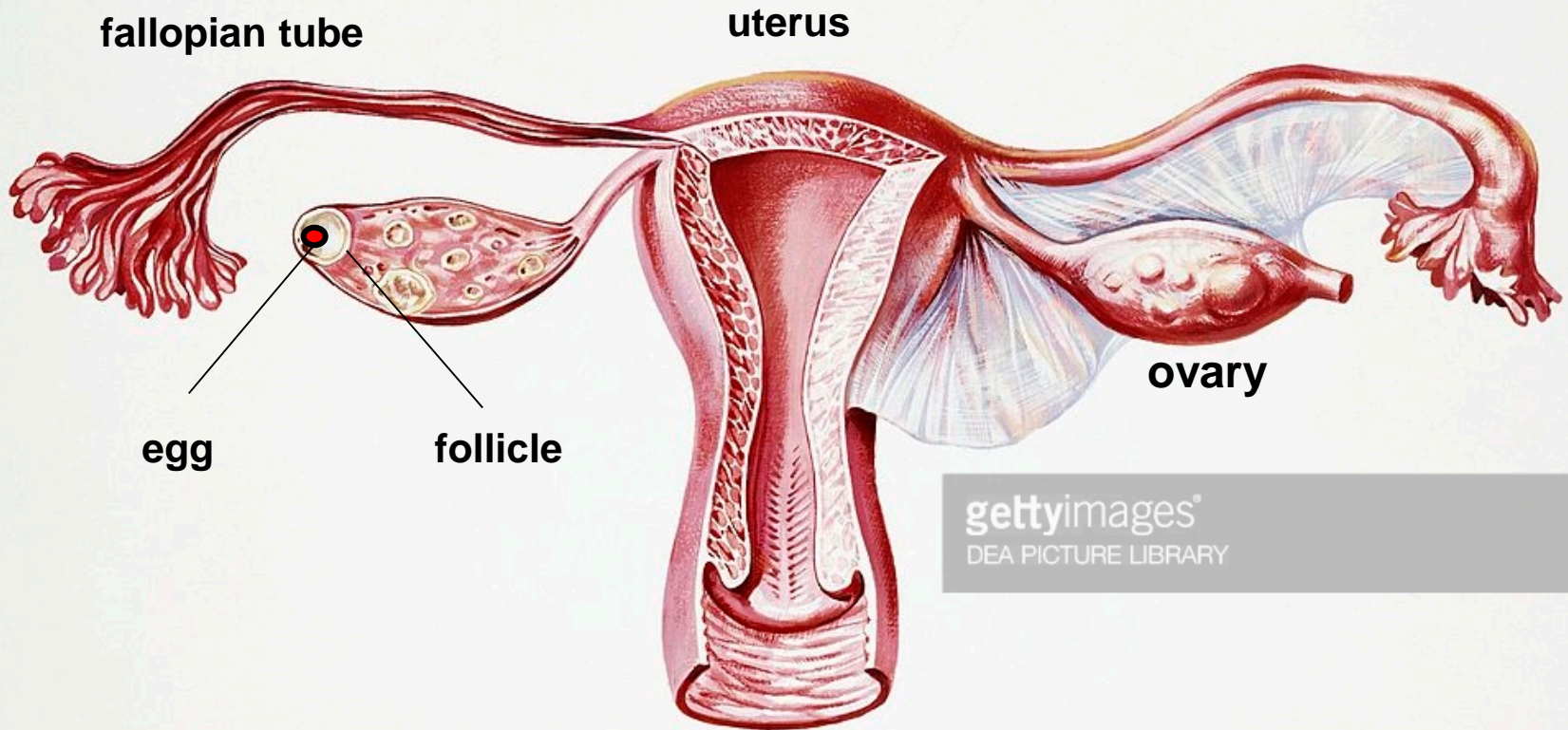
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Female reproductive organs



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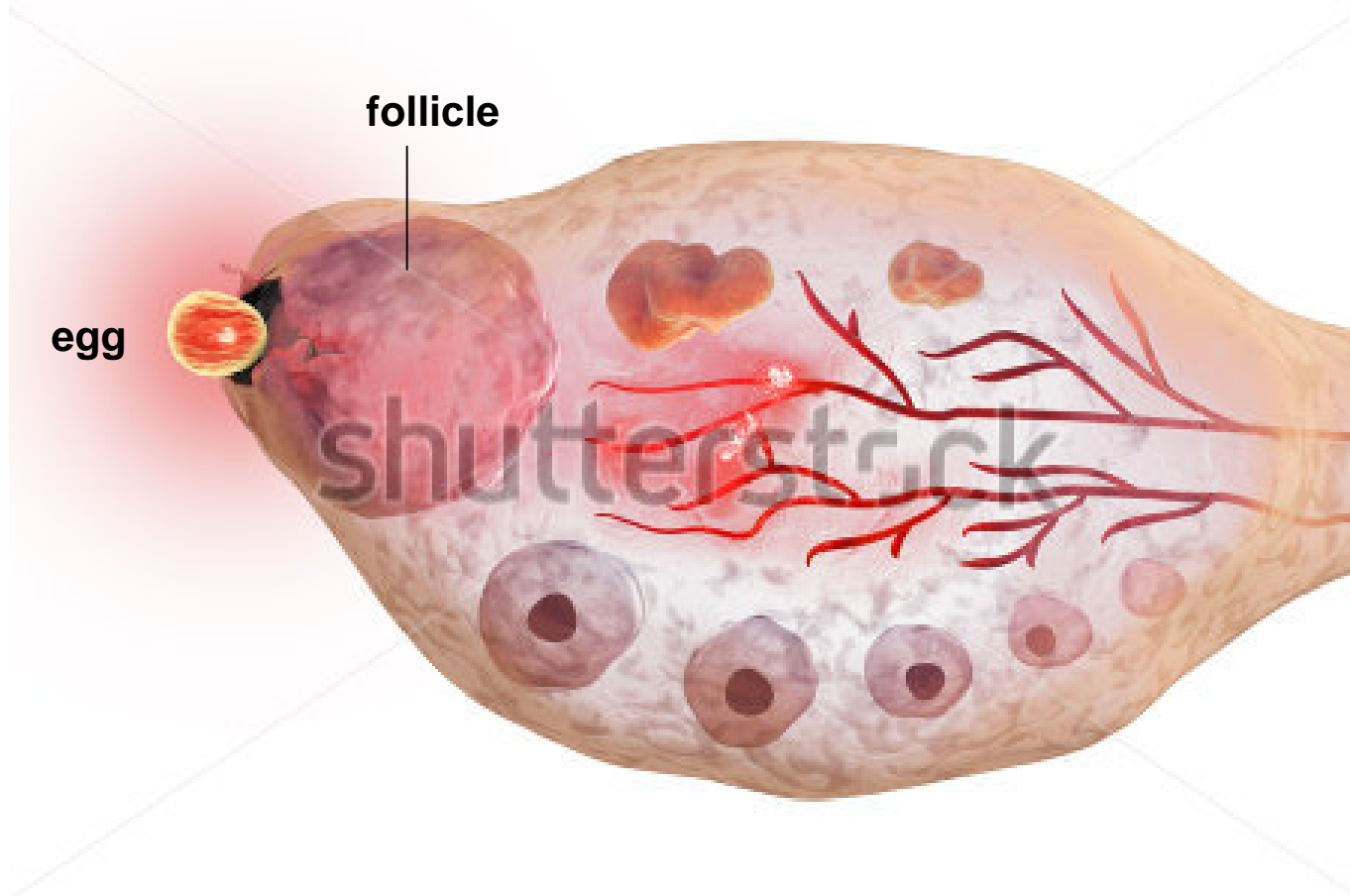




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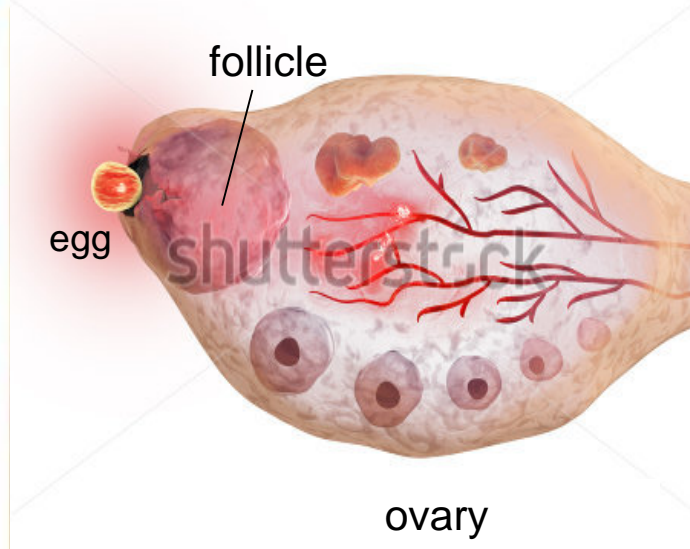
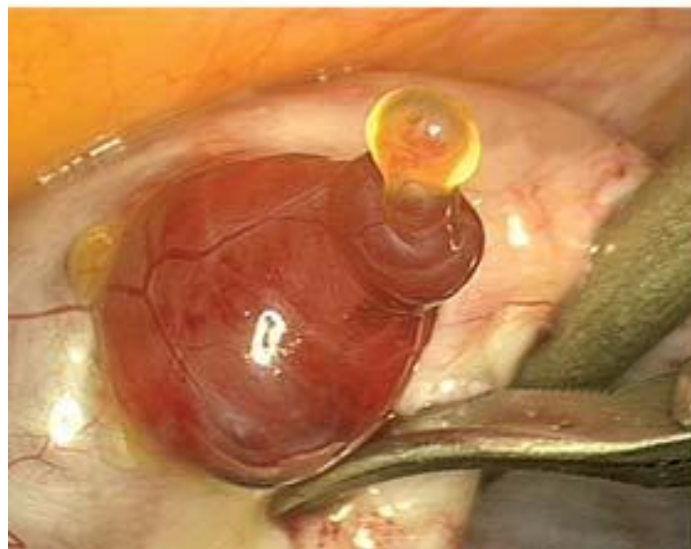
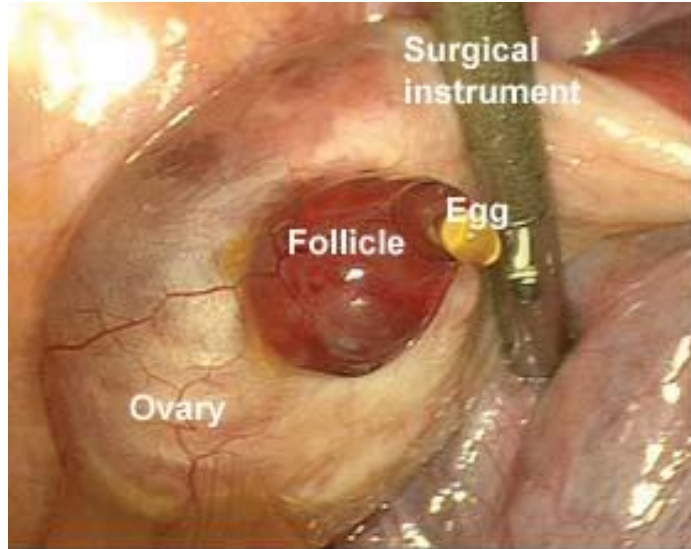
Ovulation

Follicle rupture and egg release



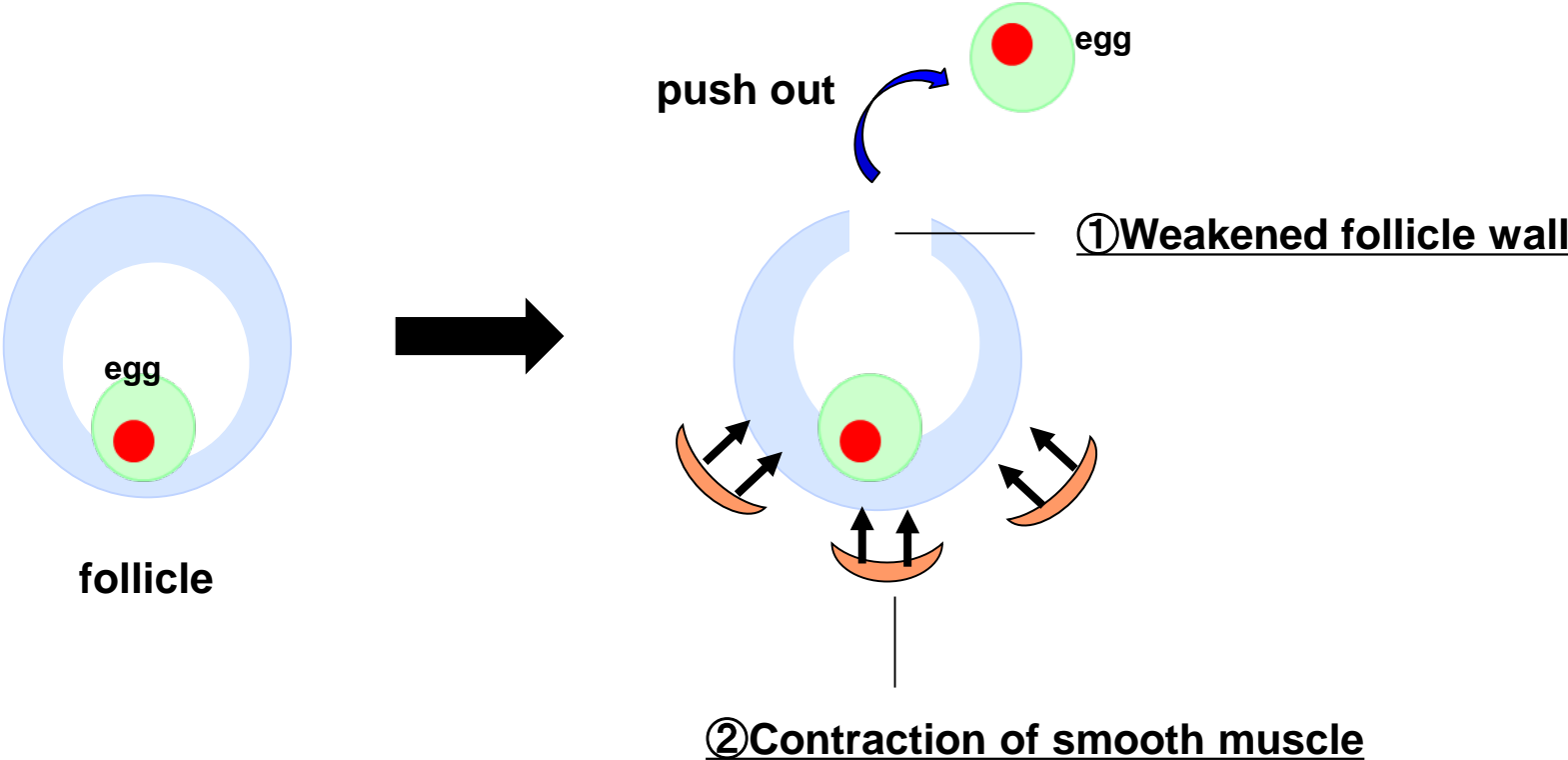
Ovulation in humans

Follicle rupture and egg release



What is the mechanism of ovulation / follicle rupture ?

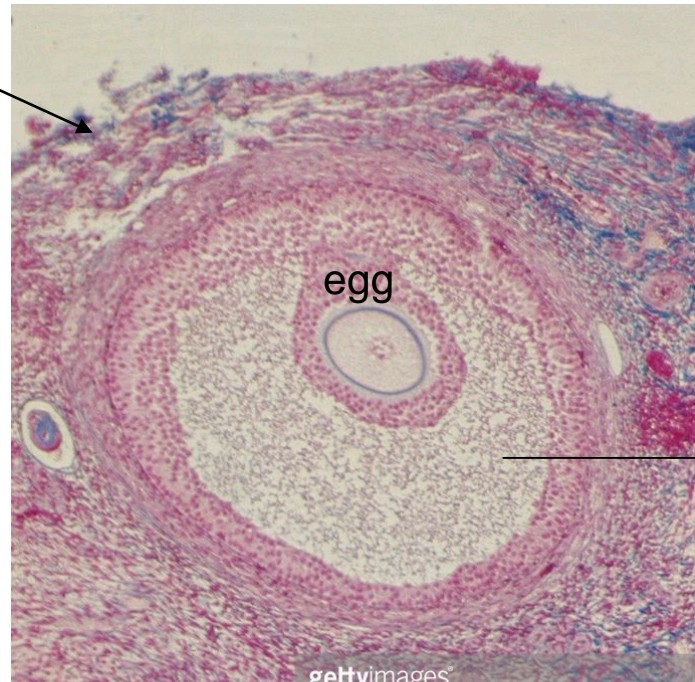
Mechanism of ovulation (follicle rupture)



Microscopic photograph of the follicle before ovulation

Local mechanism for follicle rupture

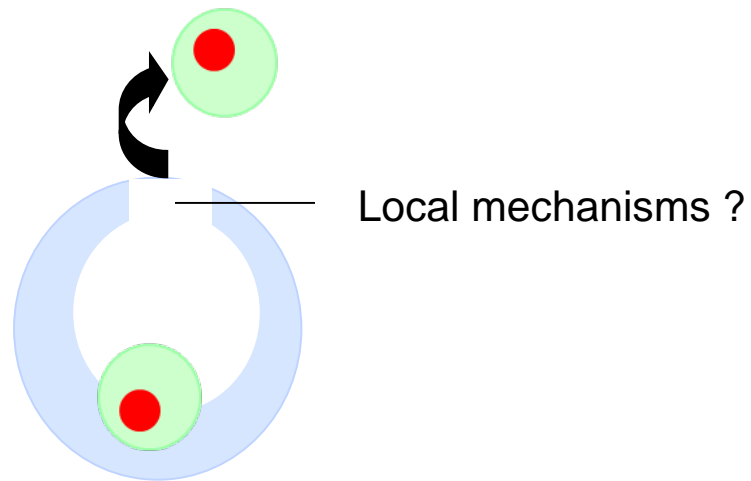
weakened follicle wall
It's getting thin.



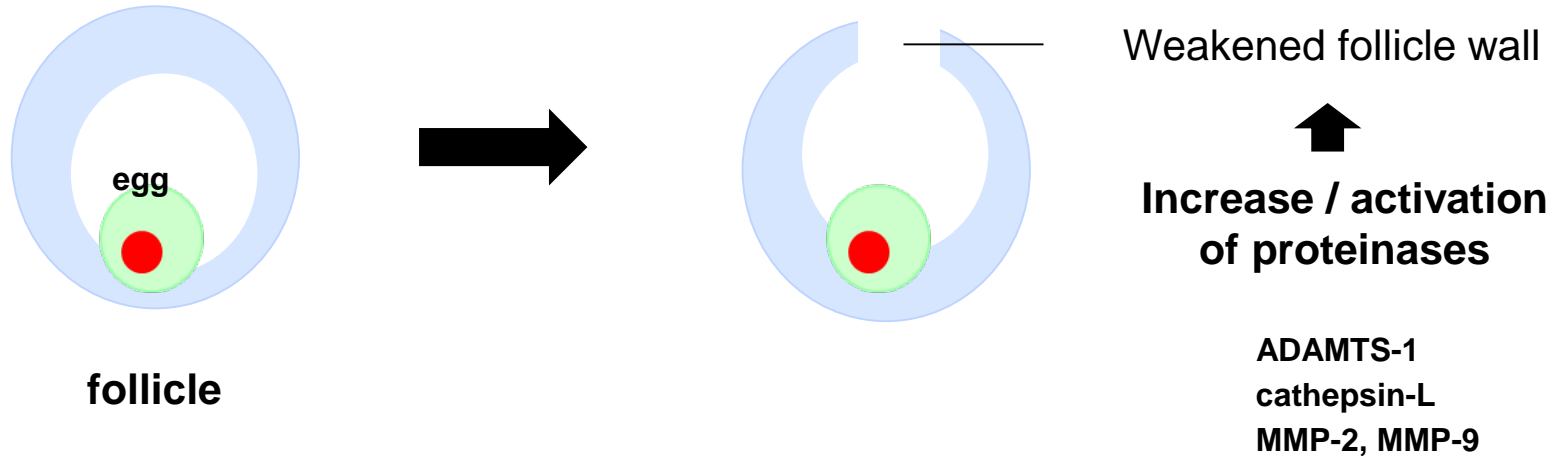
follicle

Follicle in the human ovary

How does the follicle wall become weakened ?



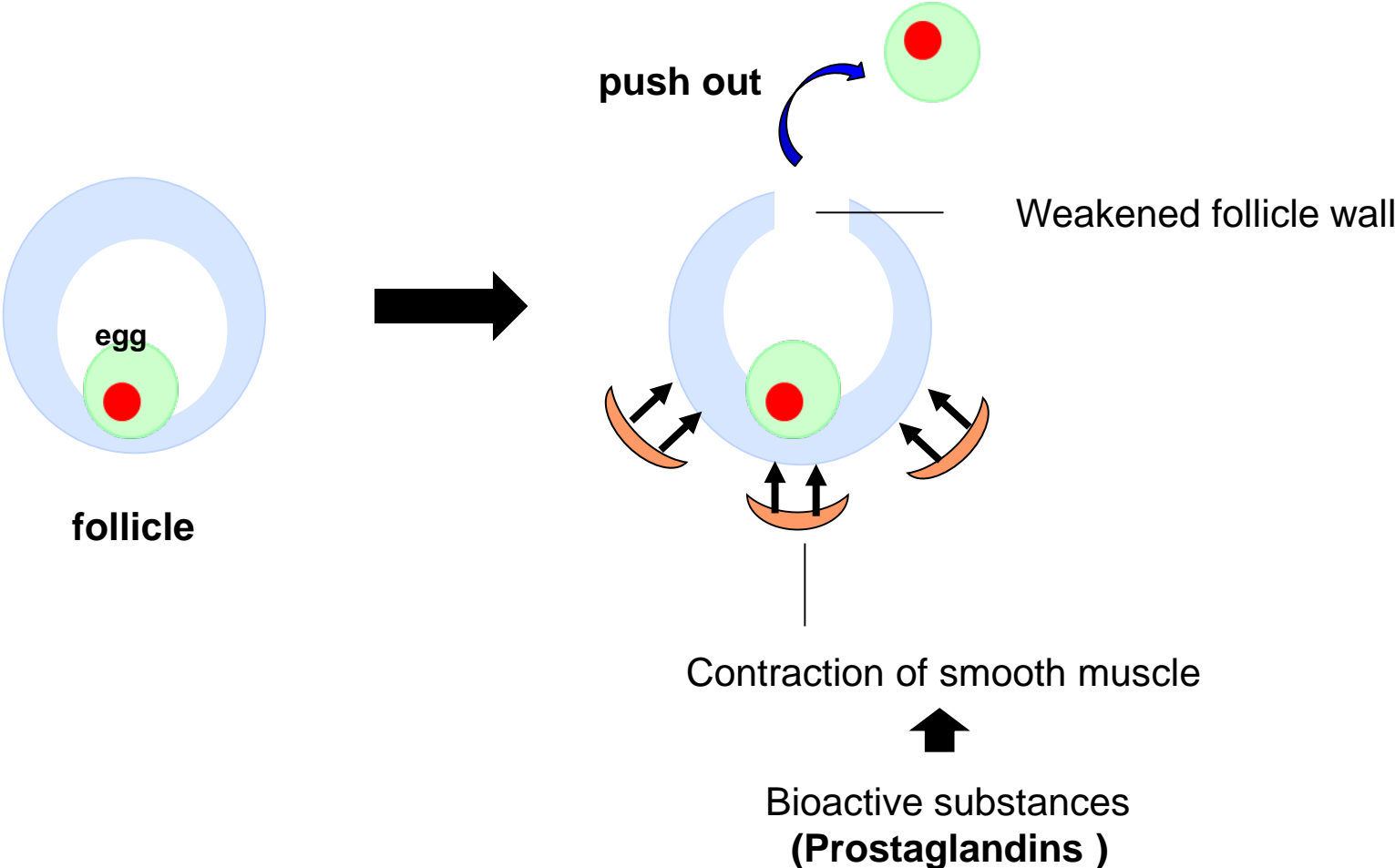
Mechanism of ovulation (follicle rupture)



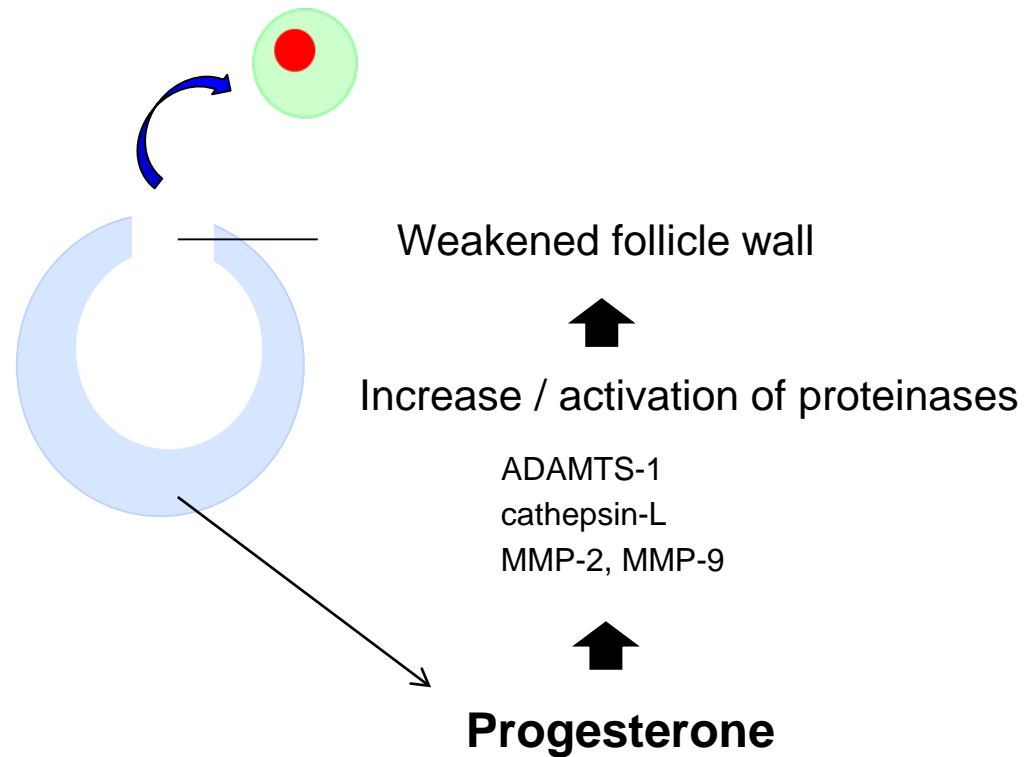
Follicle wall (membrane): consists of proteins

Proteinase: an enzyme that breaks down proteins

Mechanism of ovulation (follicle rupture)



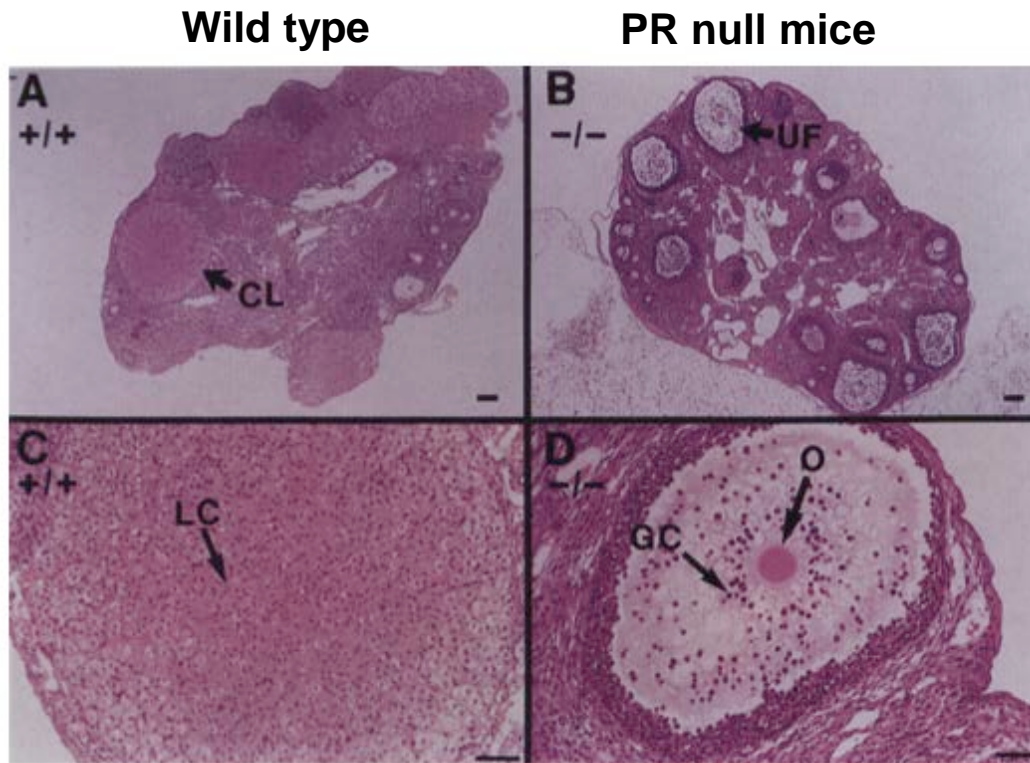
What stimulates the proteinases ?



Impaired rupture of pre-ovulatory follicles in PR-null mice

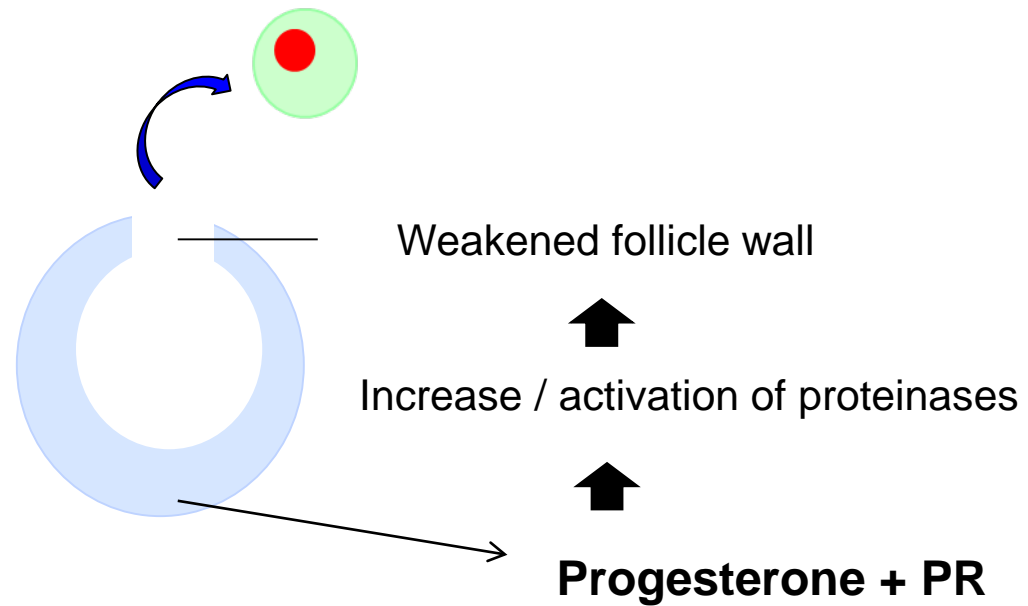
PR: Progesterone Receptor

PR-null mice lack the gene of Progesterone Receptor.
PR-null mice lack progesterone actions.



Lydon et al. Genes Dev, 1995

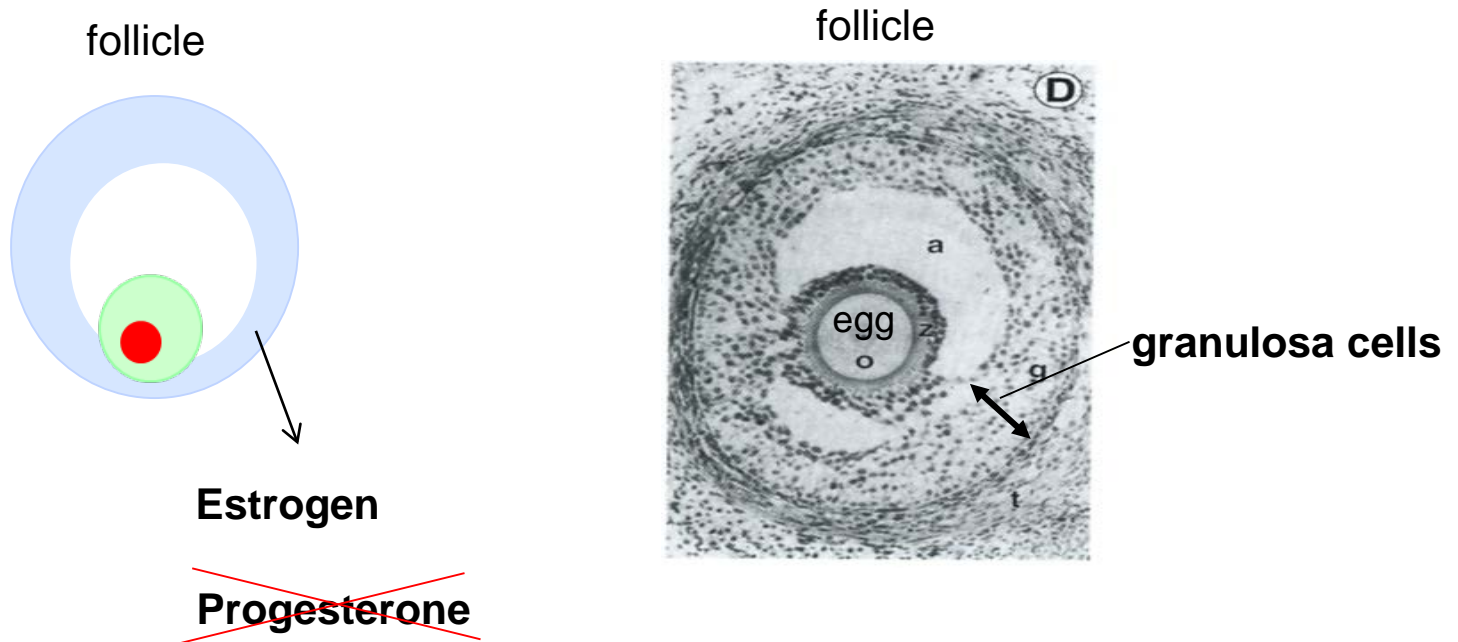
Progesterone is essential for follicle rupture (ovulation)



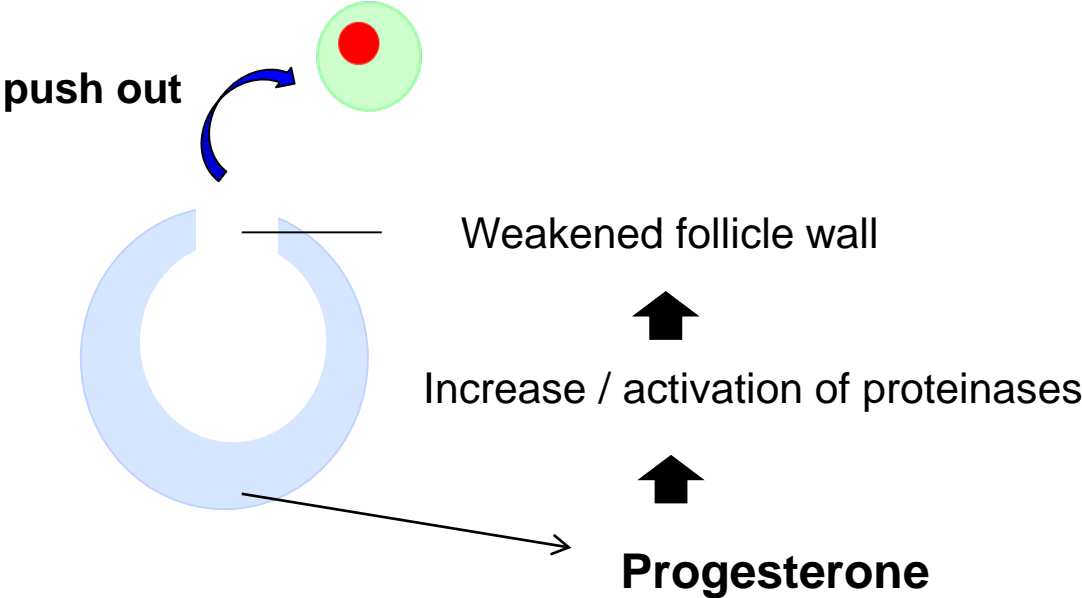
Production of female hormones (estrogen and progesterone)

Microscopic photograph of the follicle before ovulation

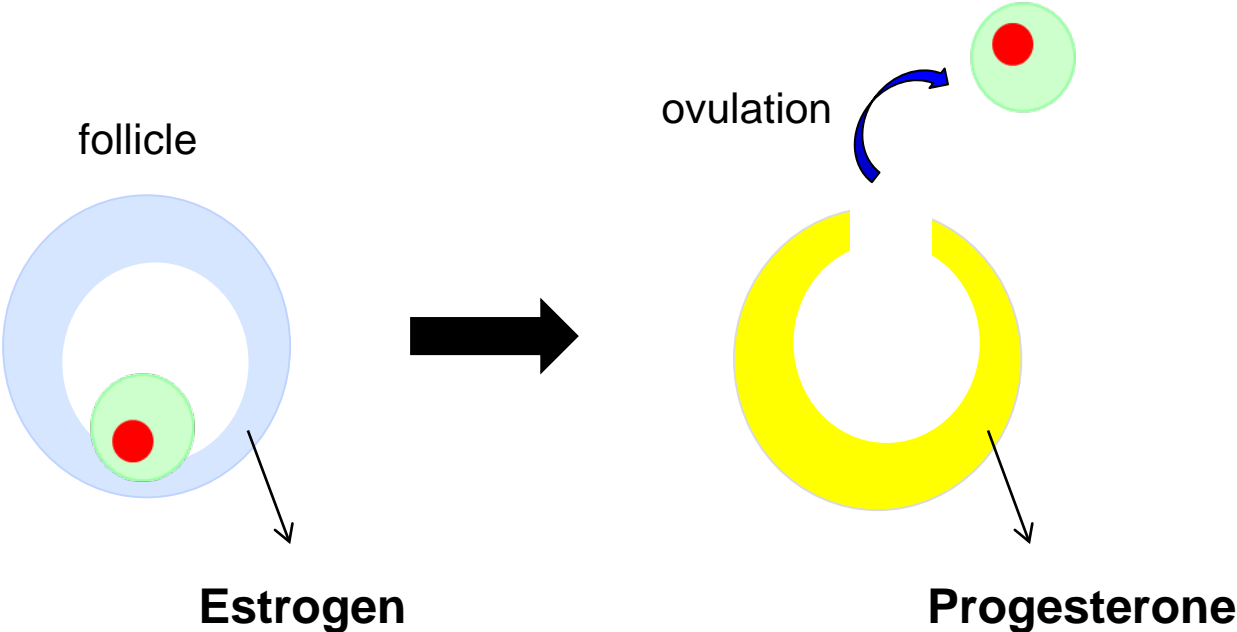
Only estrogen is produced before ovulation



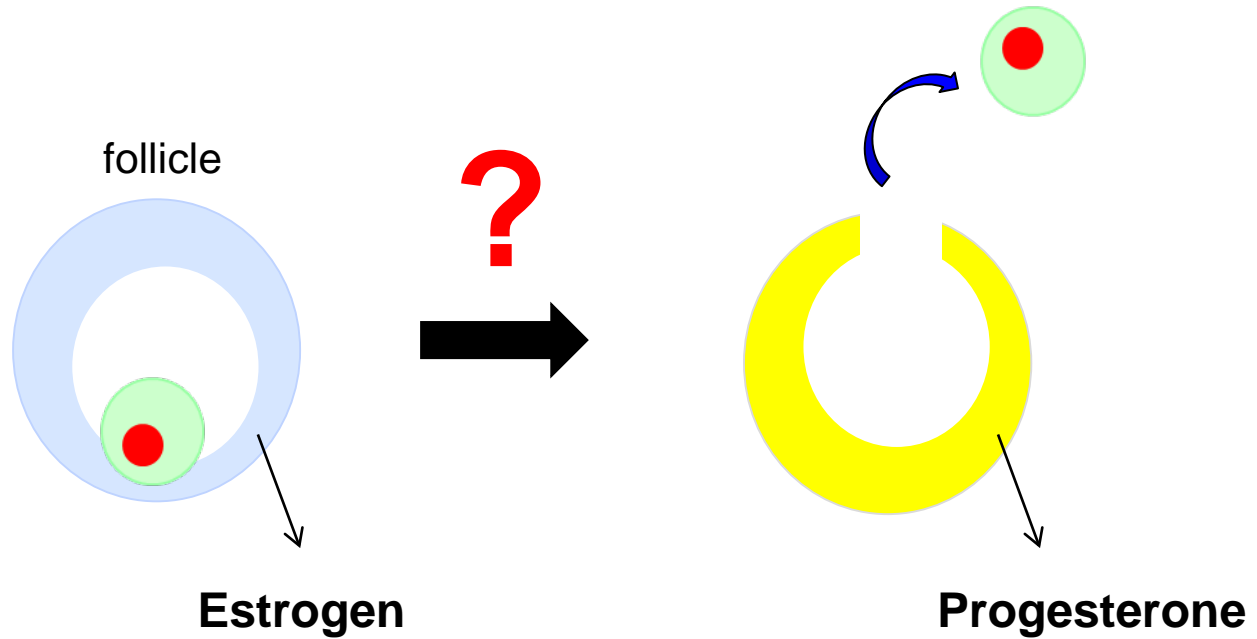
Progesterone is essential for ovulation



Granulosa cells have to change the hormone production from estrogen to progesterone to induce ovulation



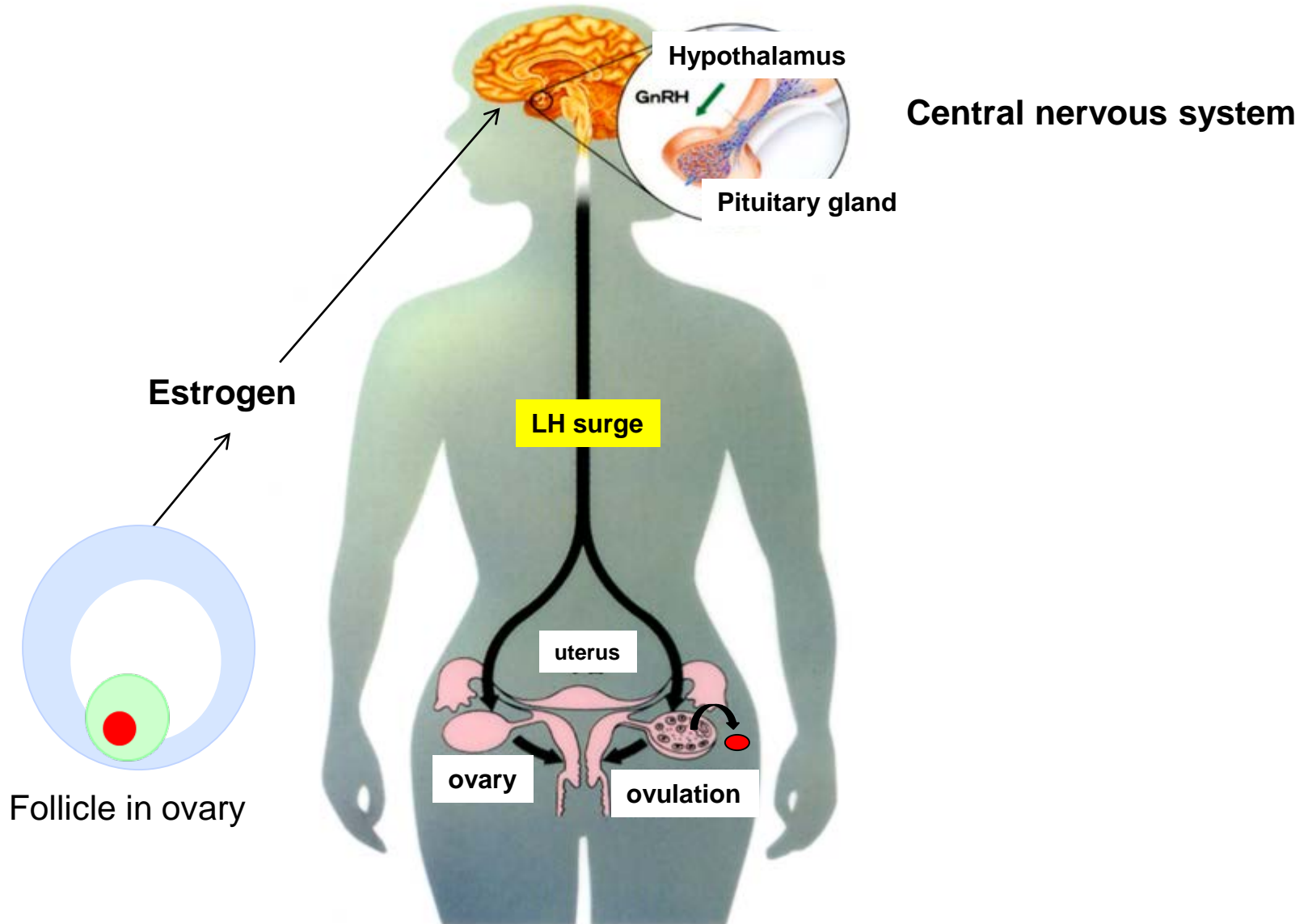
What is the signal (trigger) for the shift from estrogen to progesterone in granulosa cells ?



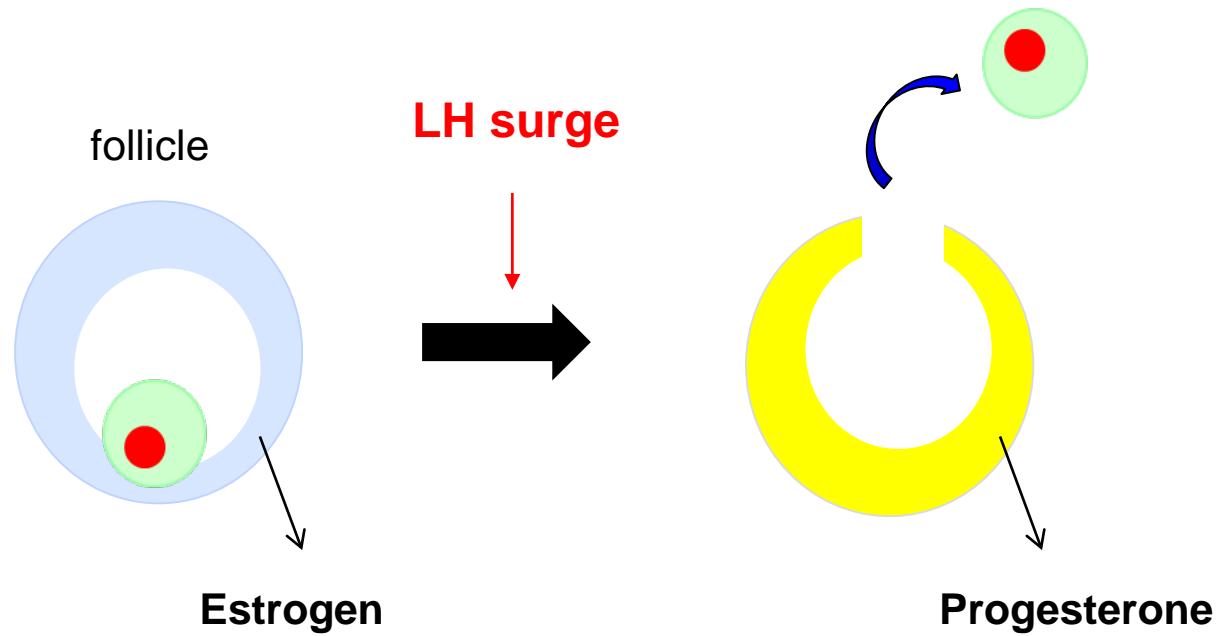
LH surge is the signal for ovulation

LH: Luteinizing hormone is produced by pituitary gland.

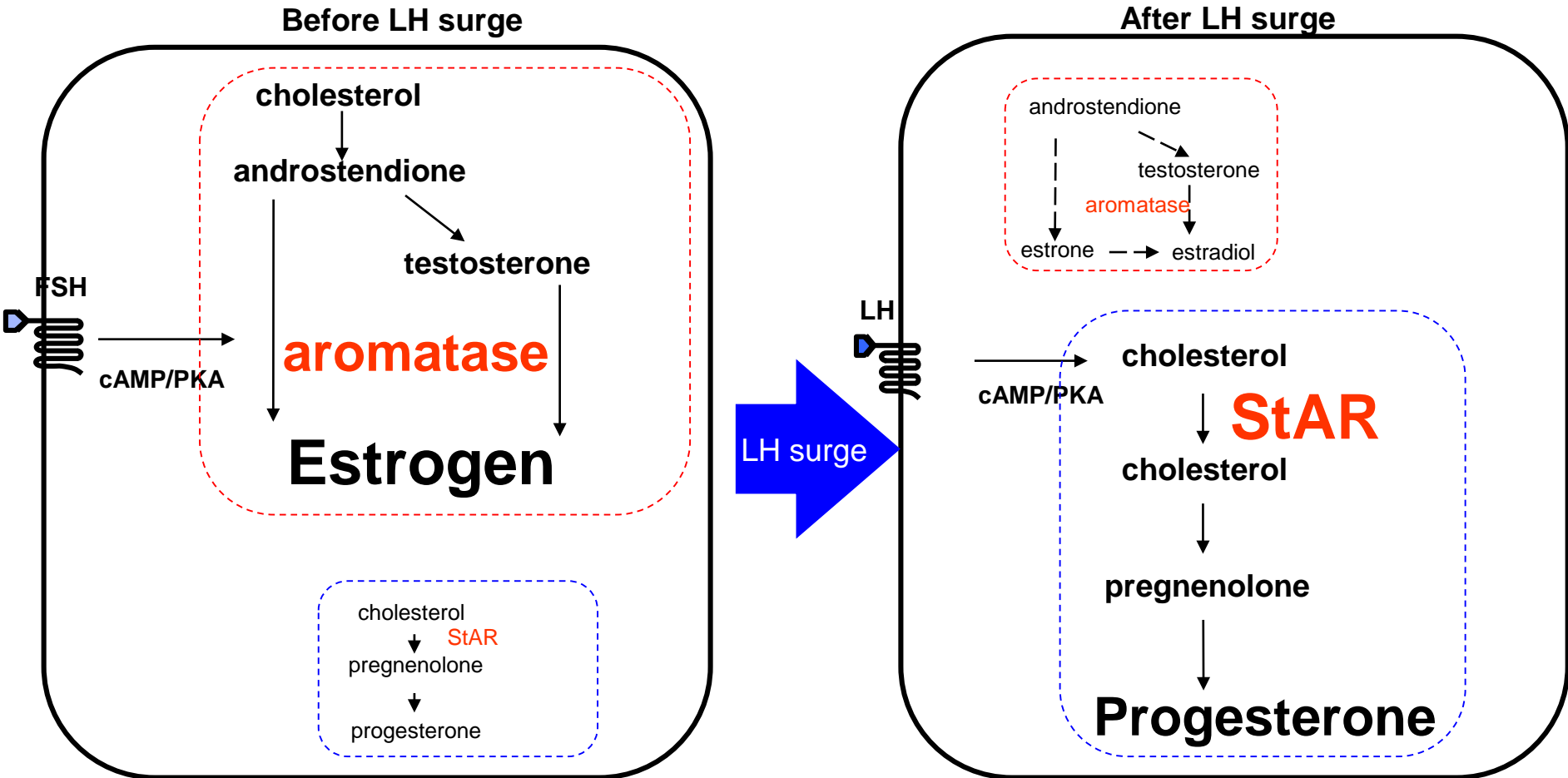
LH surge: large amount of LH is rapidly secreted.



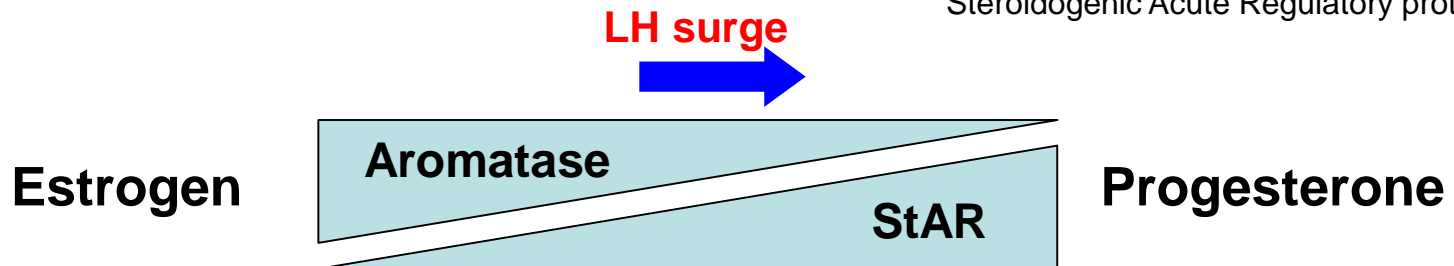
LH surge shifts female hormone production from estrogen to progesterone



Changes in hormone production in granulosa cells by LH surge

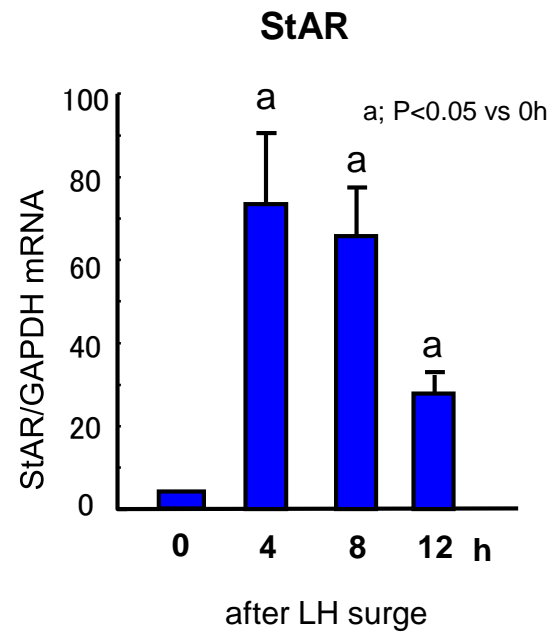
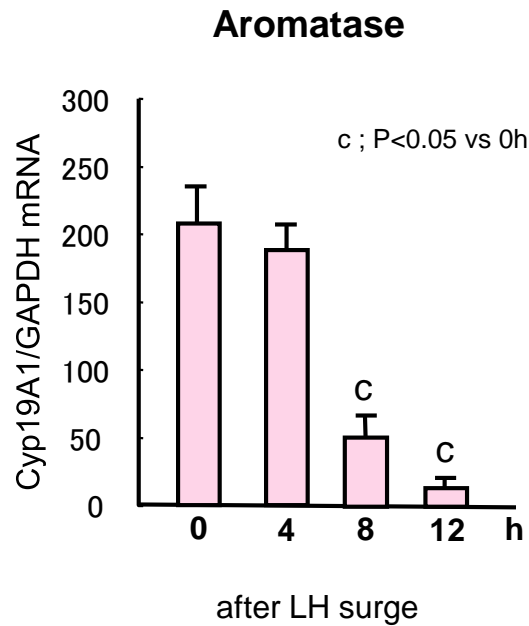


Steroidogenic Acute Regulatory protein (StAR)



**How rapidly do Aromatase and StAR change
by the LH surge ?**

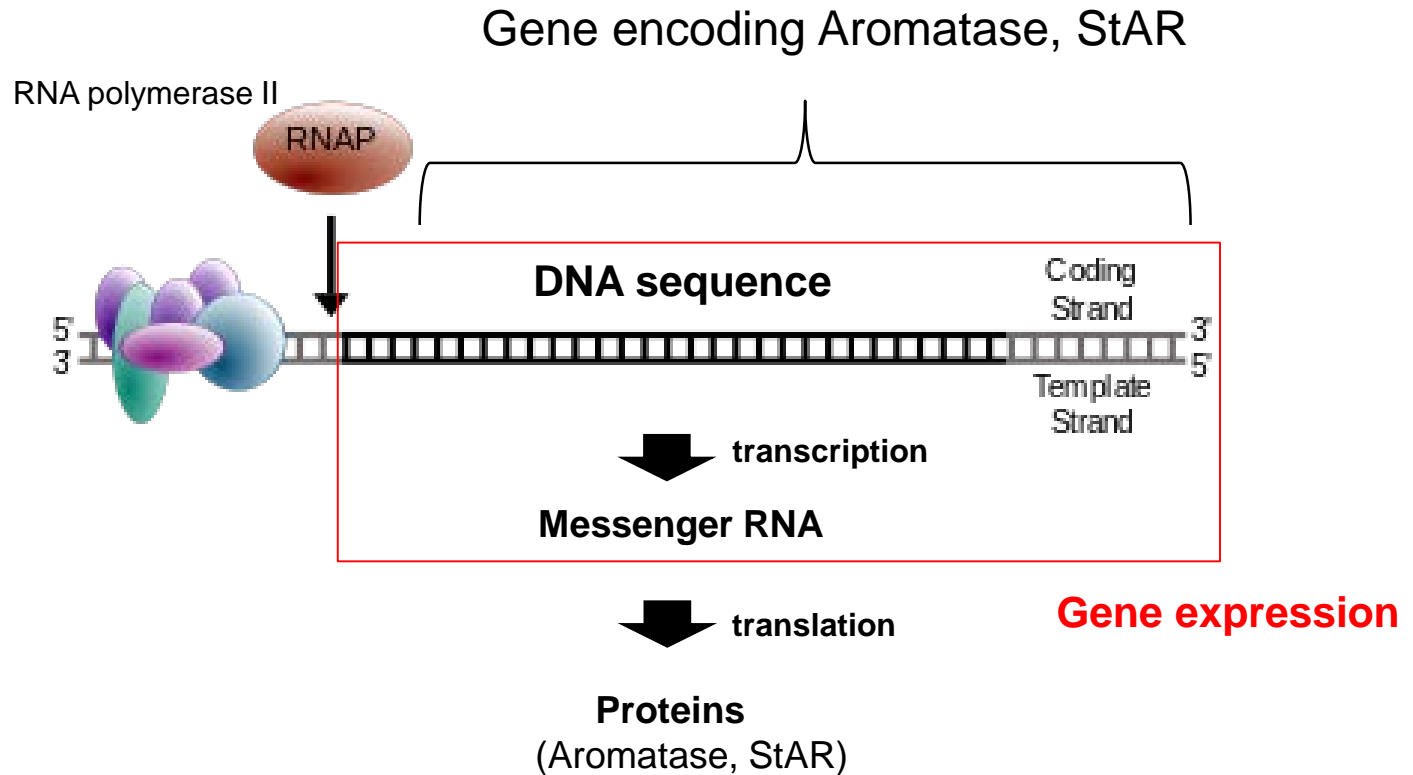
Rapid changes in Aromatase and StAR by the LH surge in rats



How are the rapid changes in Aromatase and StAR regulated ?

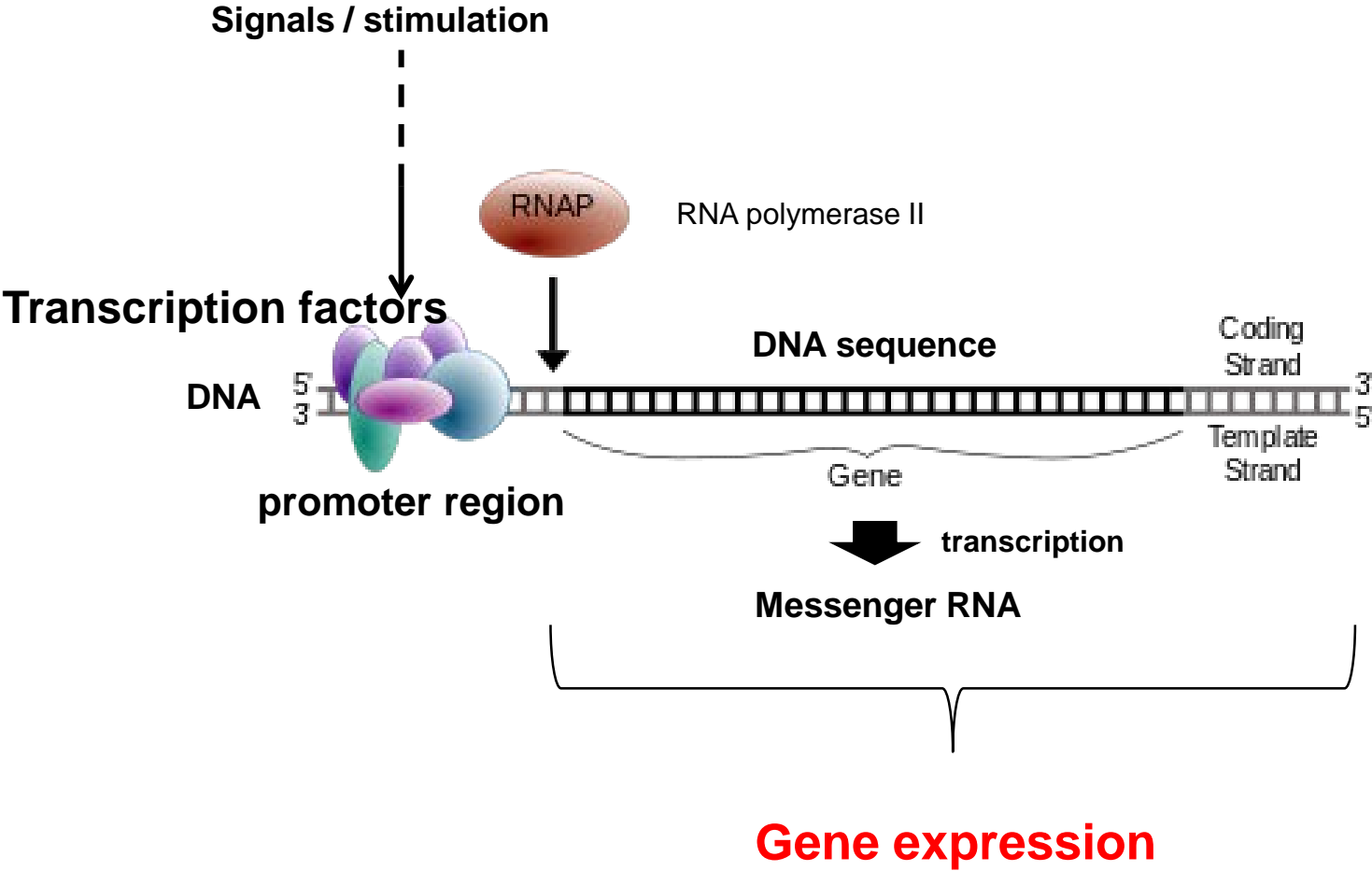
Protein production is regulated in the level of DNA of the genes

Genes consist of DNA.

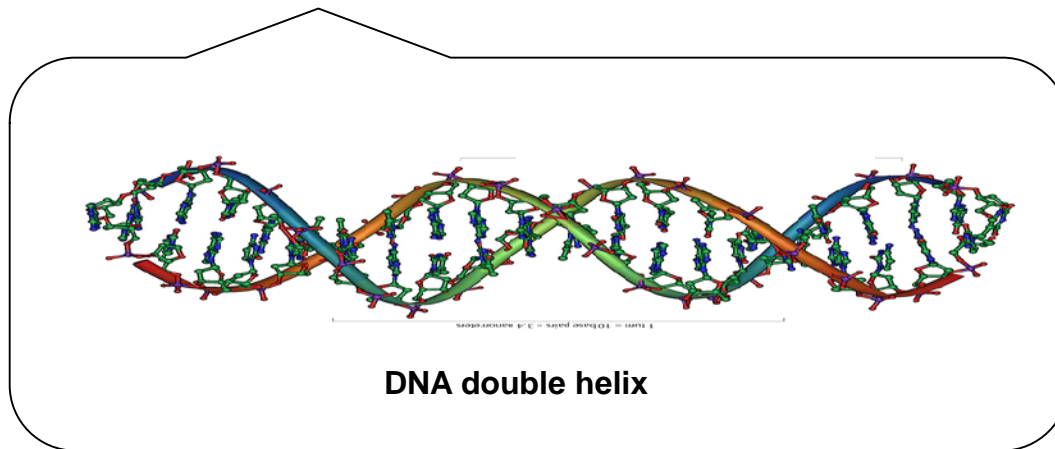
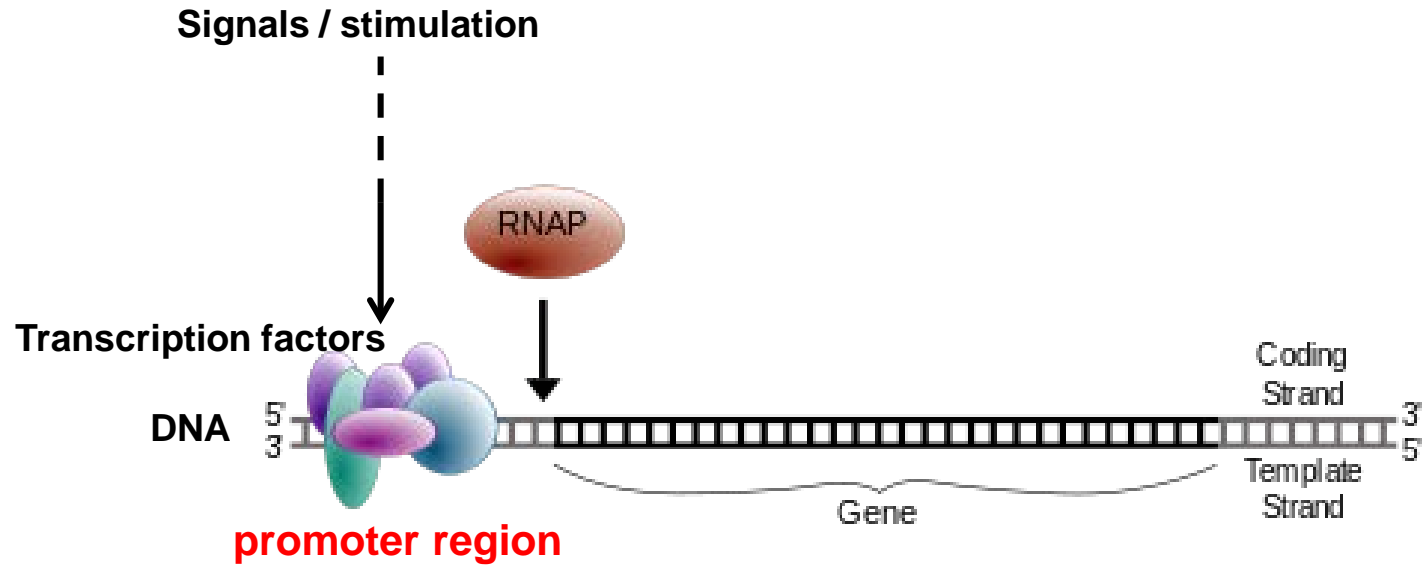


How is the gene expression regulated ?

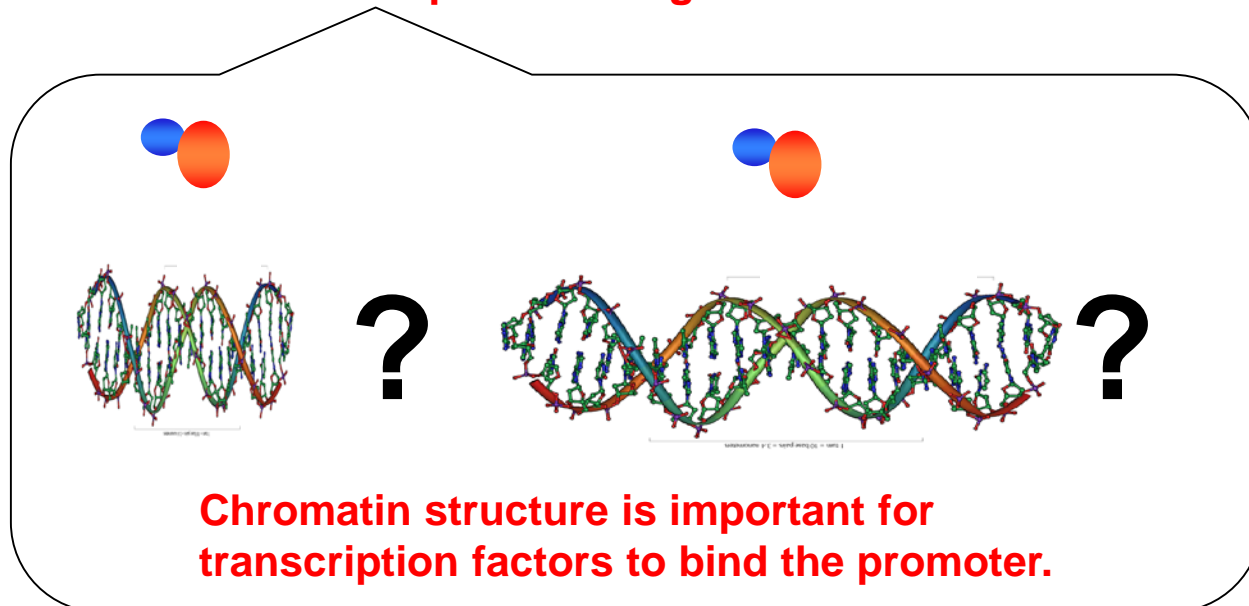
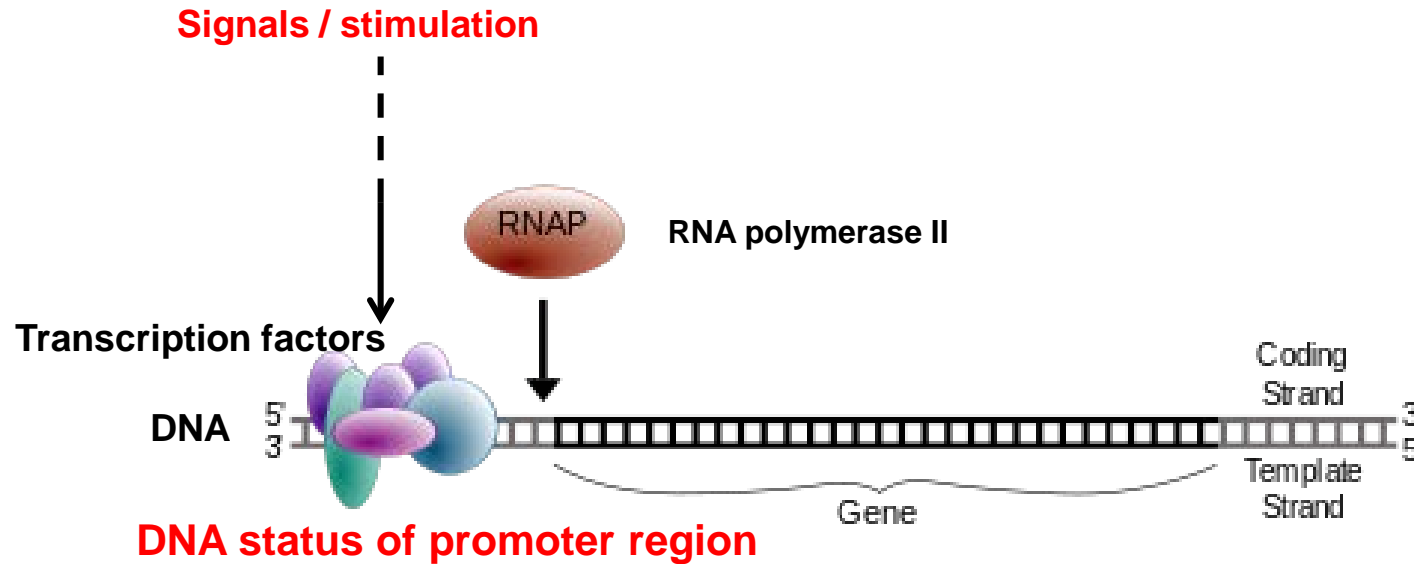
Regulation of gene expression by transcription factors



Regulation of gene expression by chromatin structure



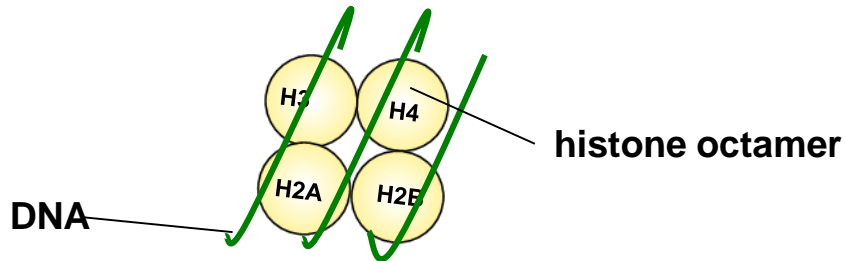
Regulation of gene expression by chromatin structure



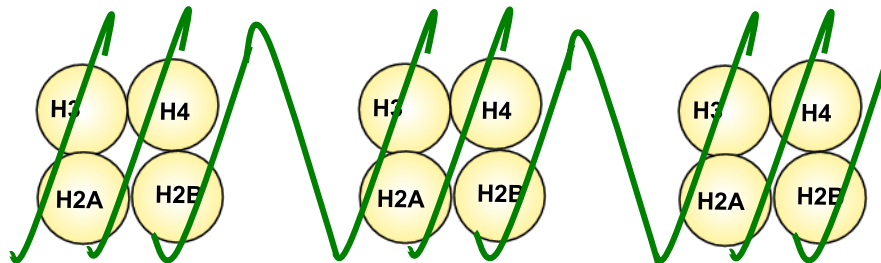
Chromatin structure

Nucleosome

The nucleosome is composed of 147 bp of DNA wrapped 1.65 turns around the histone octamer.

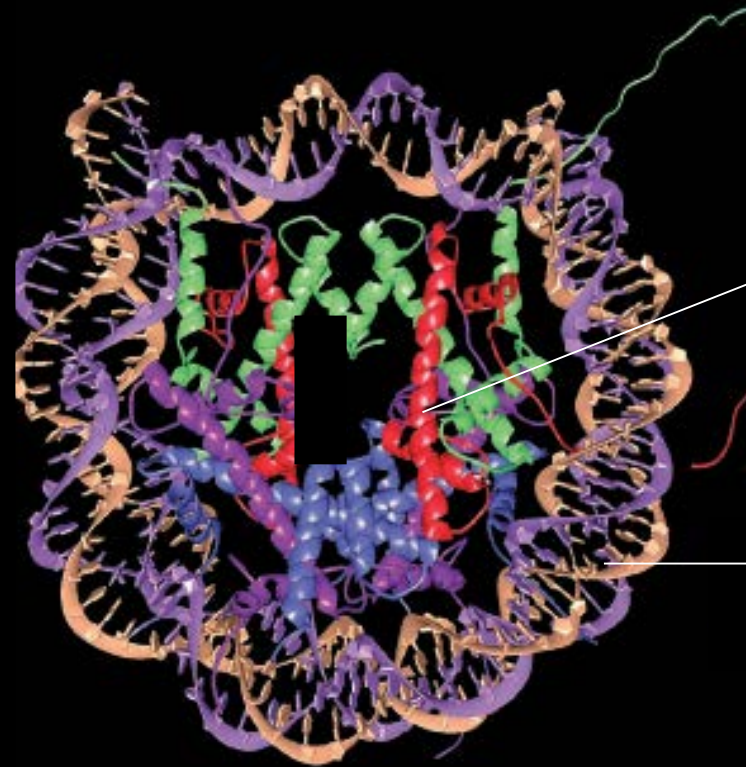


Chromatin is composed of nucleosomes.



Chromatin structure

Open chromatin

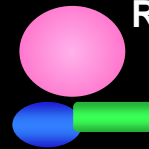


histones

DNA

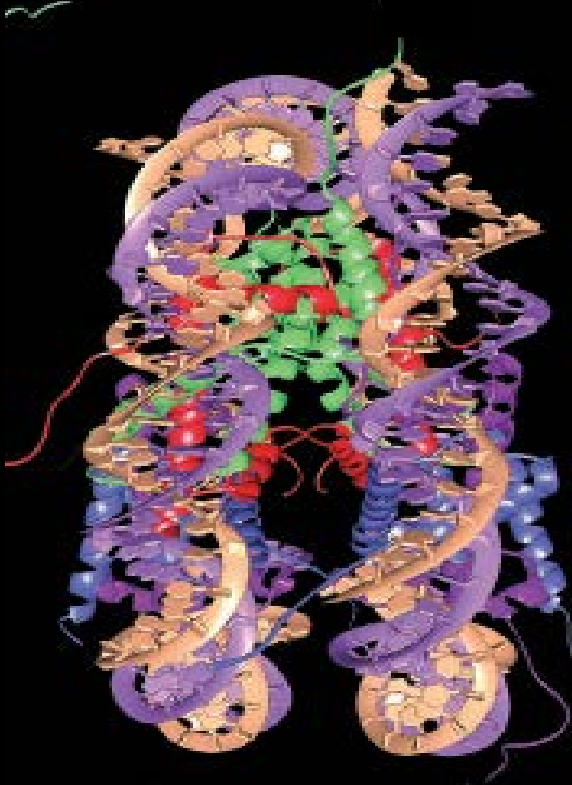


Transcription factor

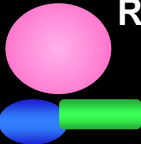


RNA Pol II

Condensed chromatin



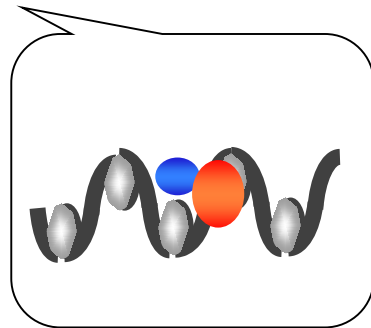
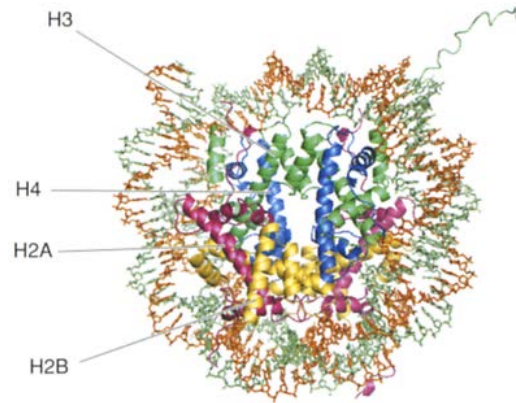
Transcription factor



RNA Pol II

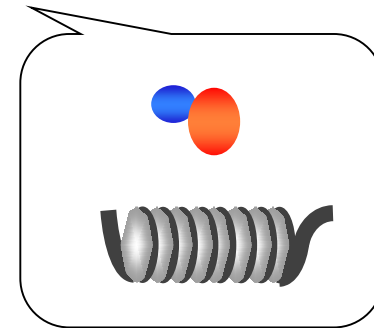
Chromatin structure is important

Open chromatin



Activating gene expression

Condensed chromatin

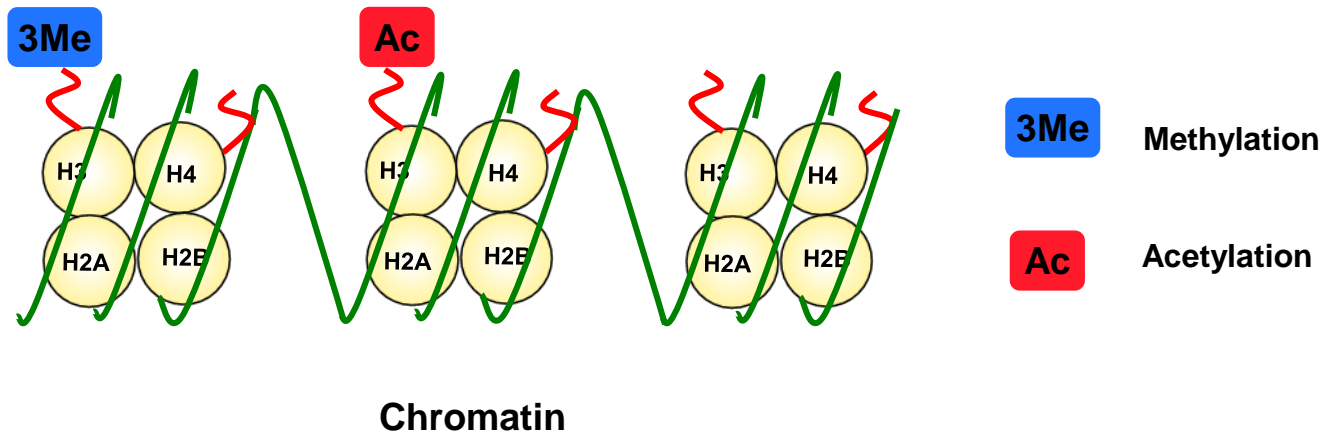
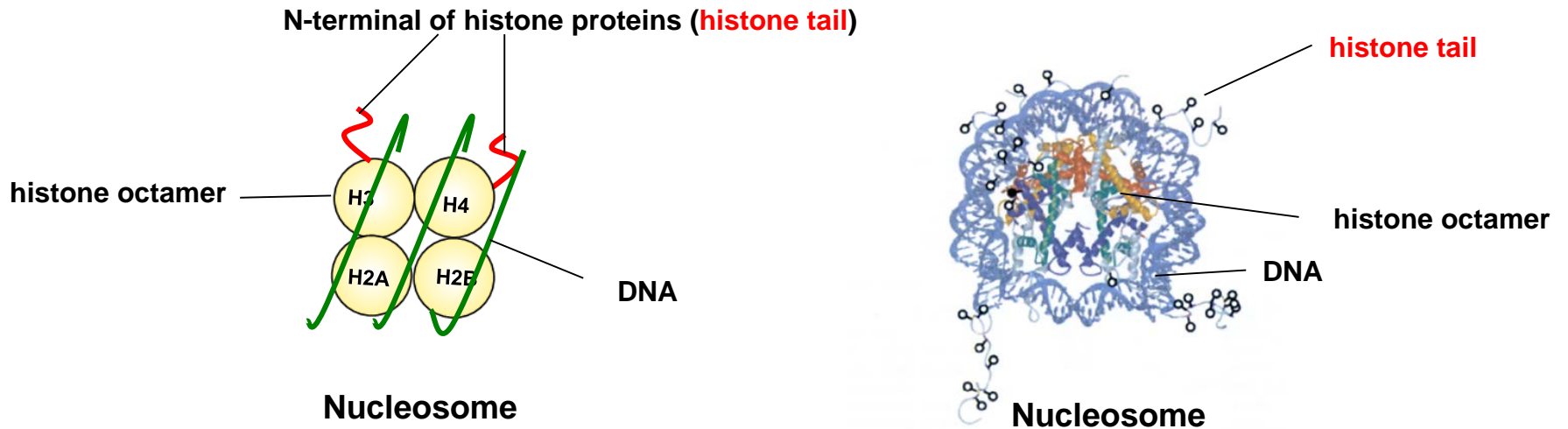


Suppressing gene expression

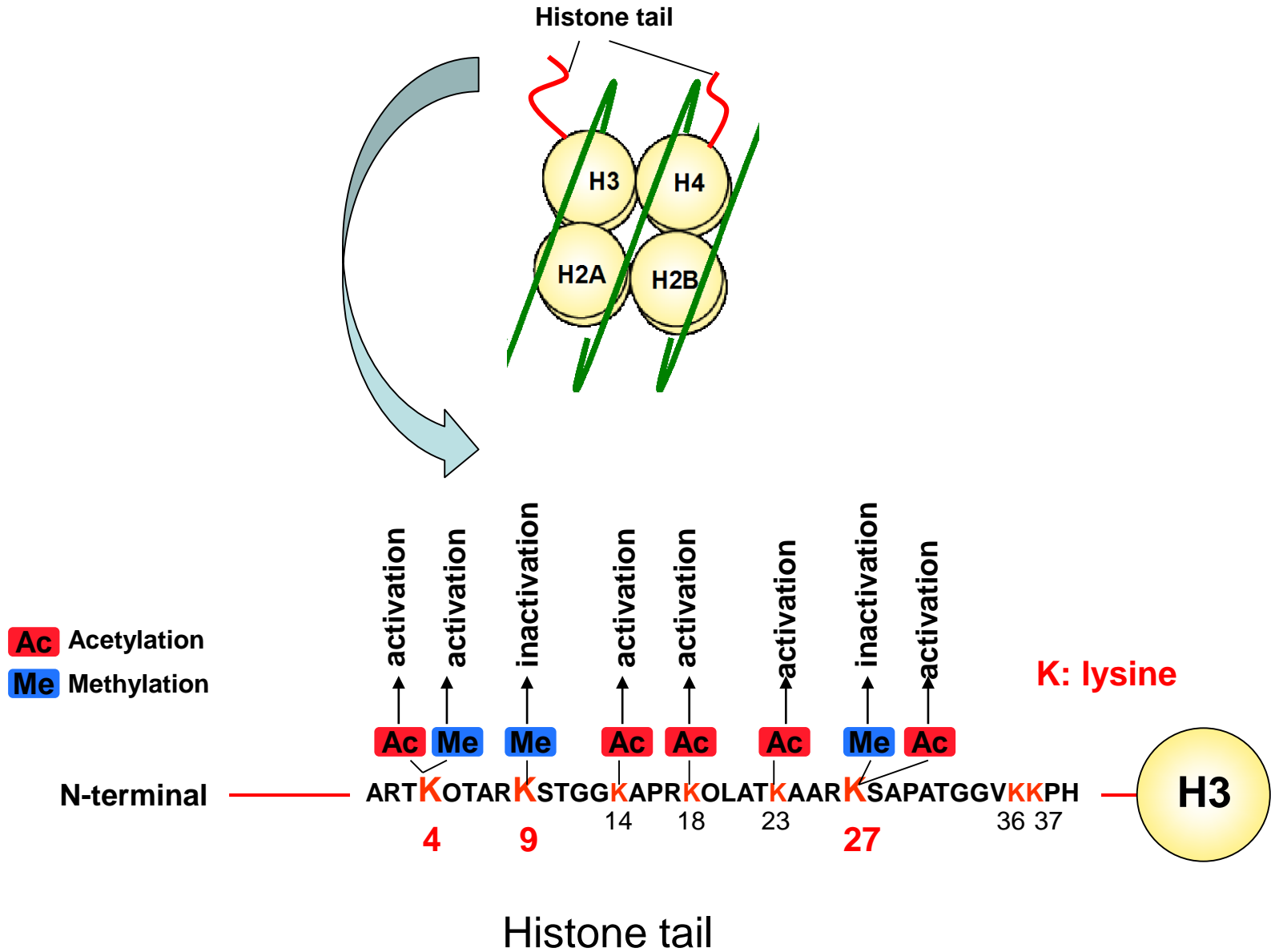
How is the chromatin structure regulated ?

Histone modifications

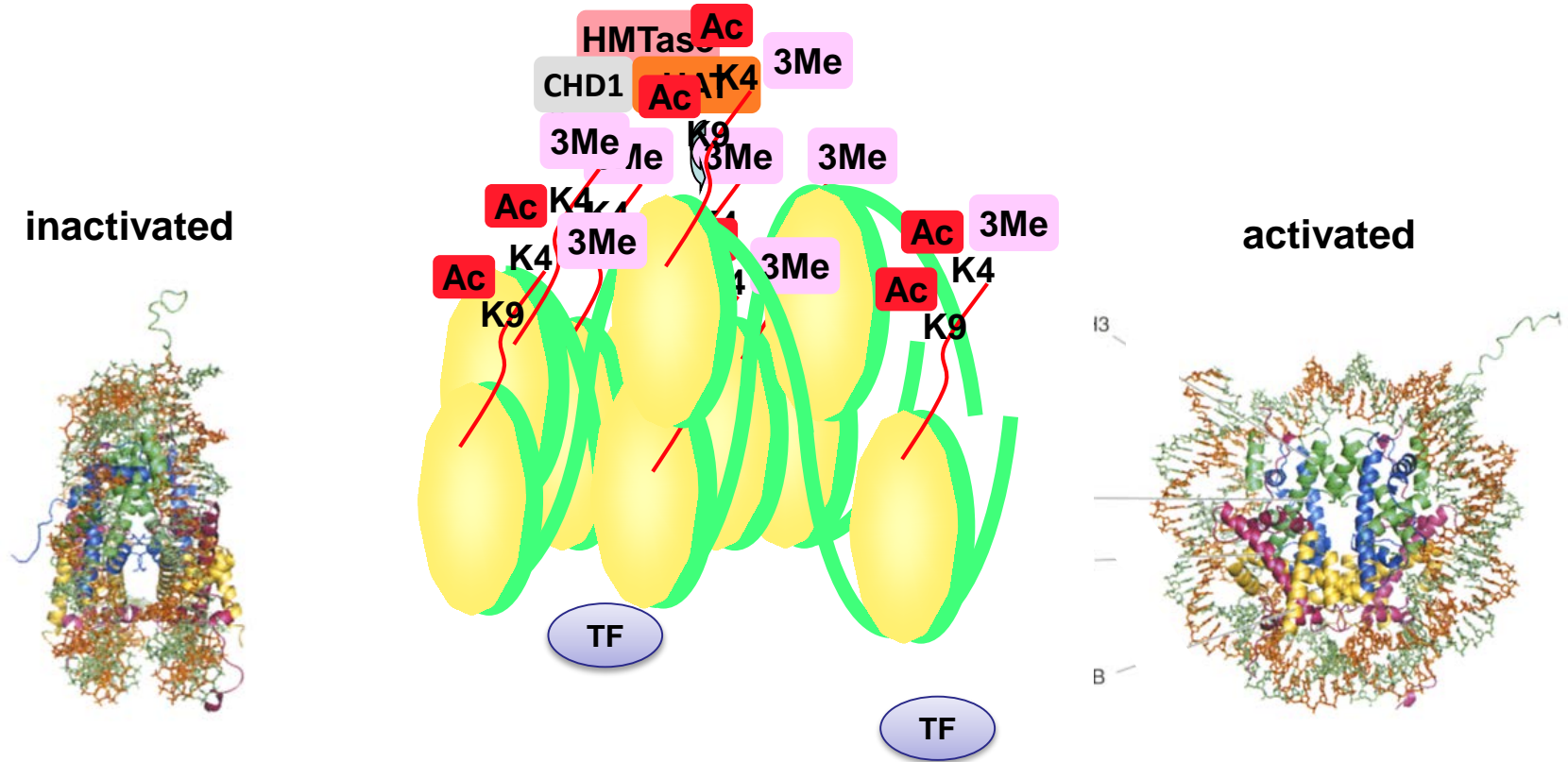
Histone modifications



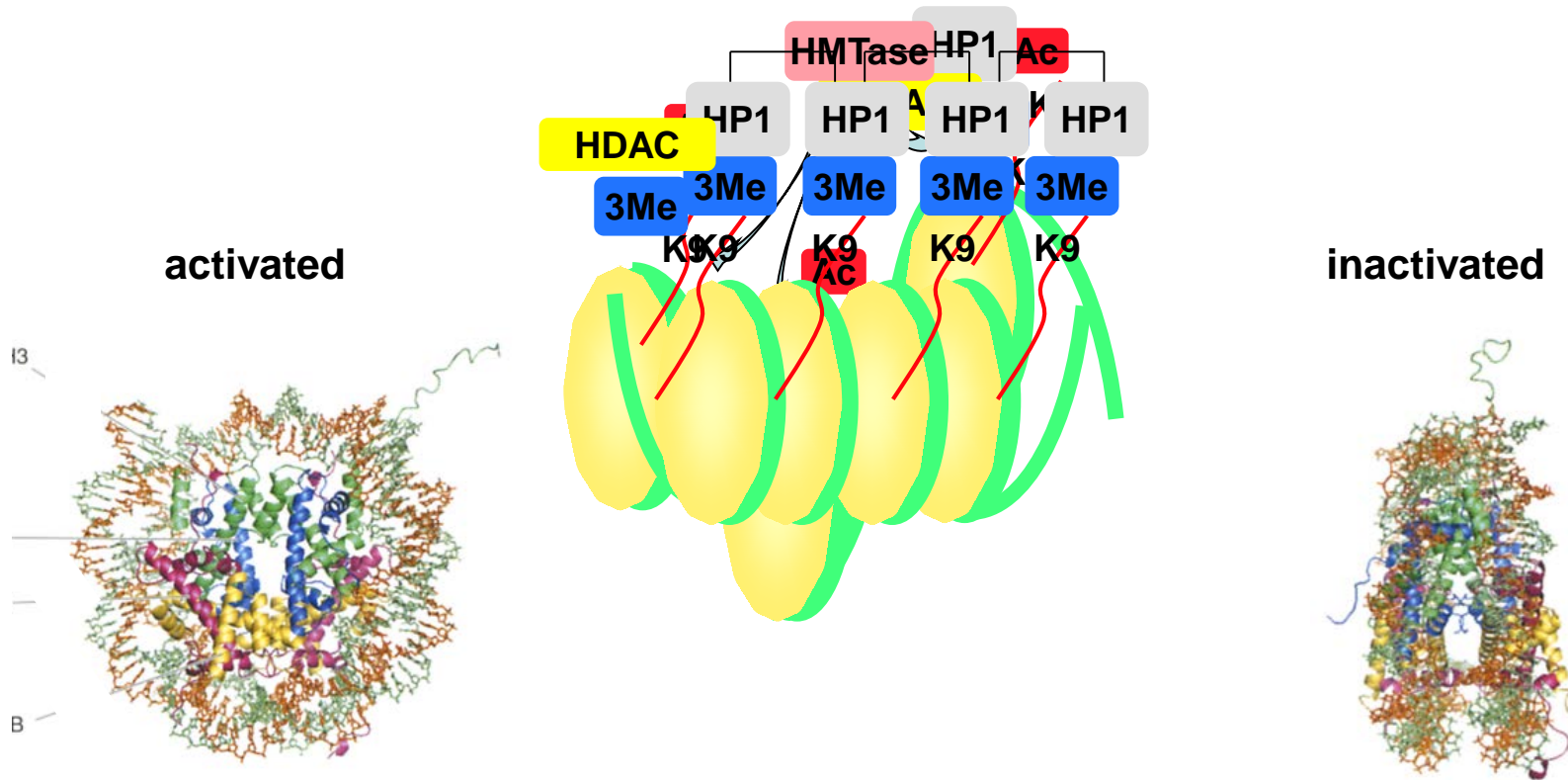
Histone modifications and transcriptional activity



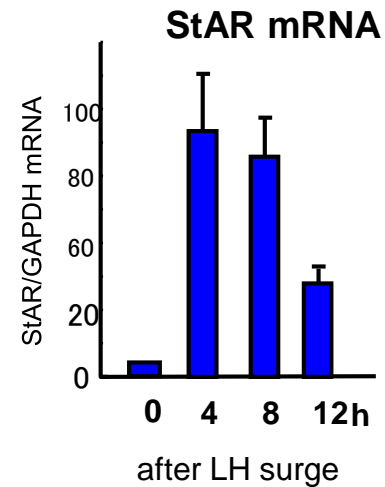
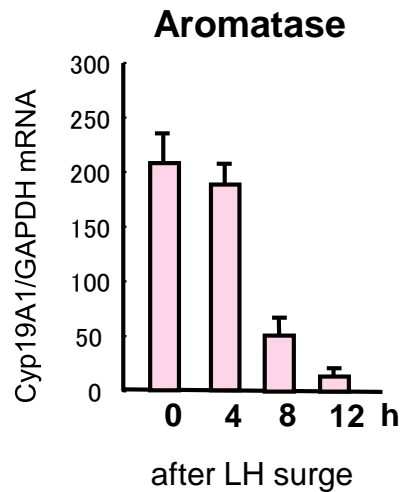
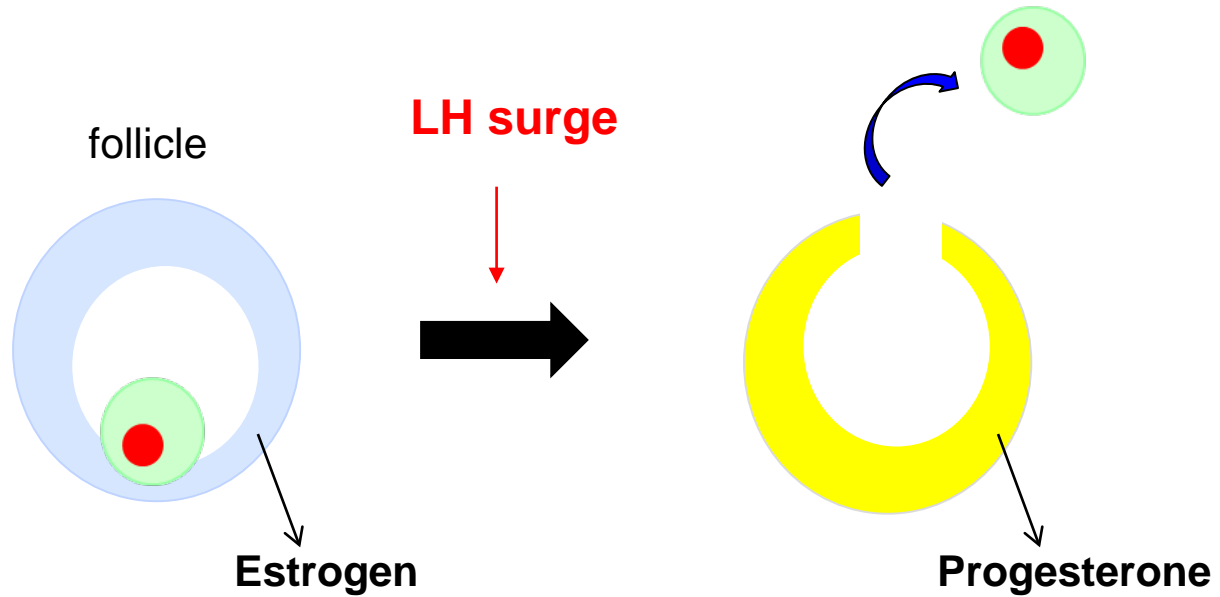
Gene activation by histone modifications



Gene inactivation by histone modifications



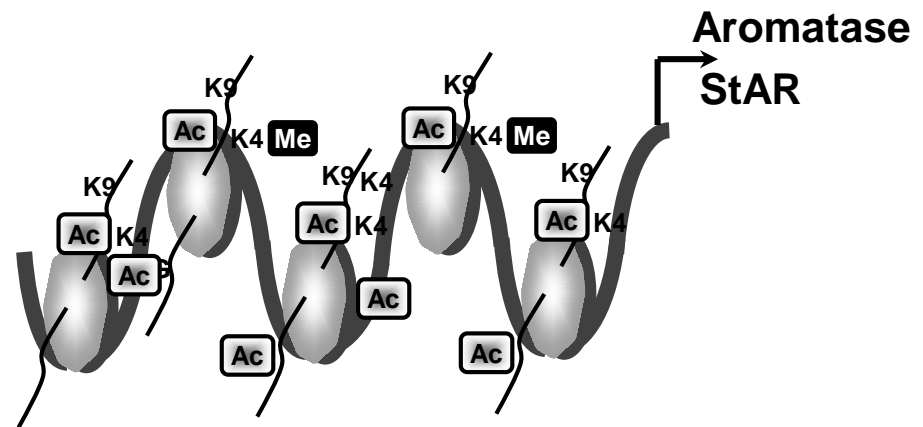
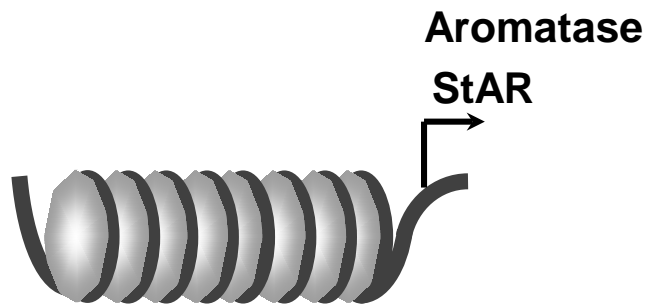
Rapid changes in Aromatase and StAR genes by the LH surge



How do histone modifications and chromatin structures of Aromatase and StAR genes change by the LH surge?

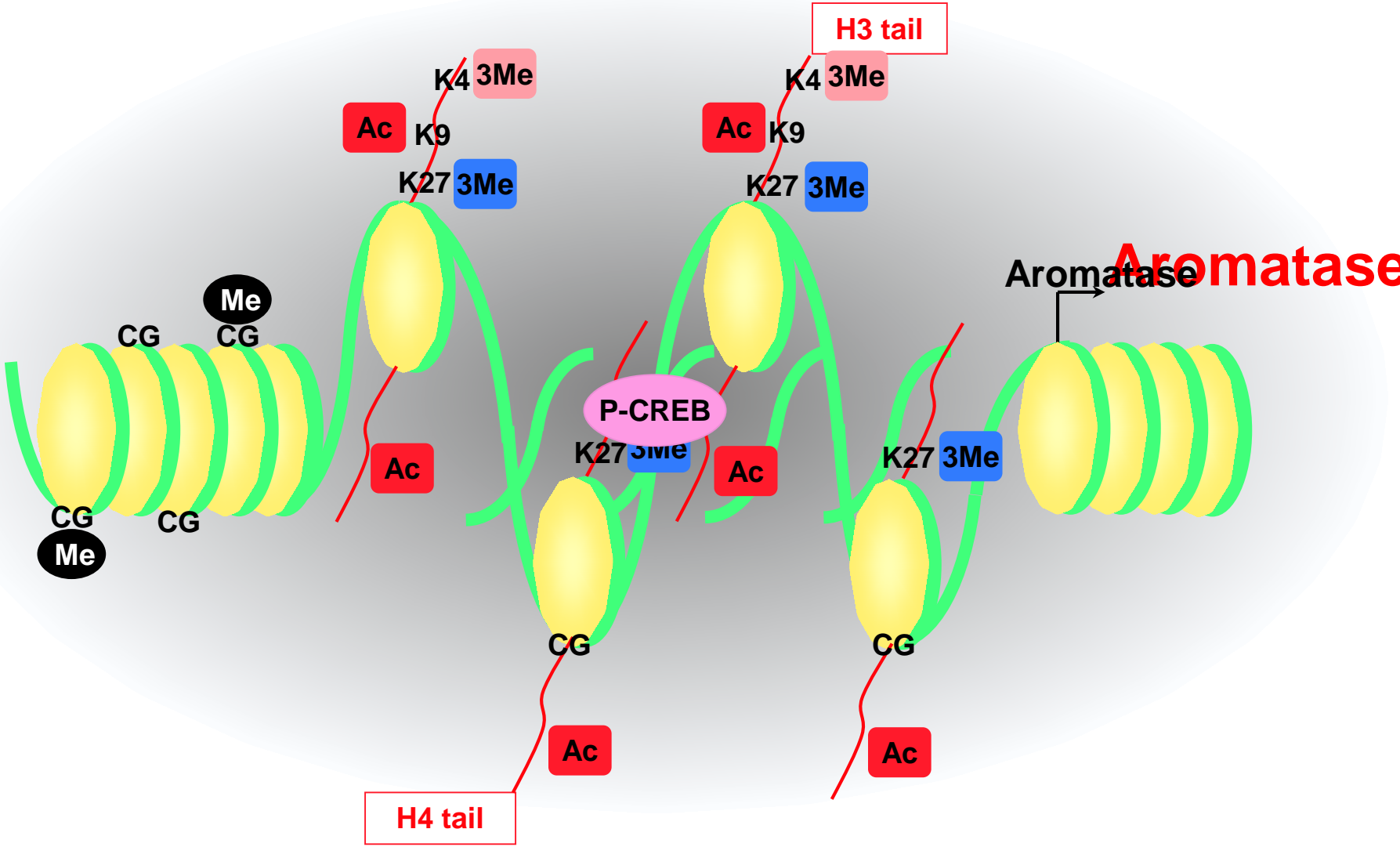
chromatin structures ?

histone modifications ?



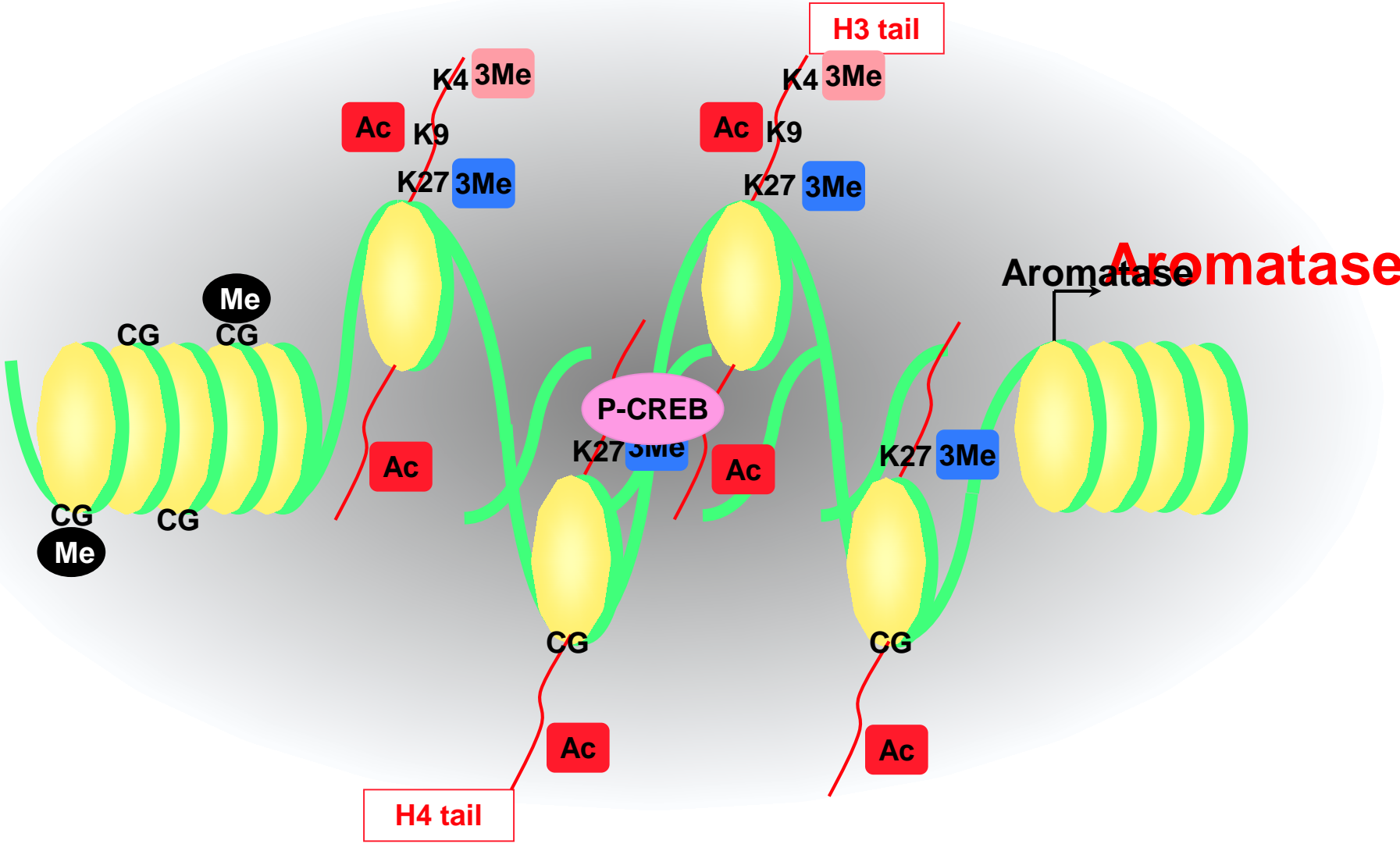
Changes in histone modifications and chromatin structures in **Aromatase** after the LH surge

After LH surge



Changes in histone modifications and chromatin structures in **Aromatase** after the LH surge

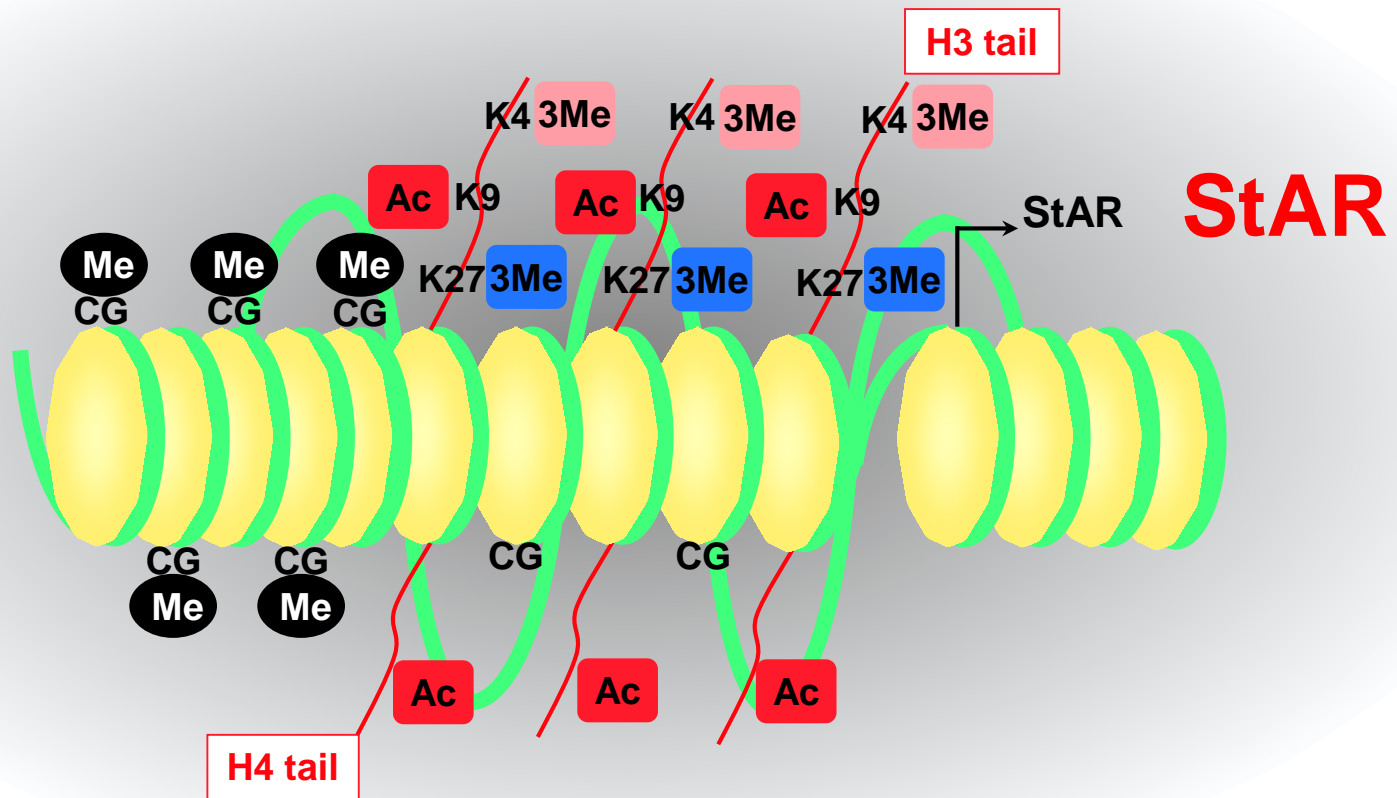
After LH surge



Changes in histone modifications and chromatin structures in **StAR** after the LH surge

After LH surge

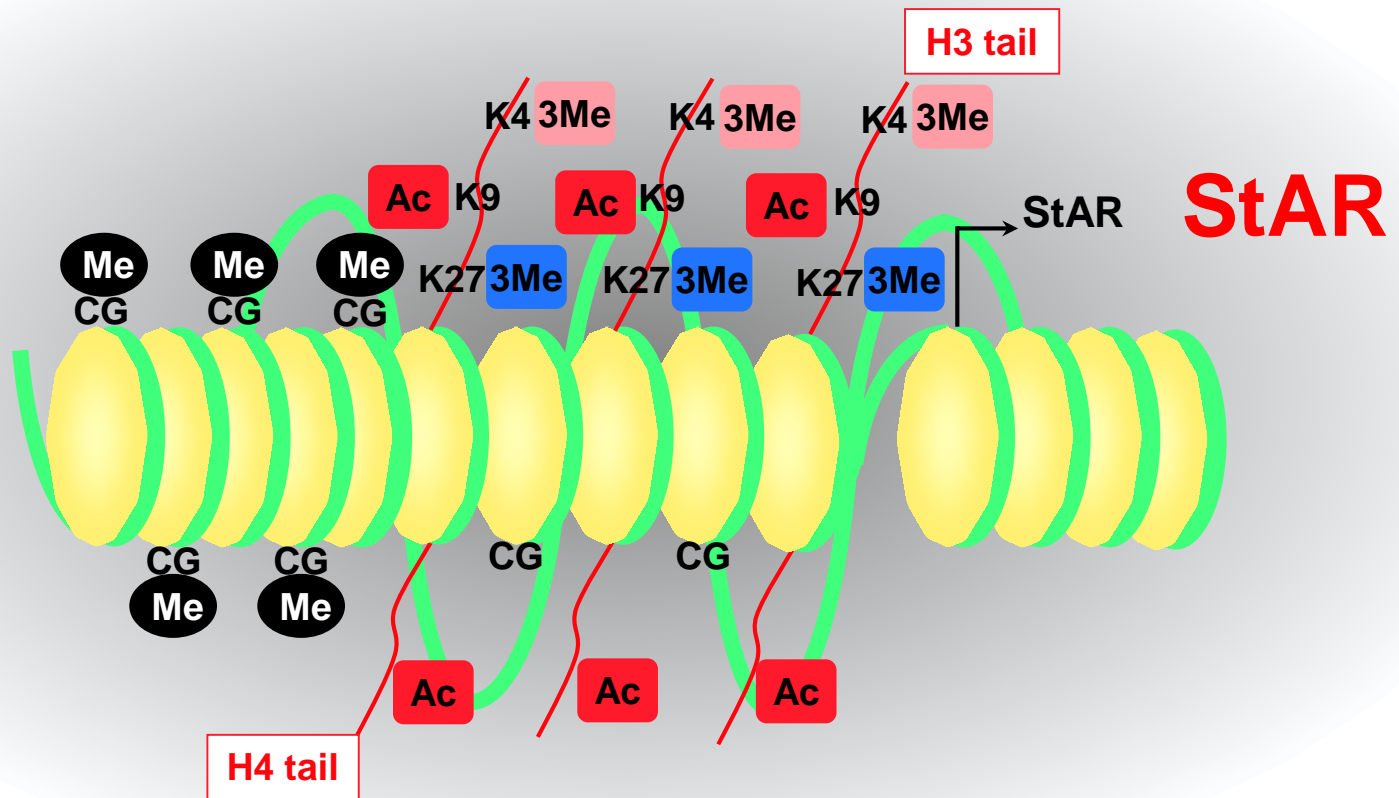
C/EBP- β



Changes in histone modifications and chromatin structures in **StAR** after the LH surge

After LH surge

C/EBP- β

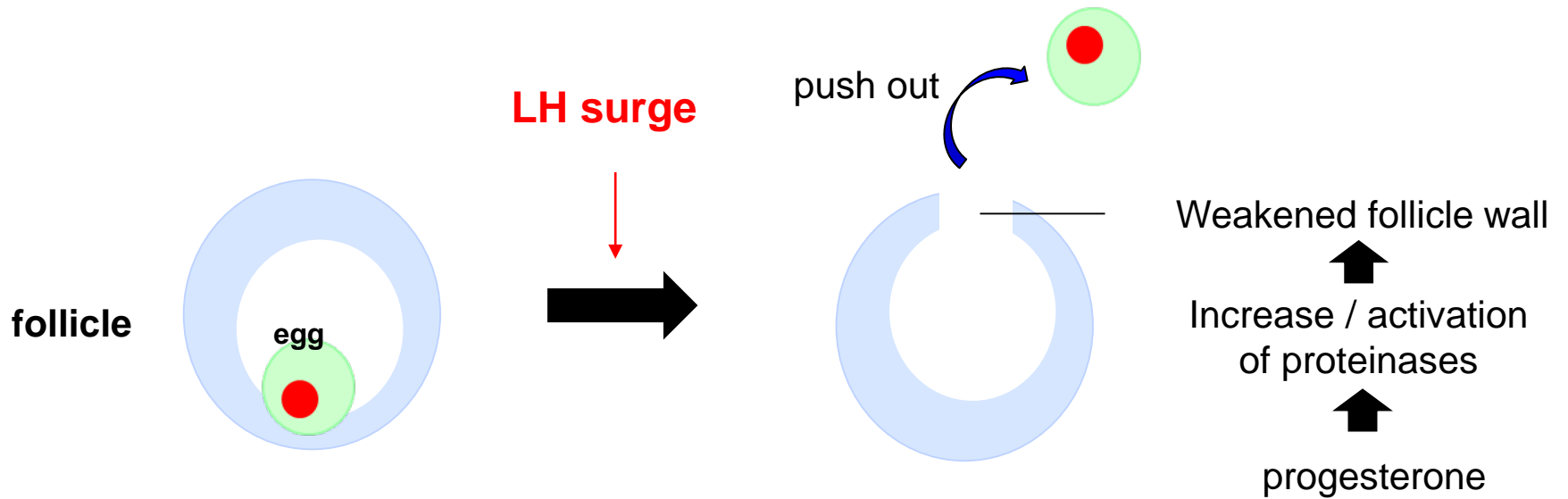


We found that:

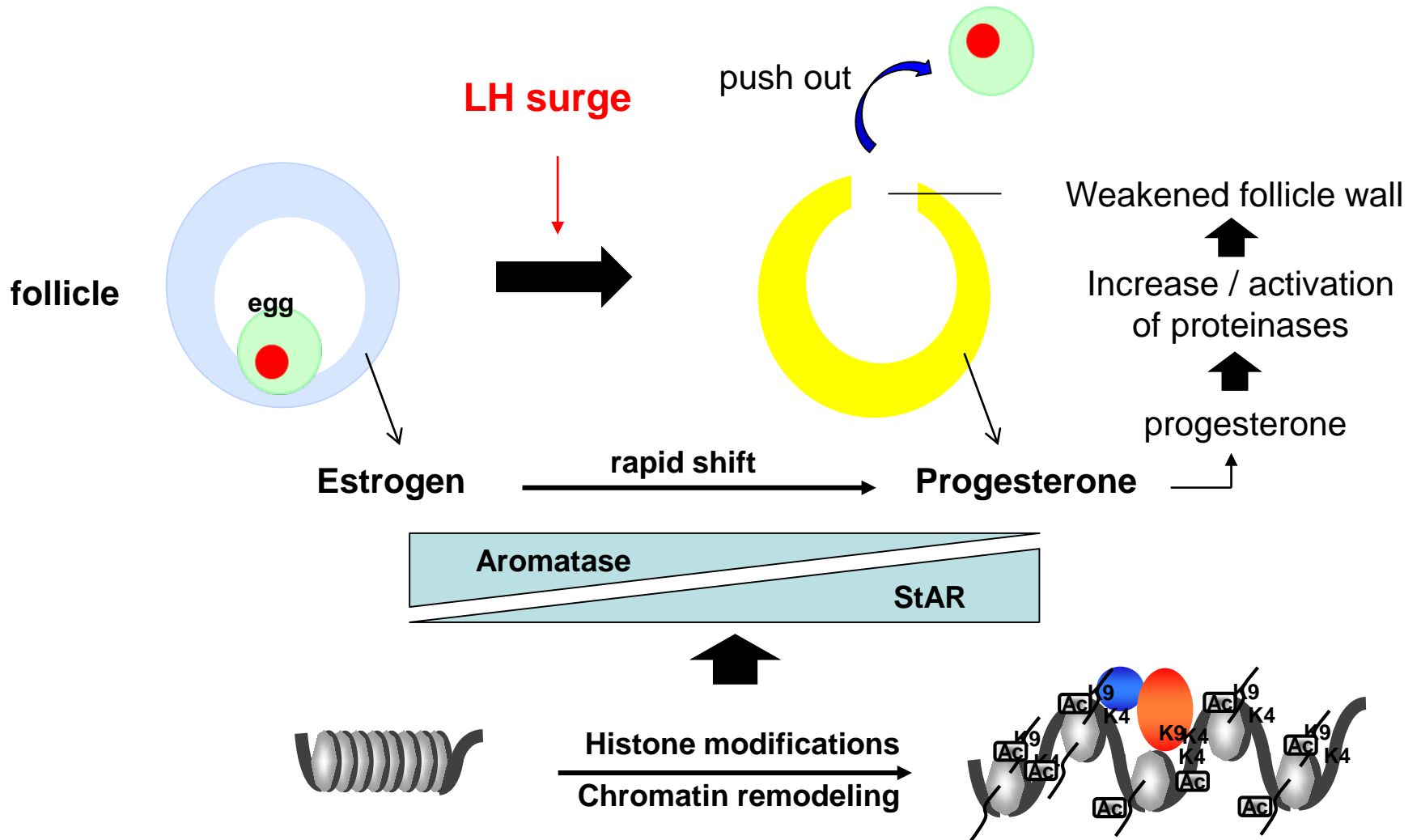
the change in the DNA side, such as chromatin remodeling by histone modifications, contributes to the rapid changes in gene expression of Aromatase and StAR in granulosa cells for ovulation after the LH surge.

Summary

Mechanism of ovulation (follicle rupture)



Molecular mechanism of ovulation



Acknowledgements

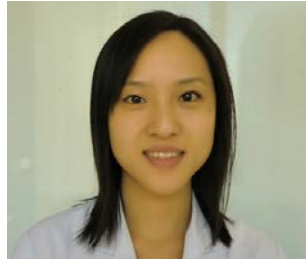
Reproductive Biology Group



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Tamura H.



Lee Lifa



Maekawa R.



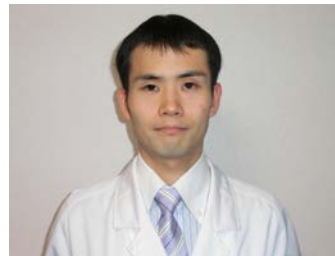
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Okada M.

Danke Schön



Molecular mechanisms of ovulation

