

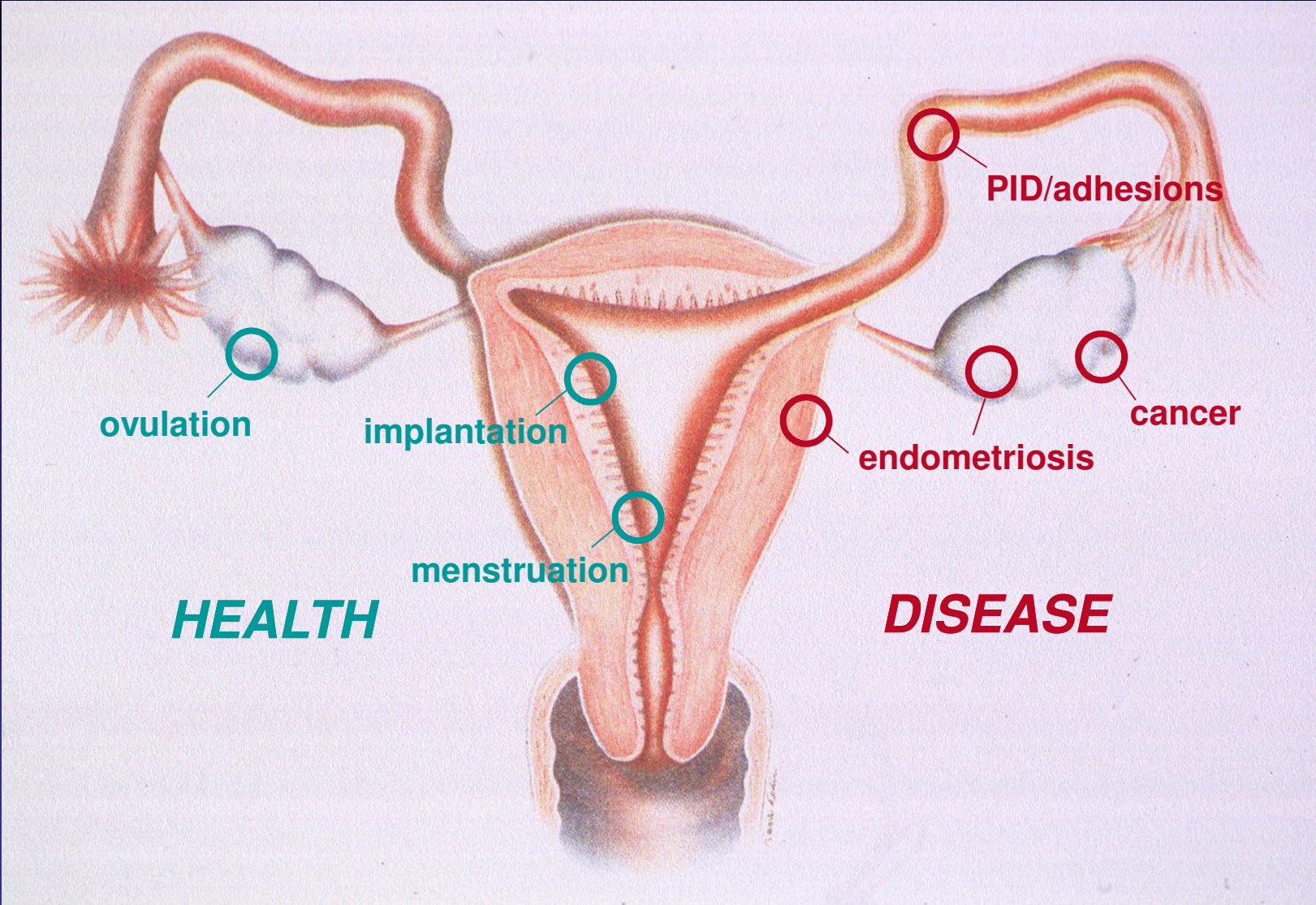
Ovulation & Ovarian Cancer

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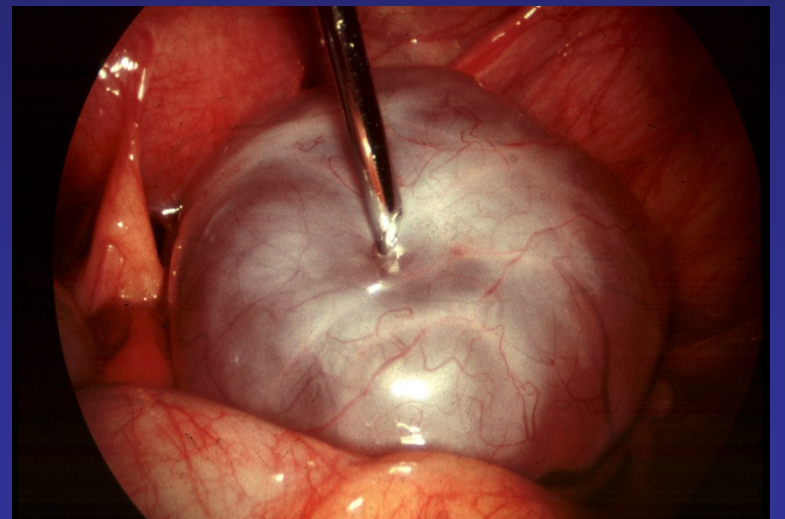
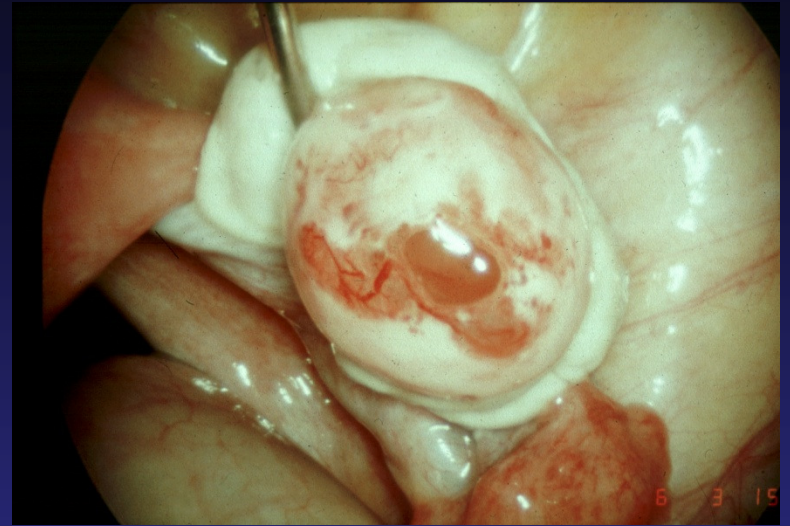
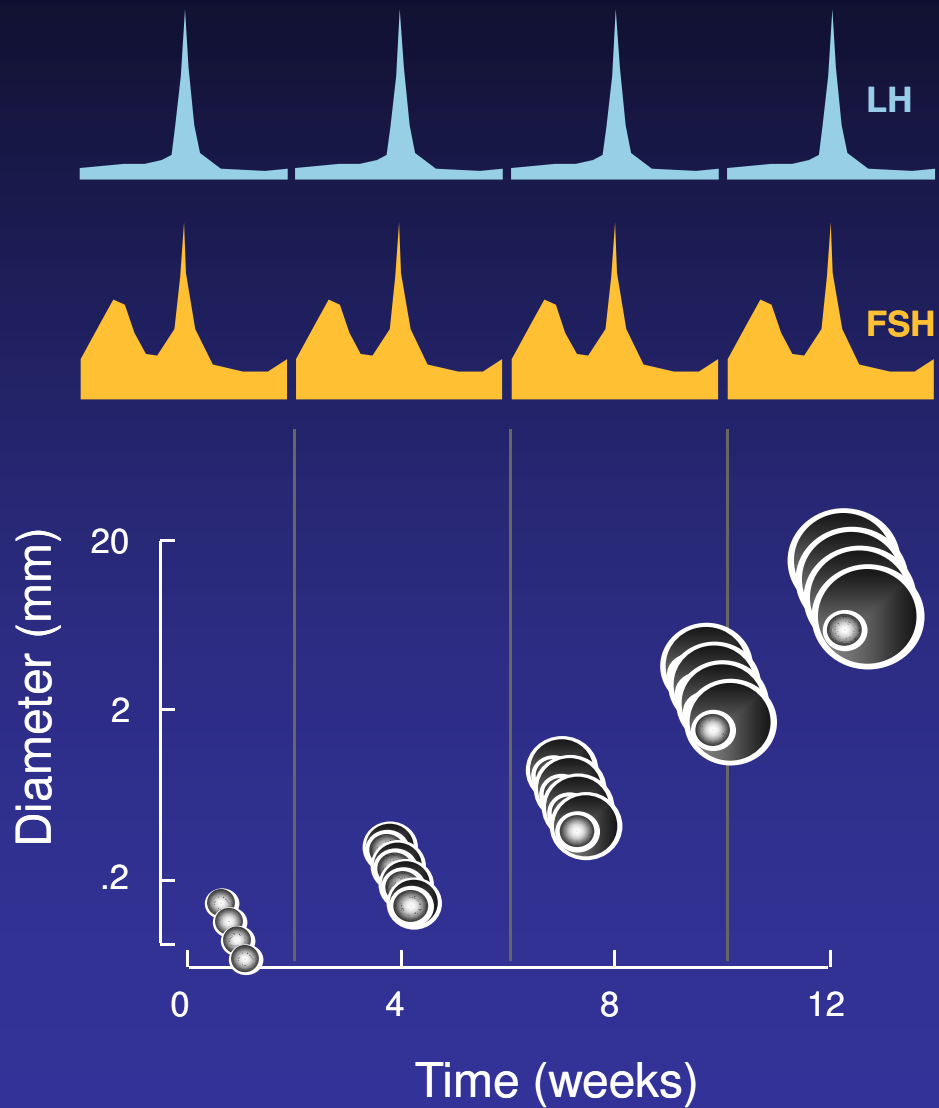
Inflammation in reproductive health and disease

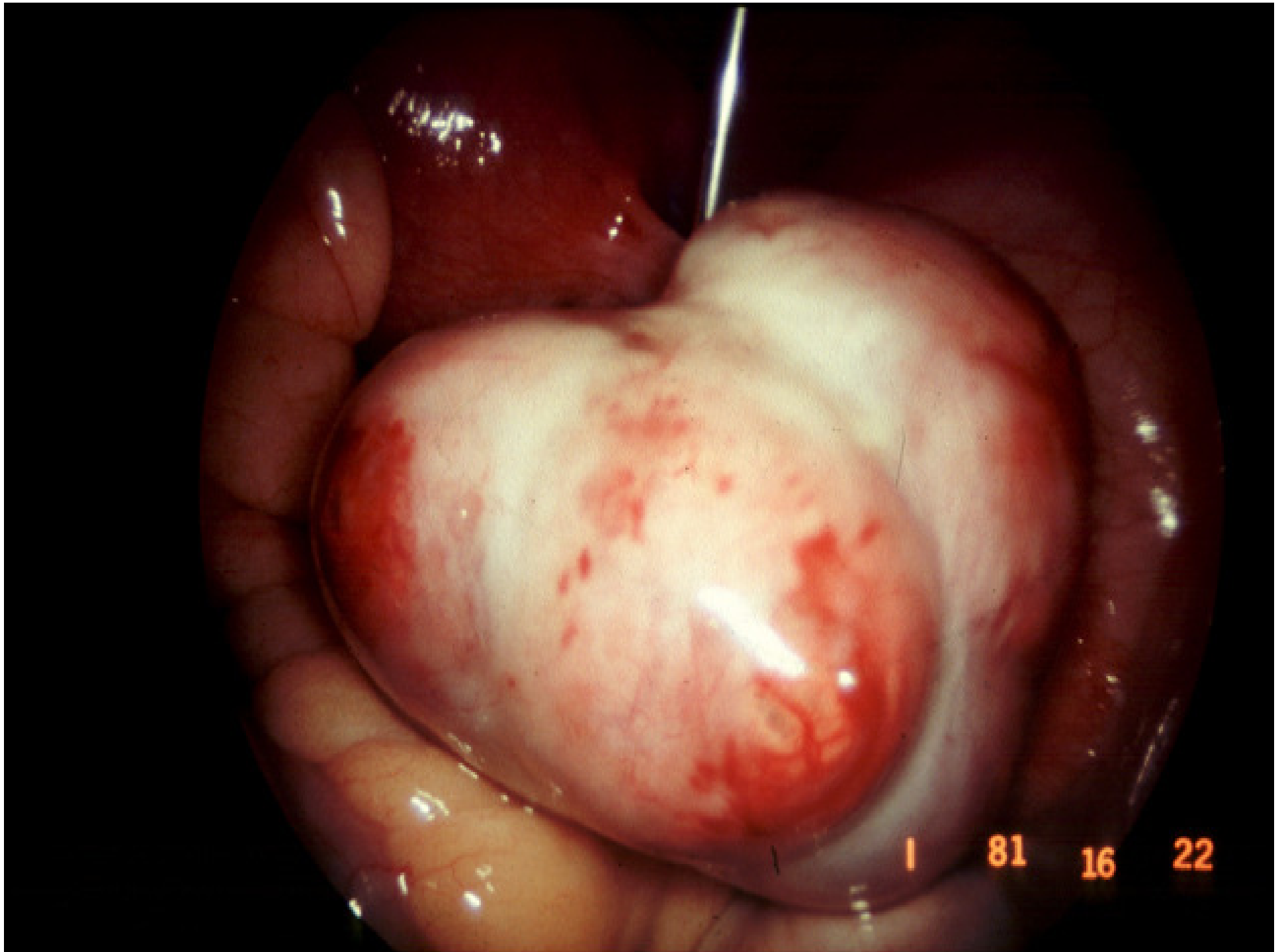


Ovulation & Ovarian Cancer

- Ovulation up close
- Ovulation as injury
- Postovulatory repair

The Follicular Lifespan

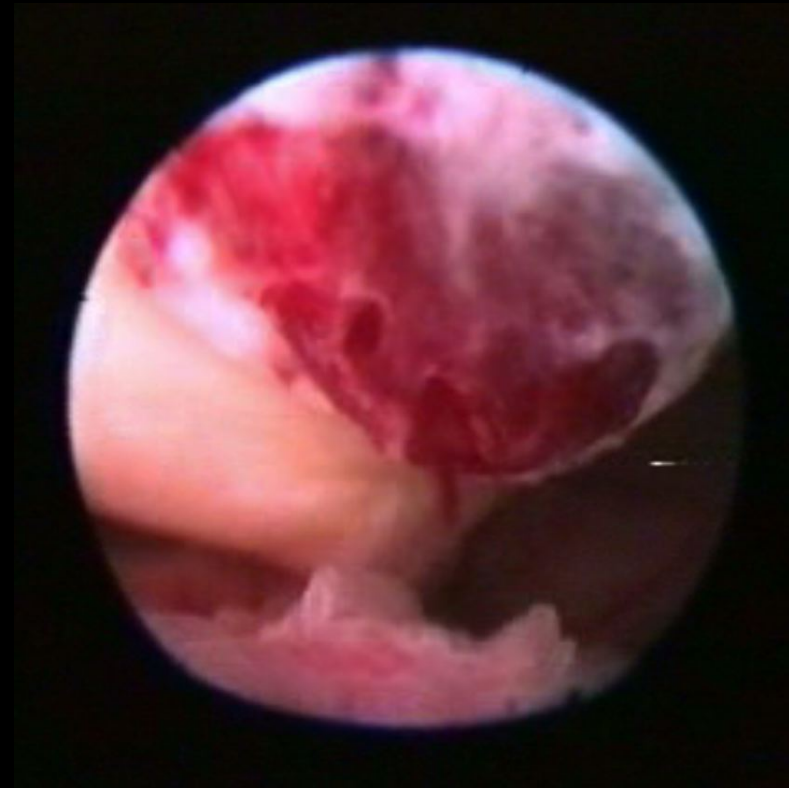
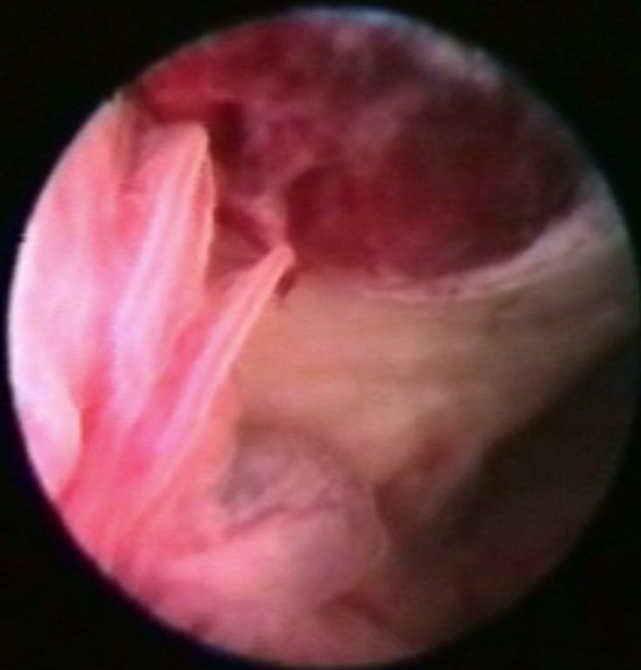
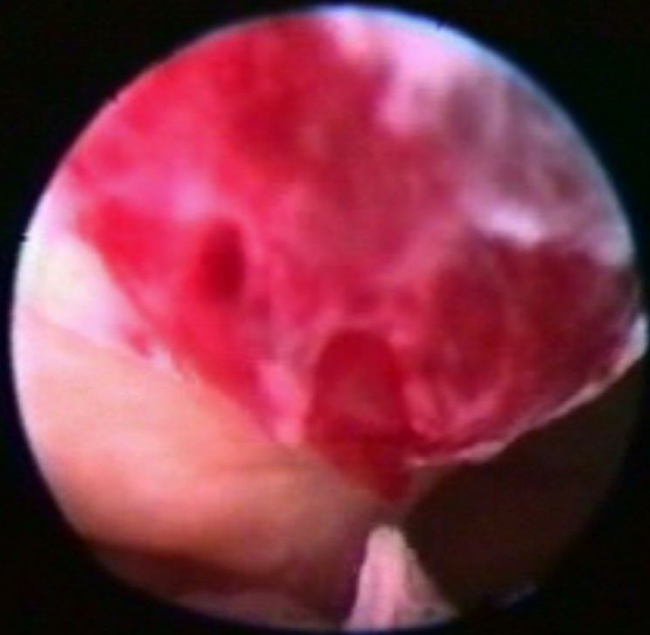




Ovulation & Ovarian Cancer

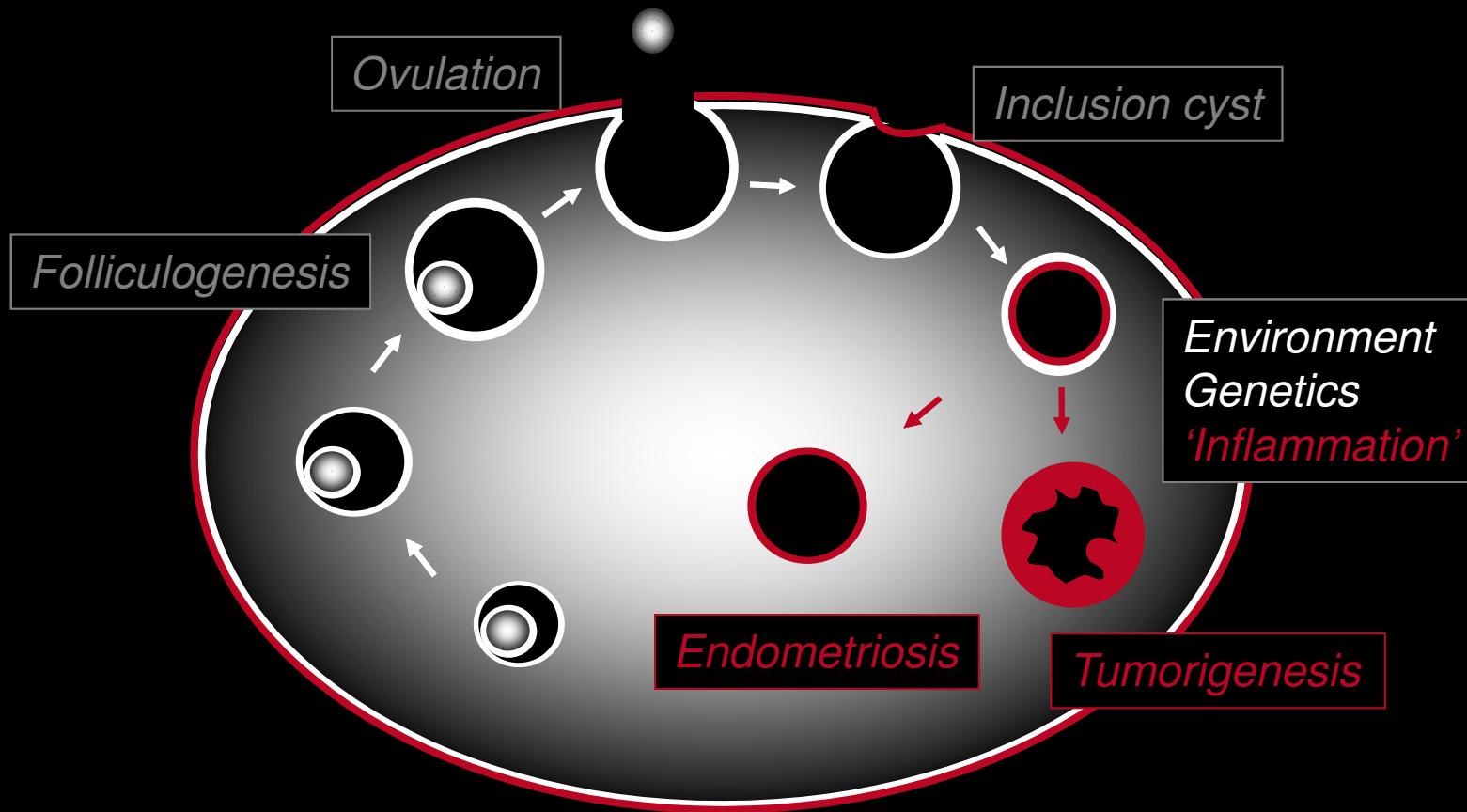
- Ovulation up close
- Ovulation as injury
- Postovulatory repair

Source: Jan Brosens

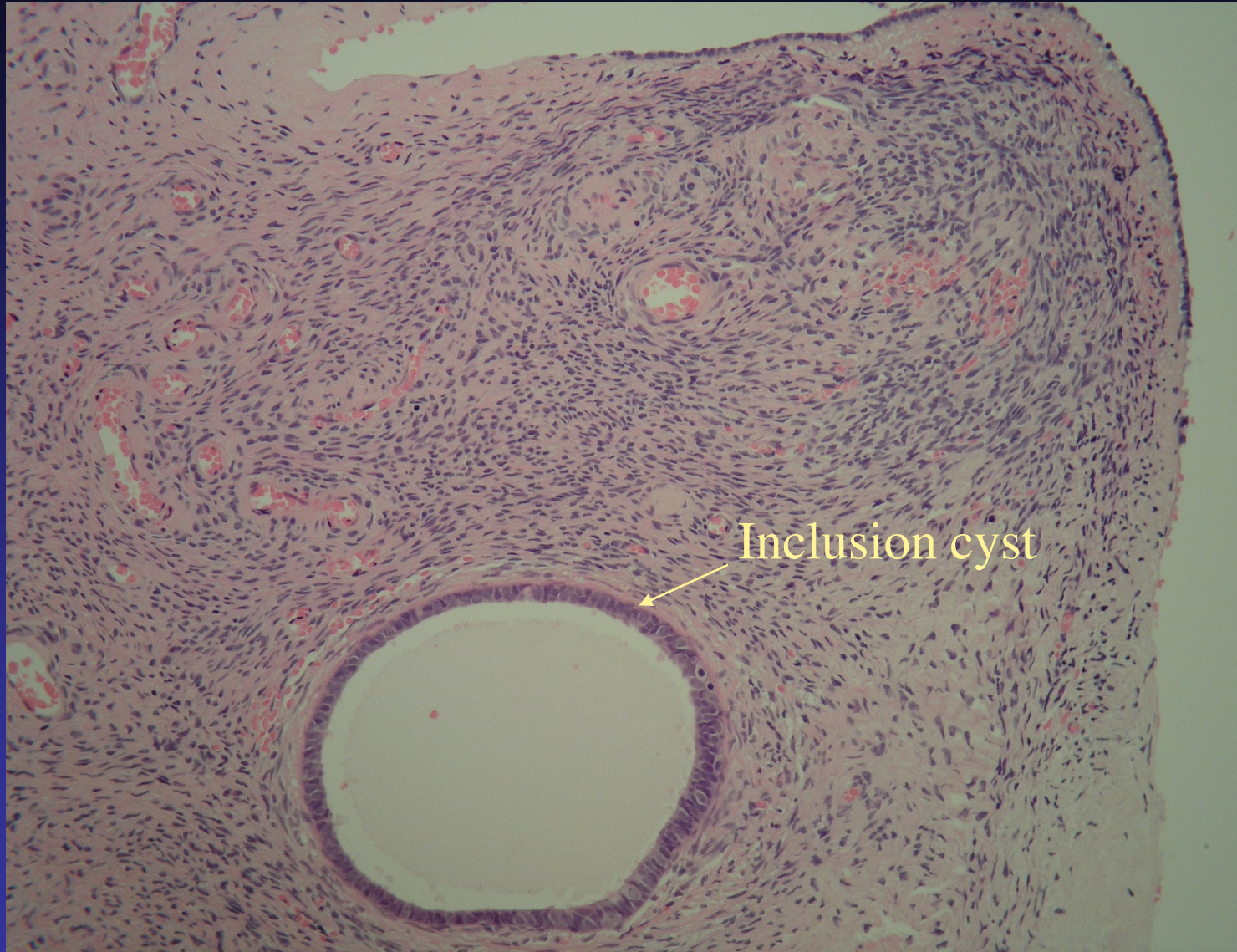


Source: Jan Brosens

Ovulation and ovarian disease



Intra-ovarian inclusion cyst

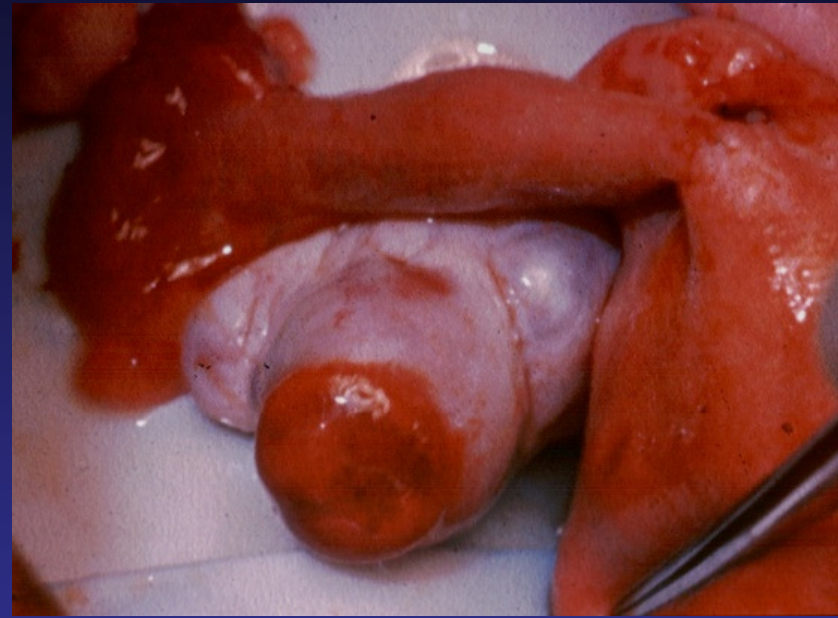
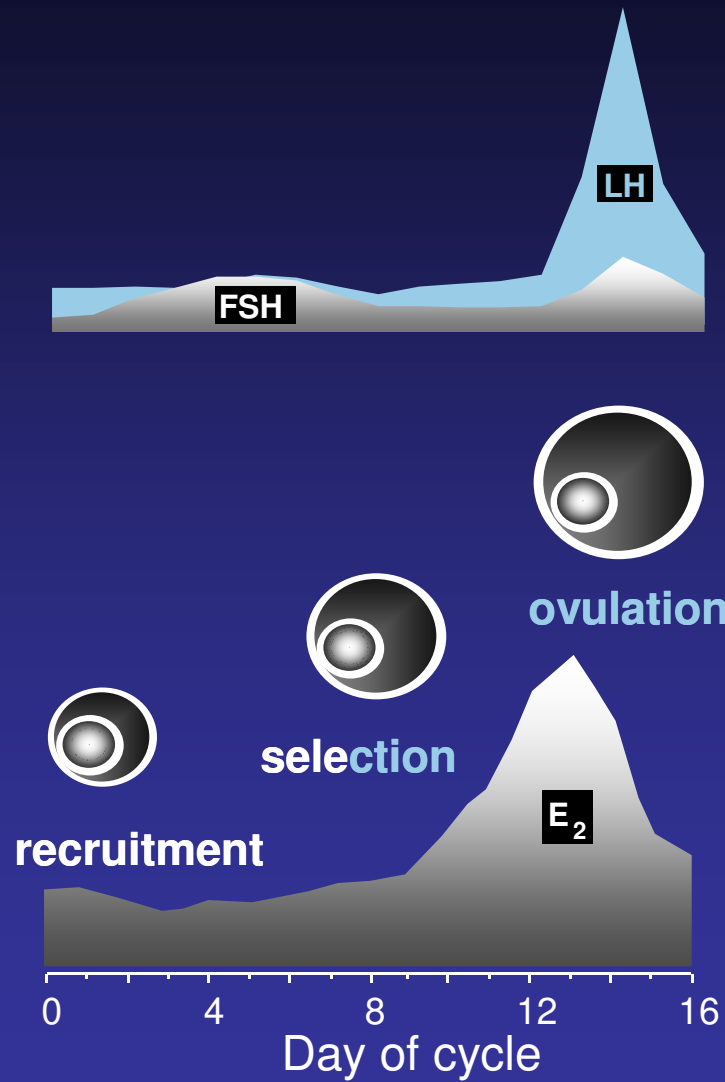


Ovarian Cancer

- 90% cases thought to arise in ovarian surface epithelium (OSE)
- incidence correlates with duration/frequency of ovulation



Ovulation = Inflammation



LH

pro-inflammation

anti-inflammation

cytokines



prostanoids



proteinases



'Injury'



?



?



?



'Repair'



Ovulation & Ovarian Cancer

- Ovulation up close
- Ovulation as injury
- Postovulatory repair

LH

pro-inflammation

anti-inflammation

cytokines



prostanoids



proteinases



'Injury'



?



?



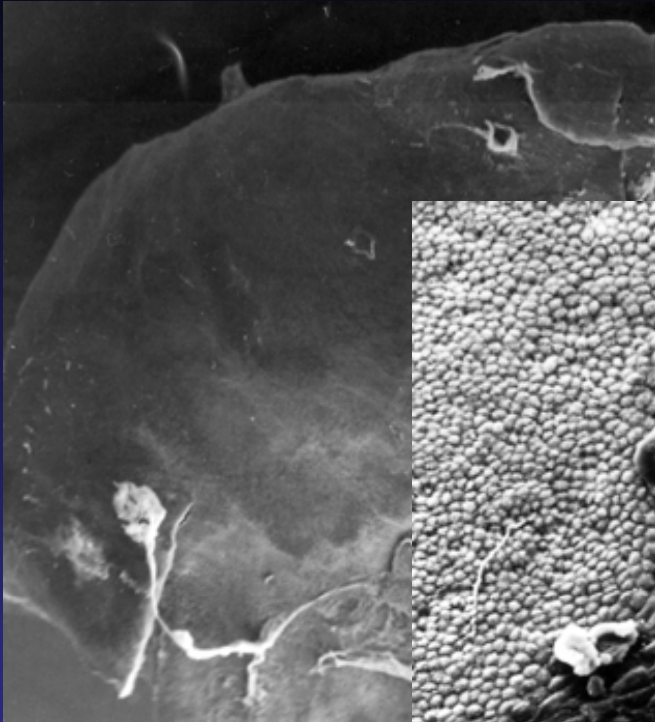
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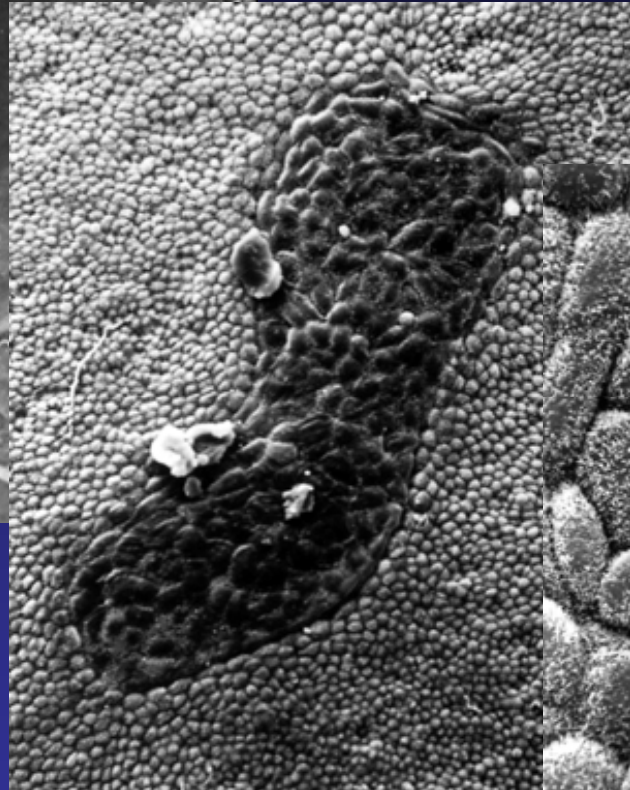
'Repair'



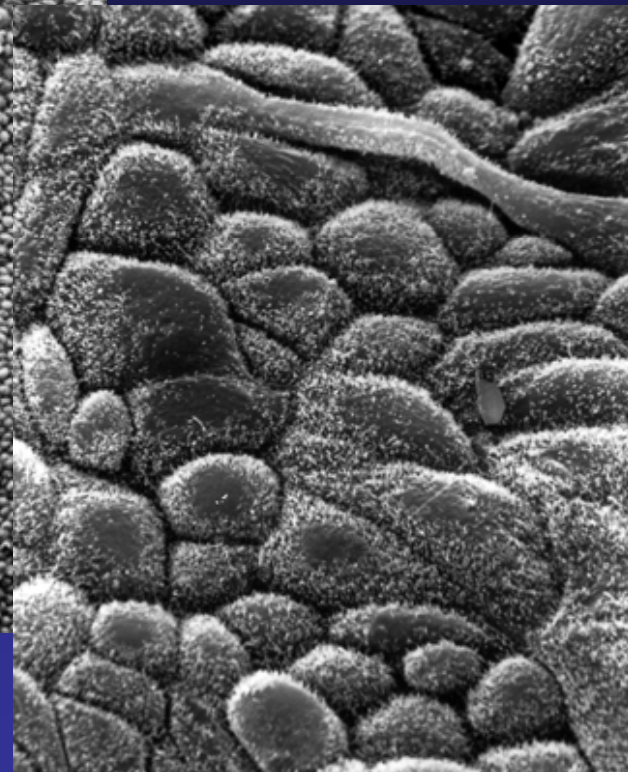
Gillett WR et al. 1991 A scanning electron microscope study of the human ovarian surface epithelium: characterization of two cell types
Human Reproduction 6:645-650



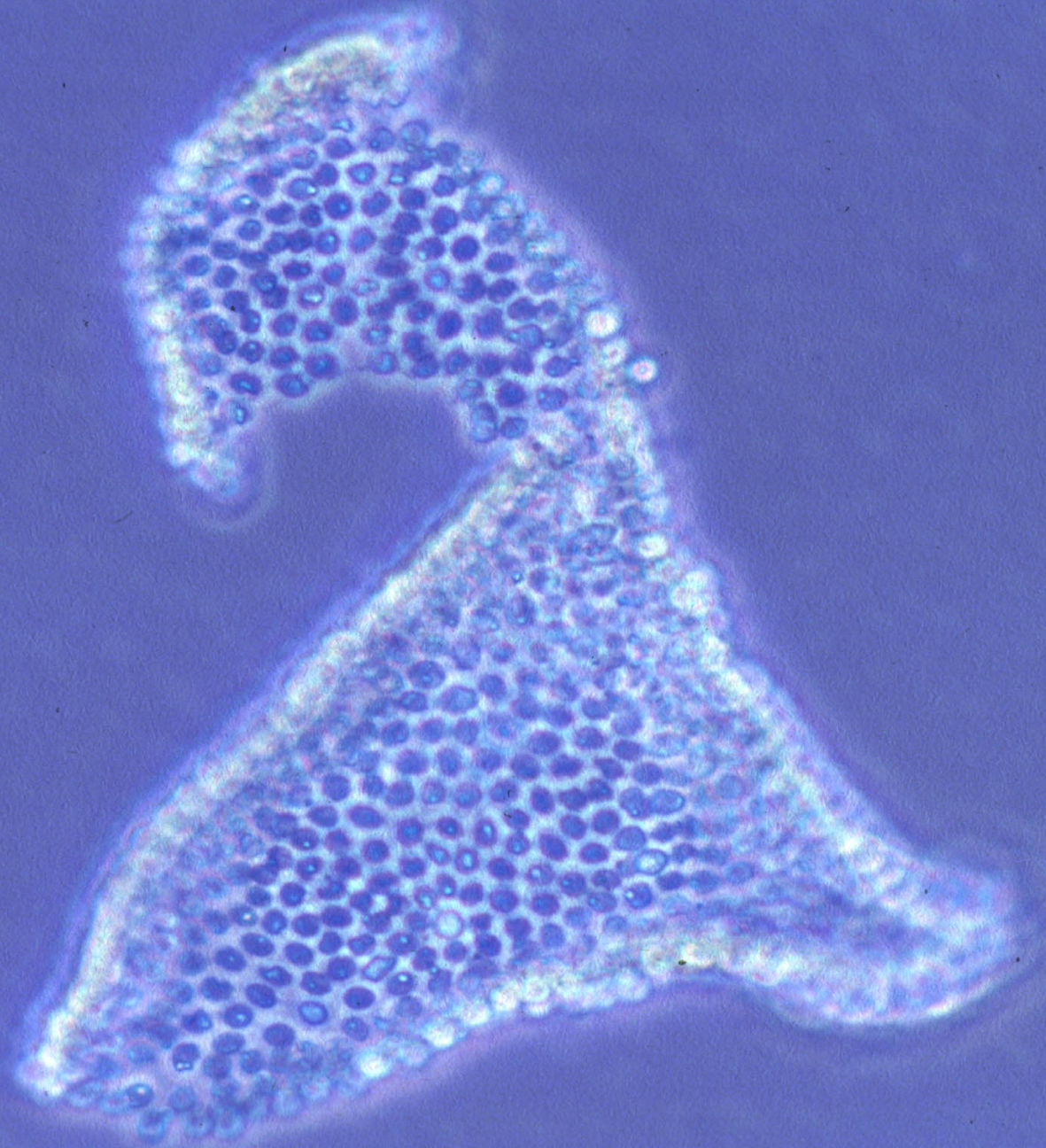
x10

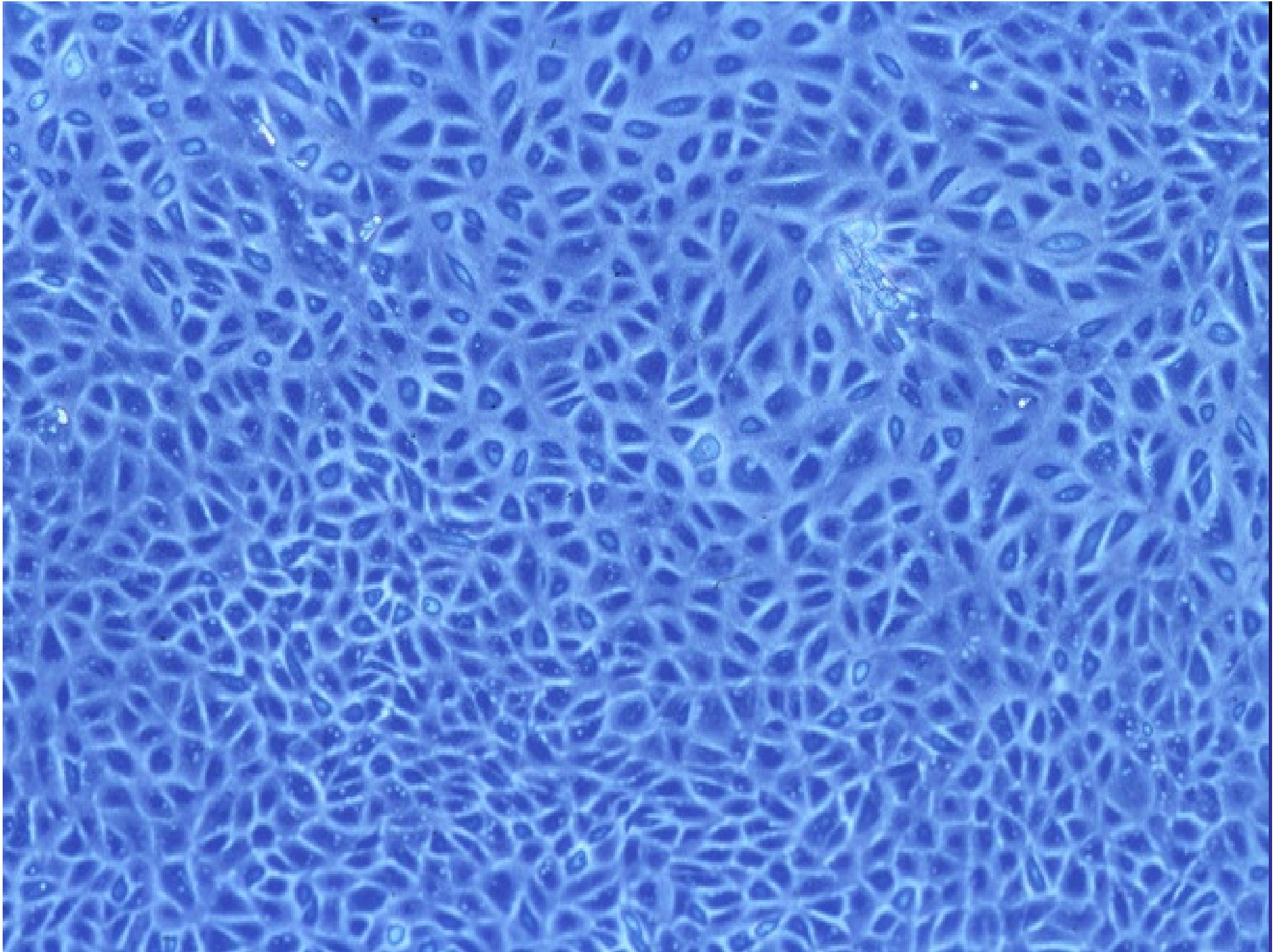


x150



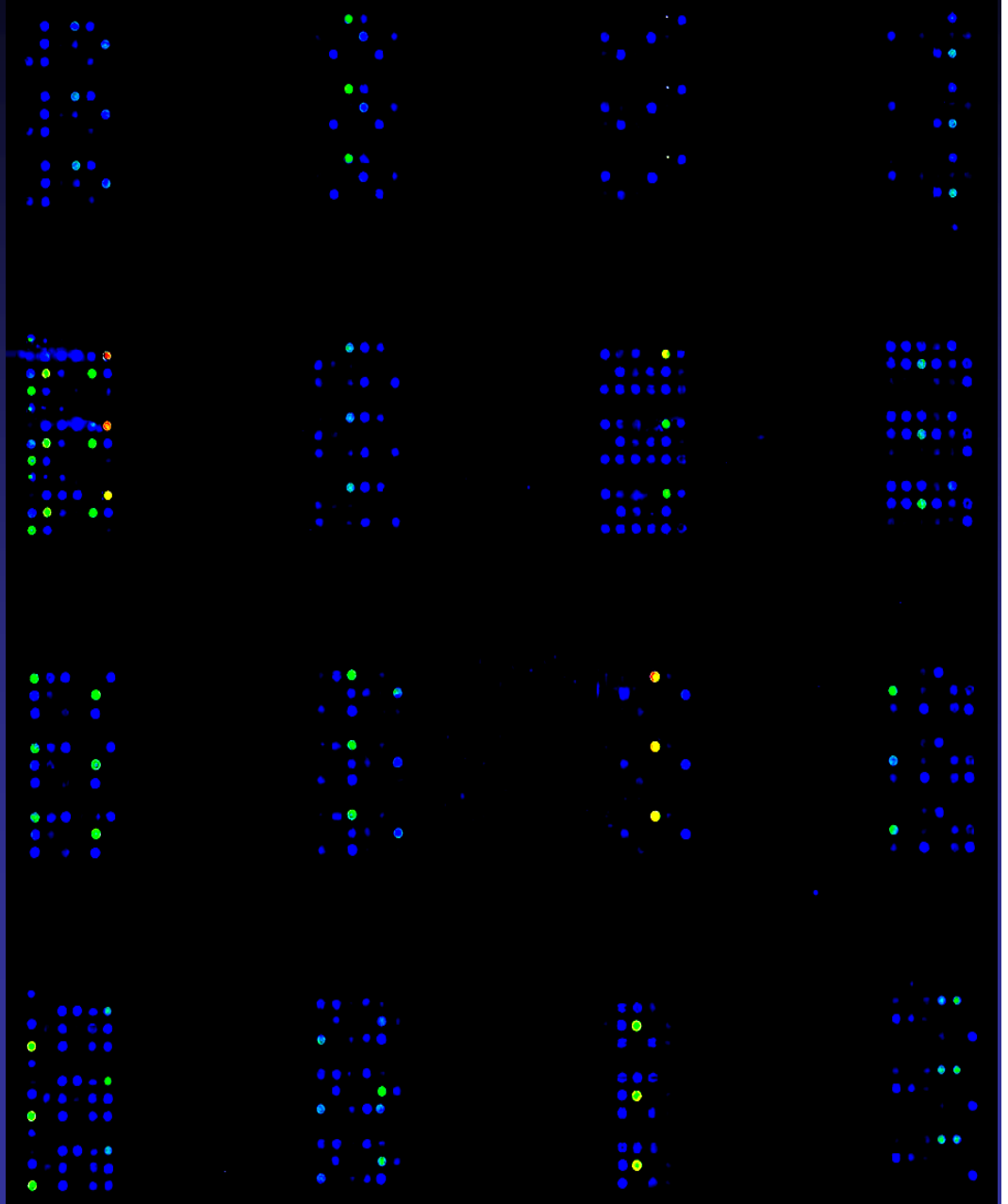
x700



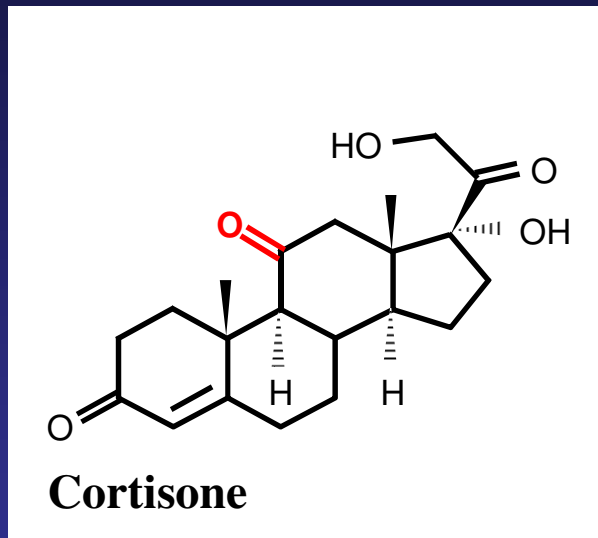


Gene expression in experimentally inflamed* OSE cells

* Treatment with Interleukin-1



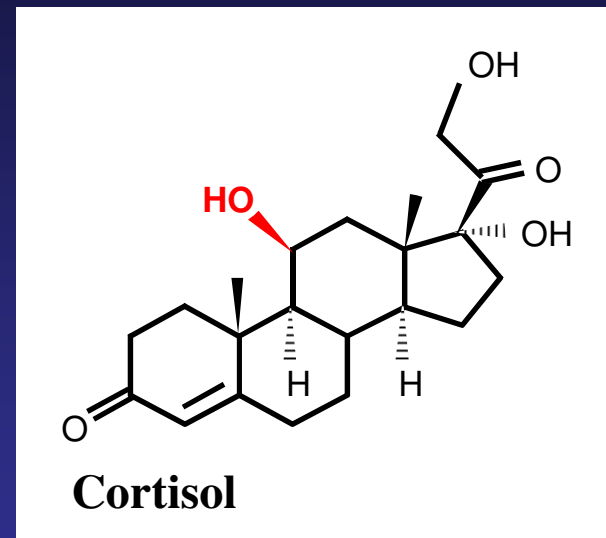
The Cortisone-Cortisol Shuttle



'INACTIVE'

11 β HSD1

\rightleftharpoons



'ACTIVE'

LH

pro-inflammation

anti-inflammation

cytokines



prostanoids



proteinases



'Injury'



?



?

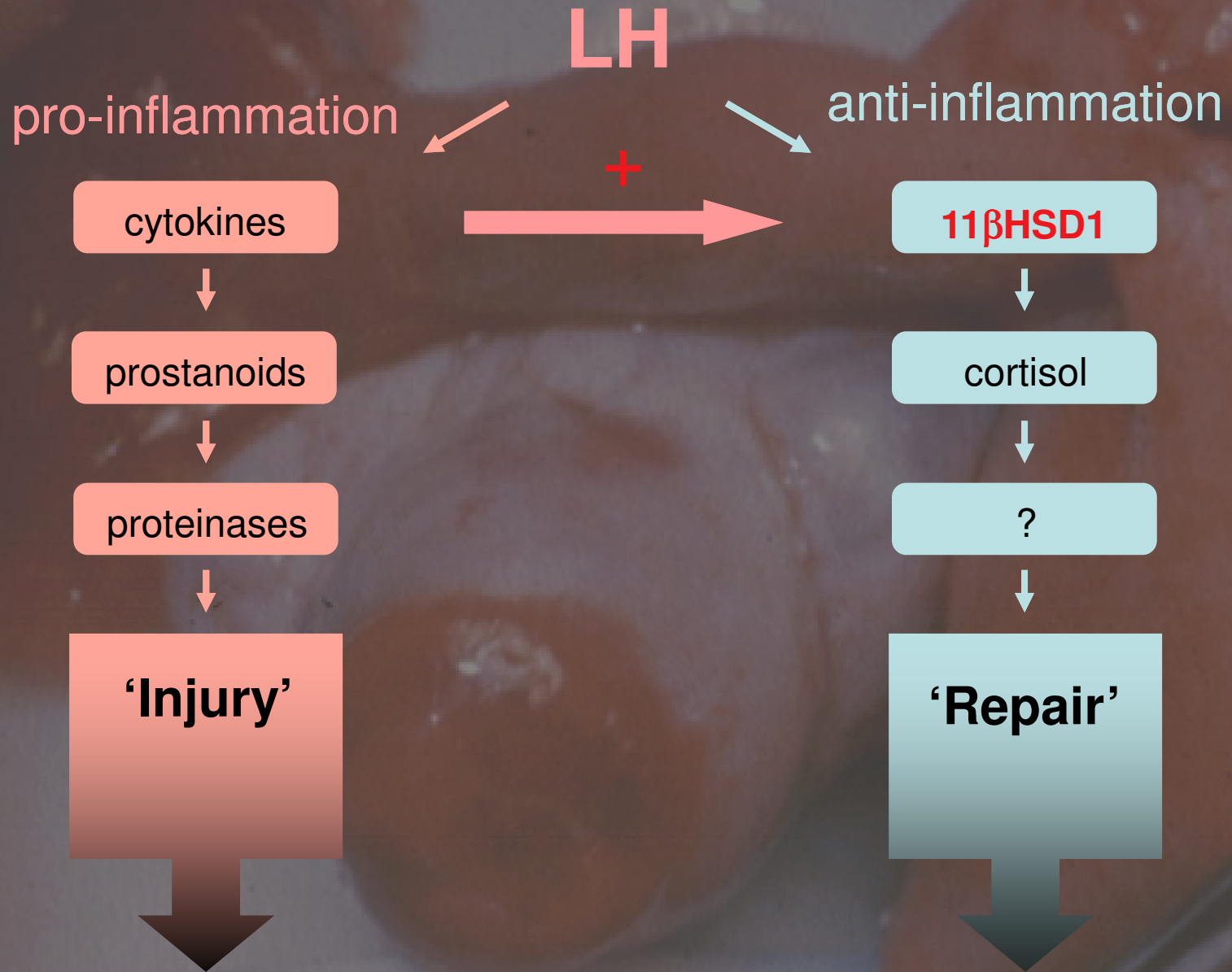


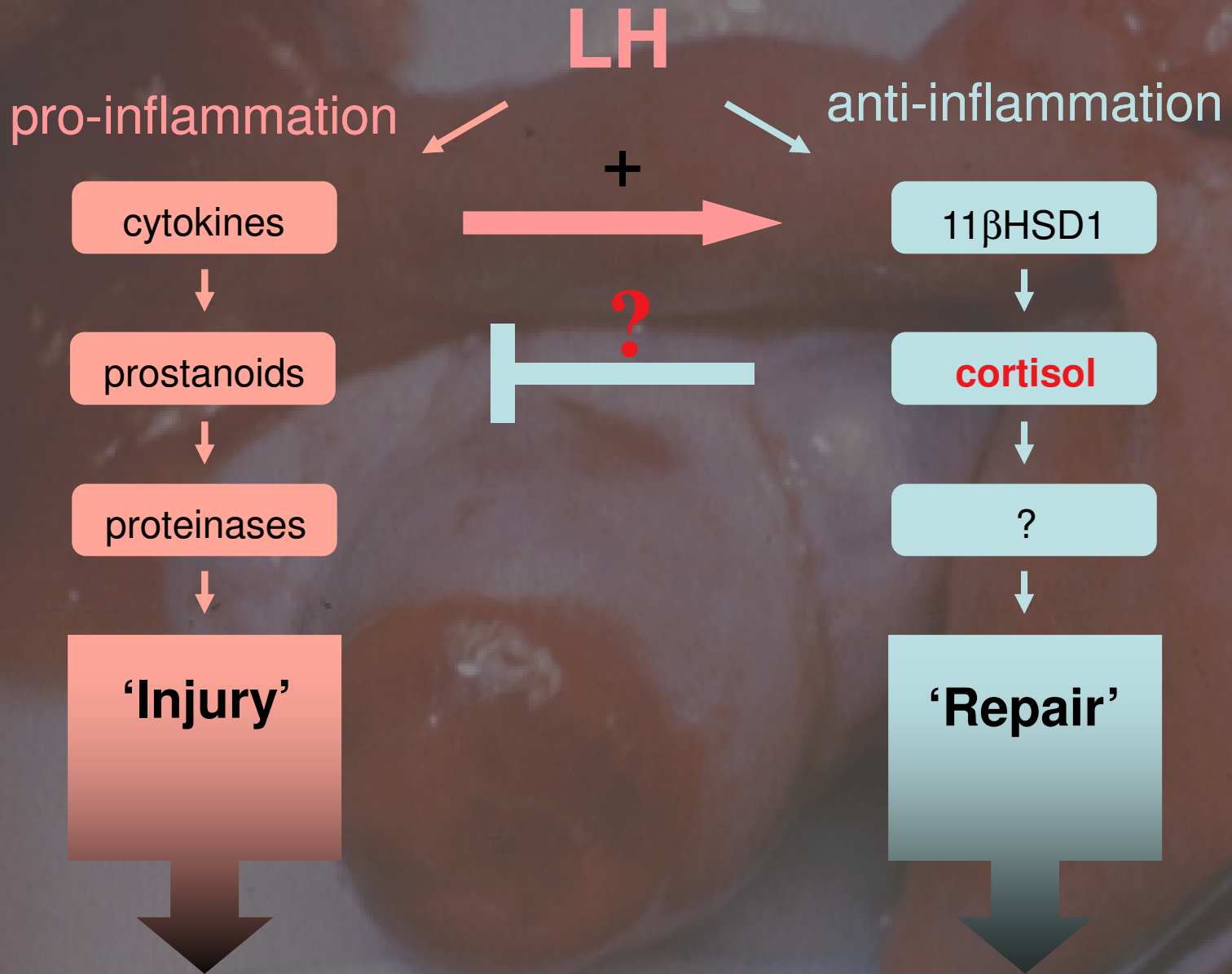
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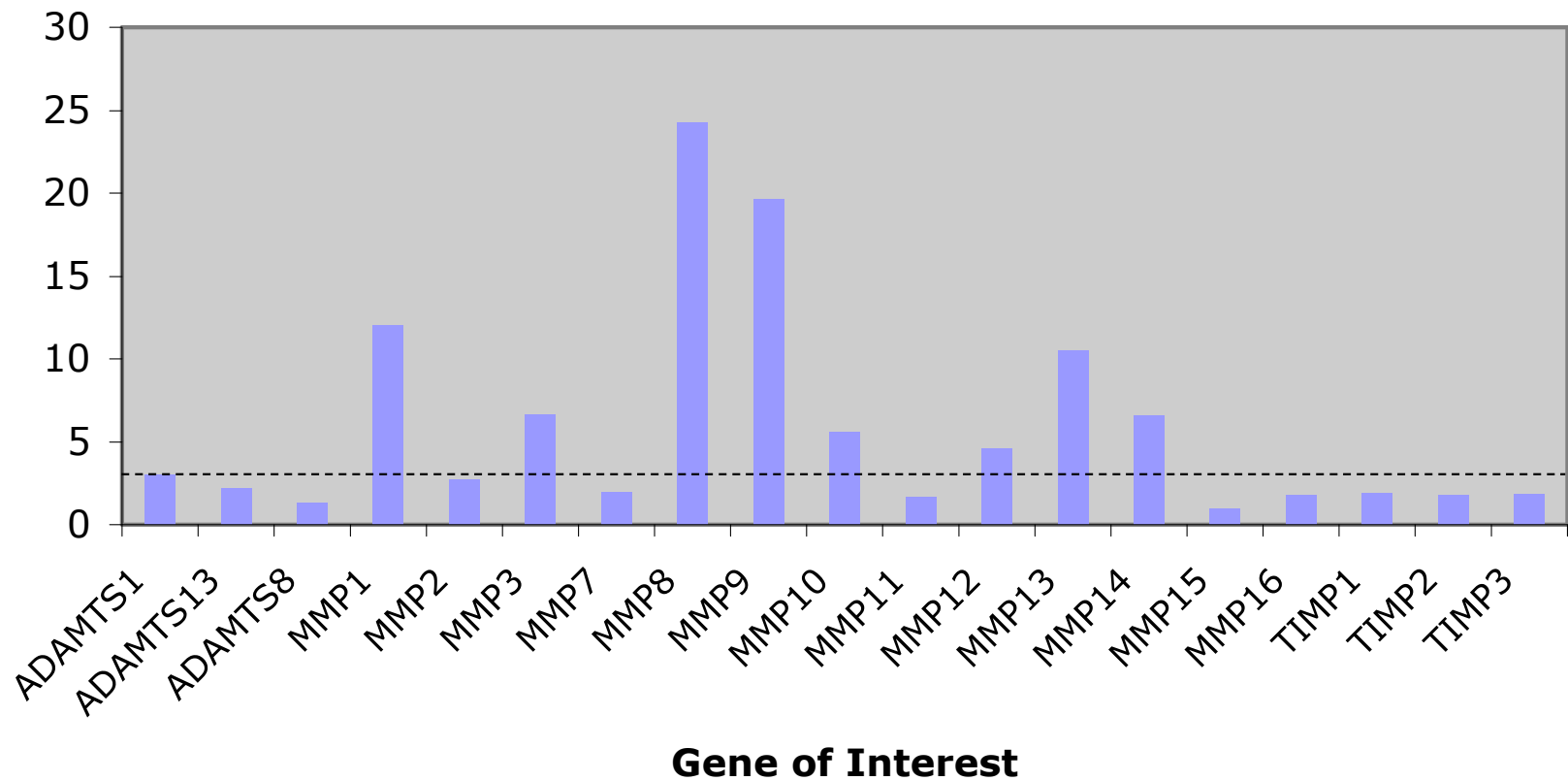
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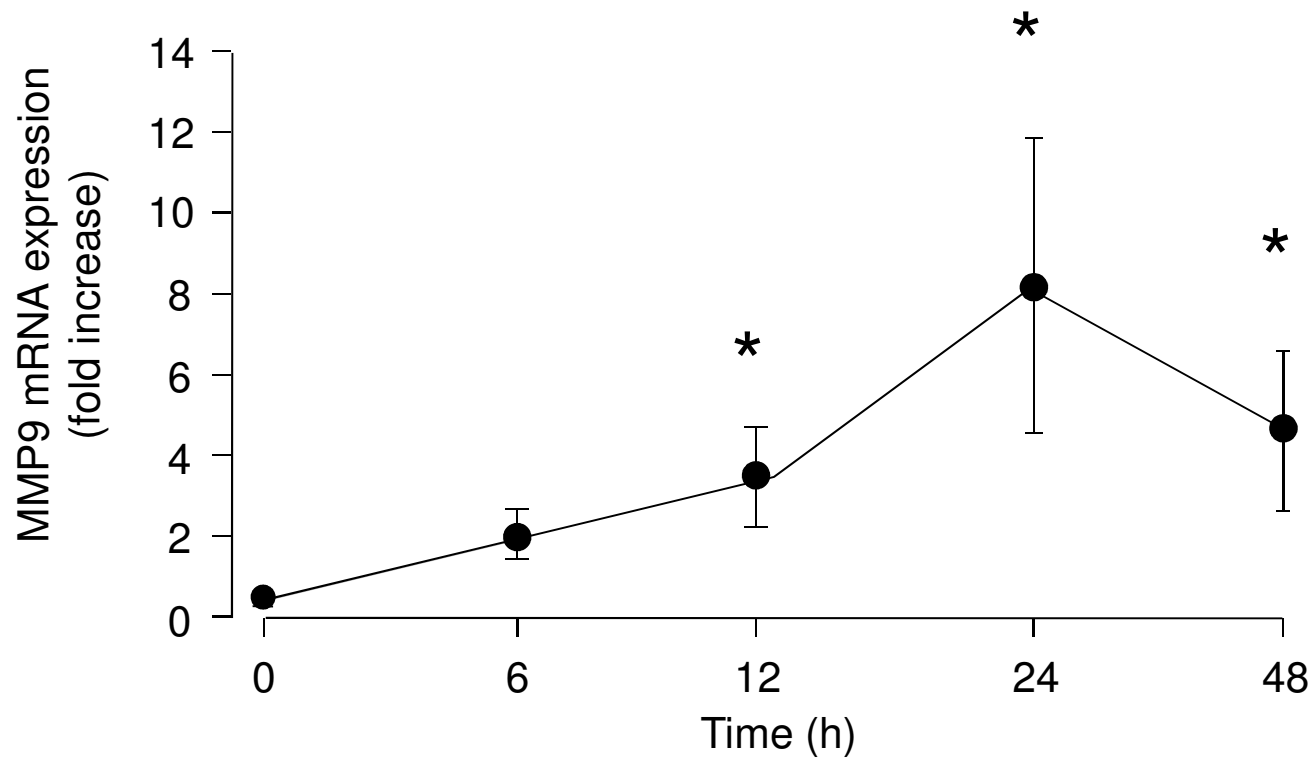




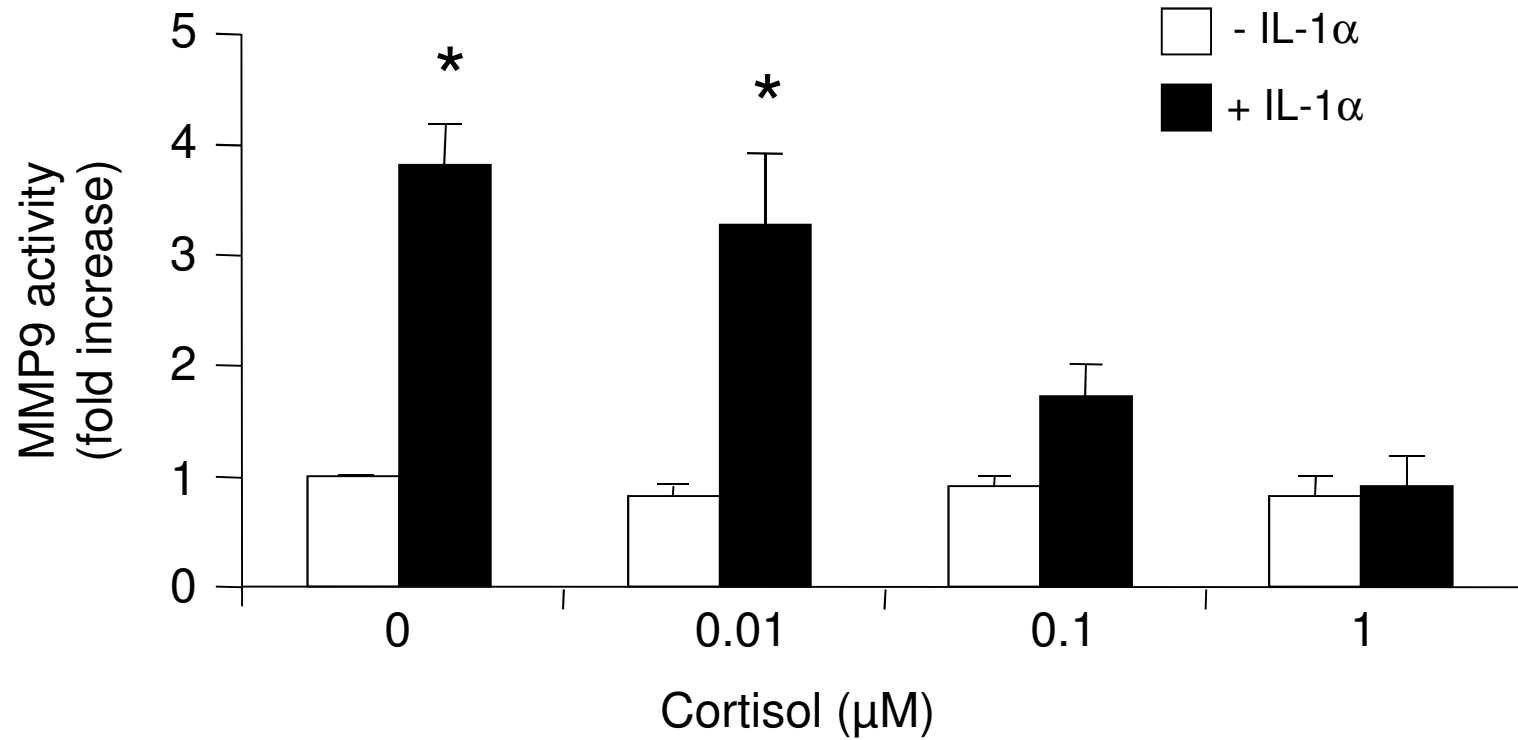
IL-1-regulated MMPs



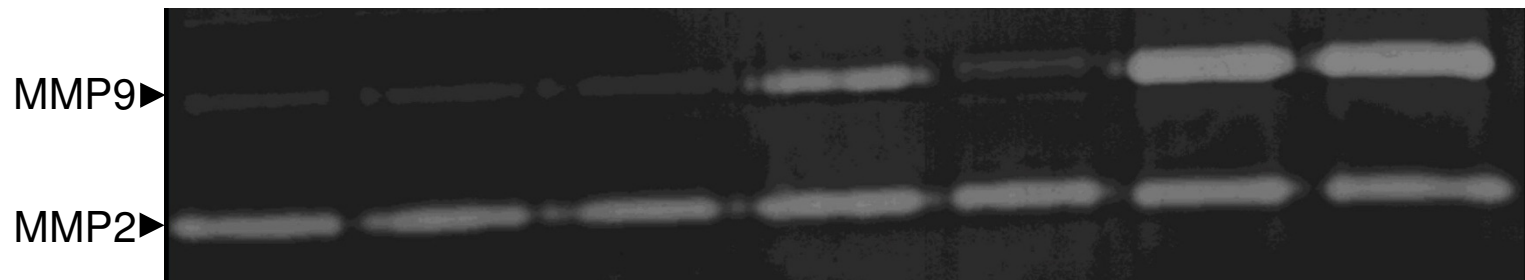
IL1-regulated MMP9



IL-1-regulated MMP9



GR-regulated MMP9

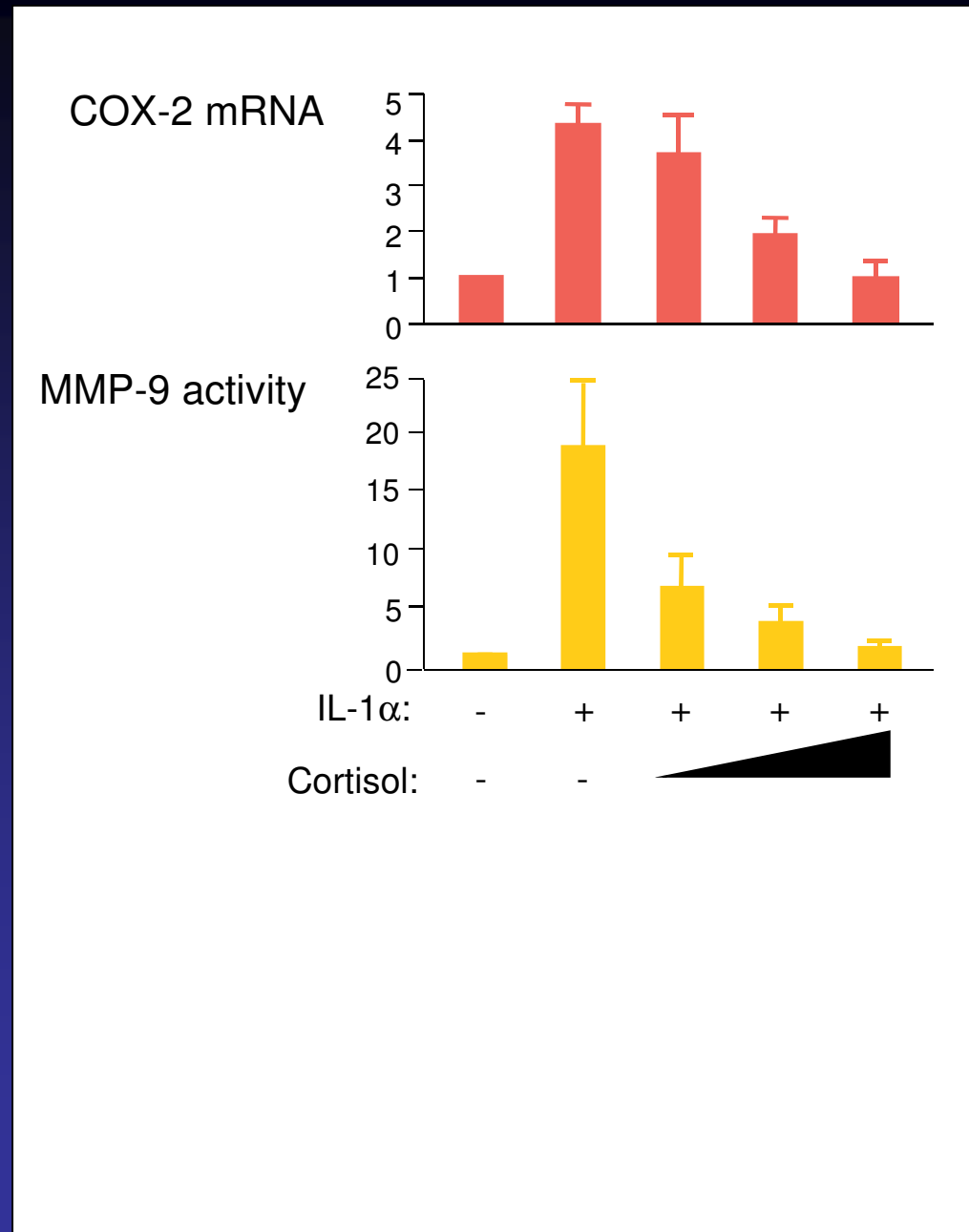


IL-1 α :	-	-	-	+	+	+	+
Cortisol	-	-	+	-	+	-	+
RU486:	-	+	-	-	-	+	+

Anti-inflammatory cortisol action in OSE cells

Rae et al. *JCEM* 2004

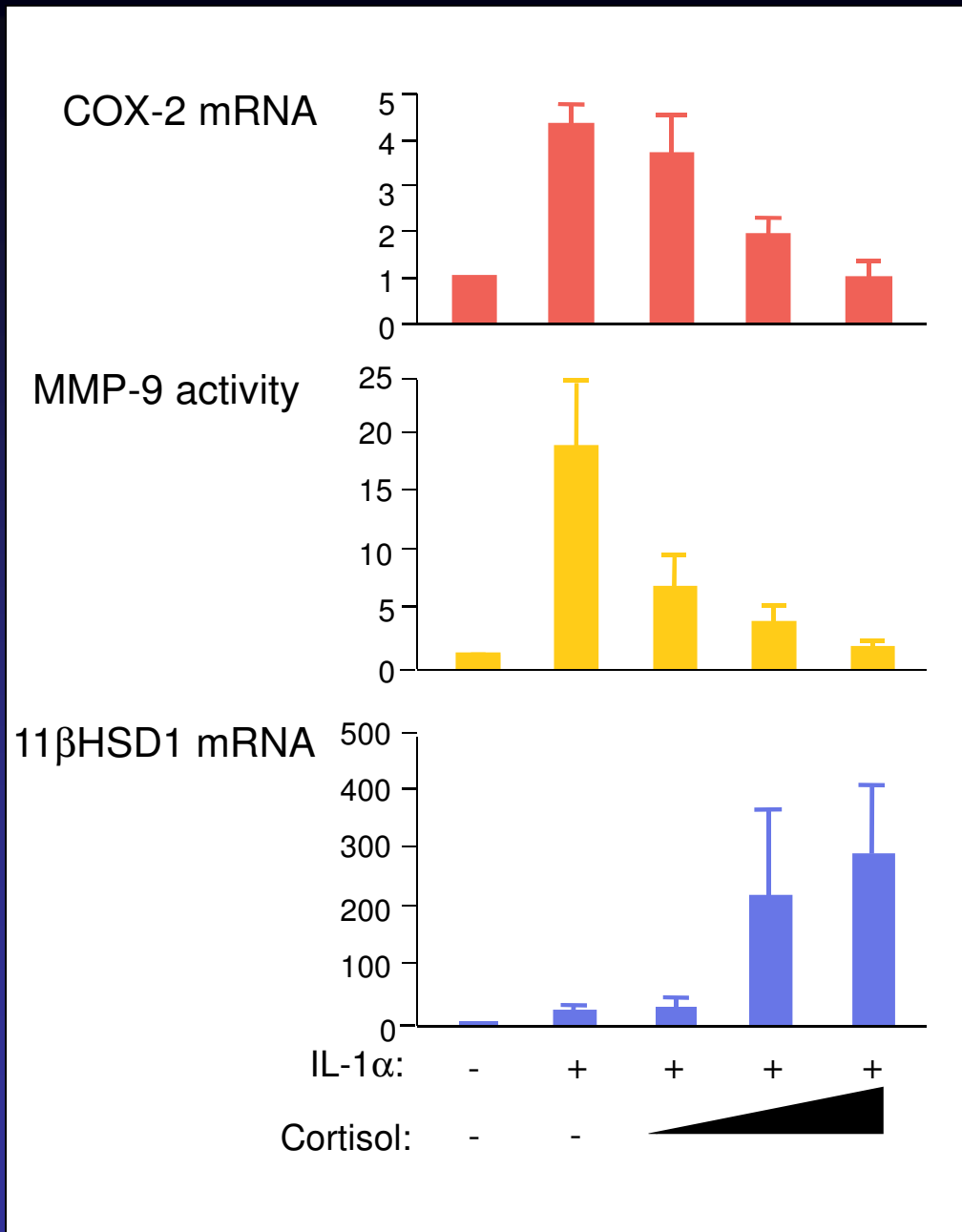
Rae et al. *Fertil Steril* 2008

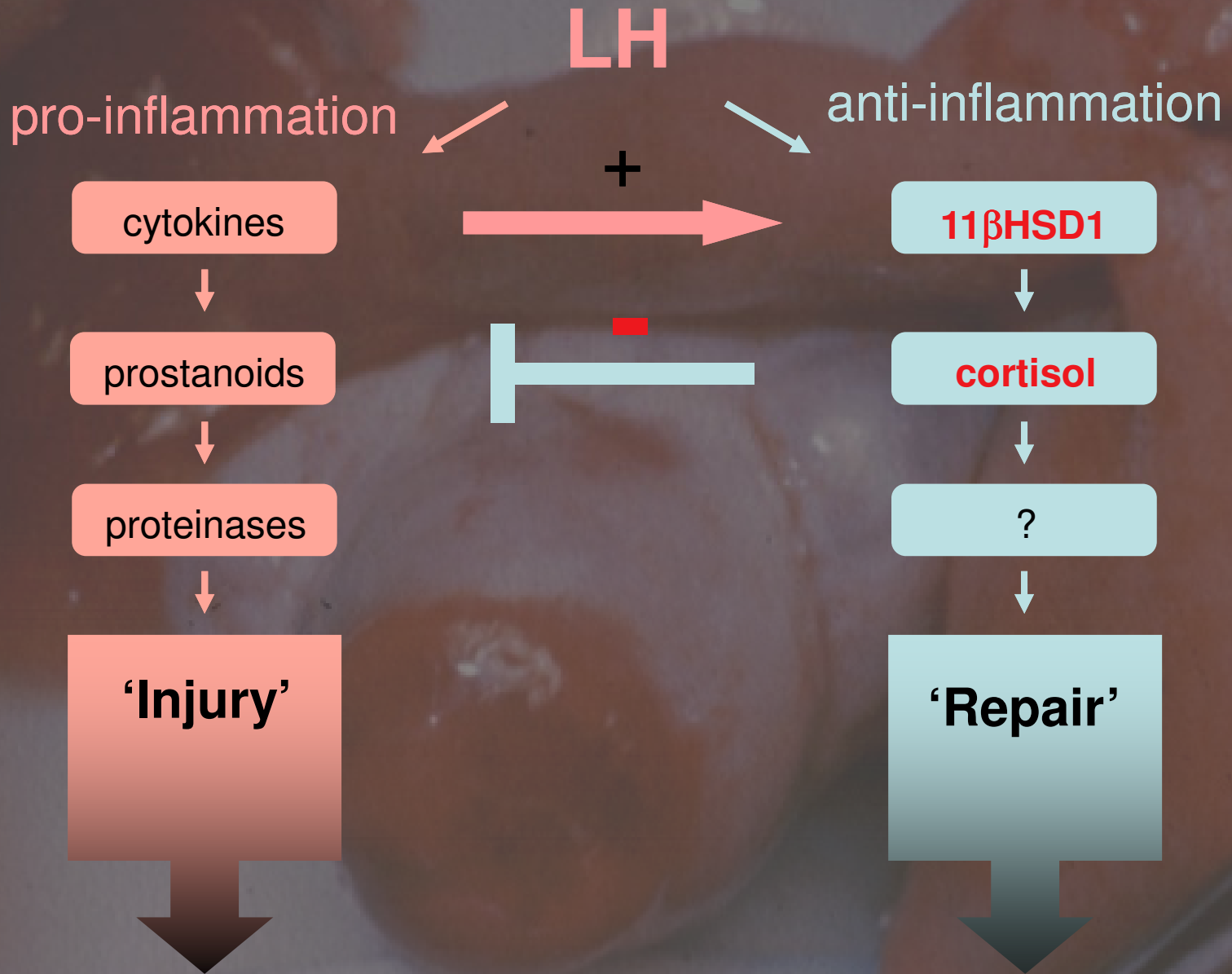


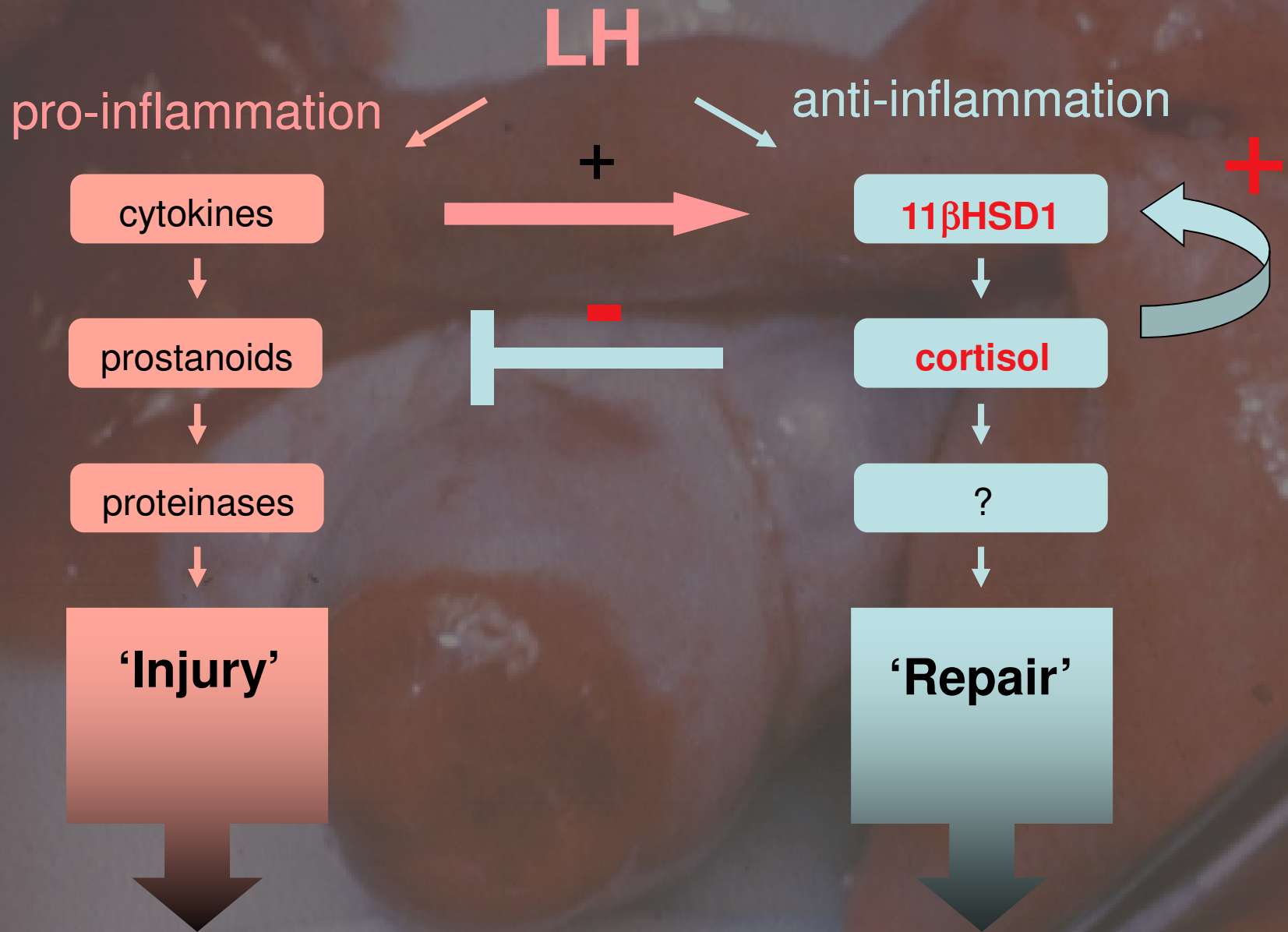
Anti-inflammatory cortisol action in OSE cells

Rae et al. *JCEM* 2004

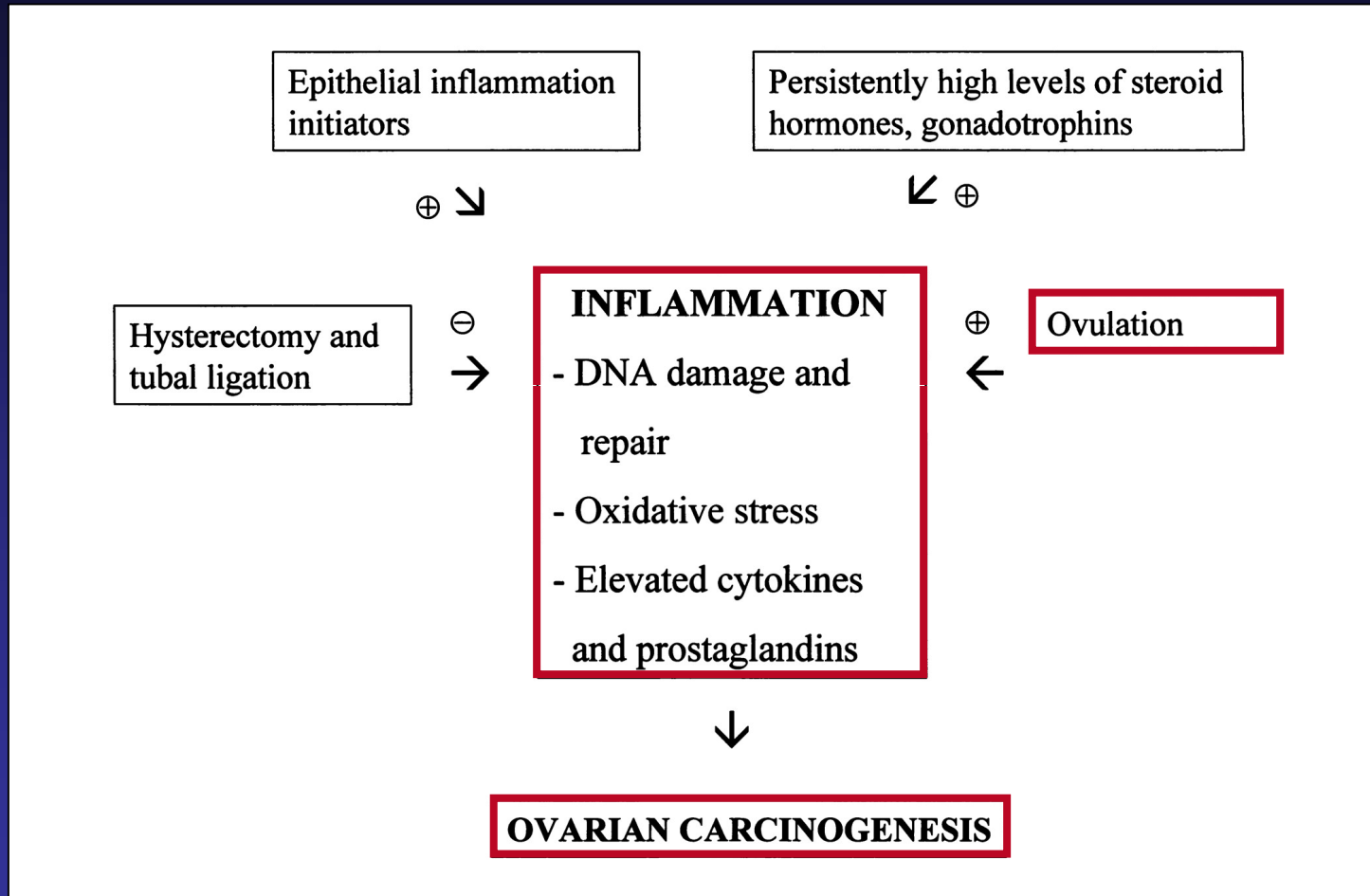
Rae et al. *Fertil Steril* 2008



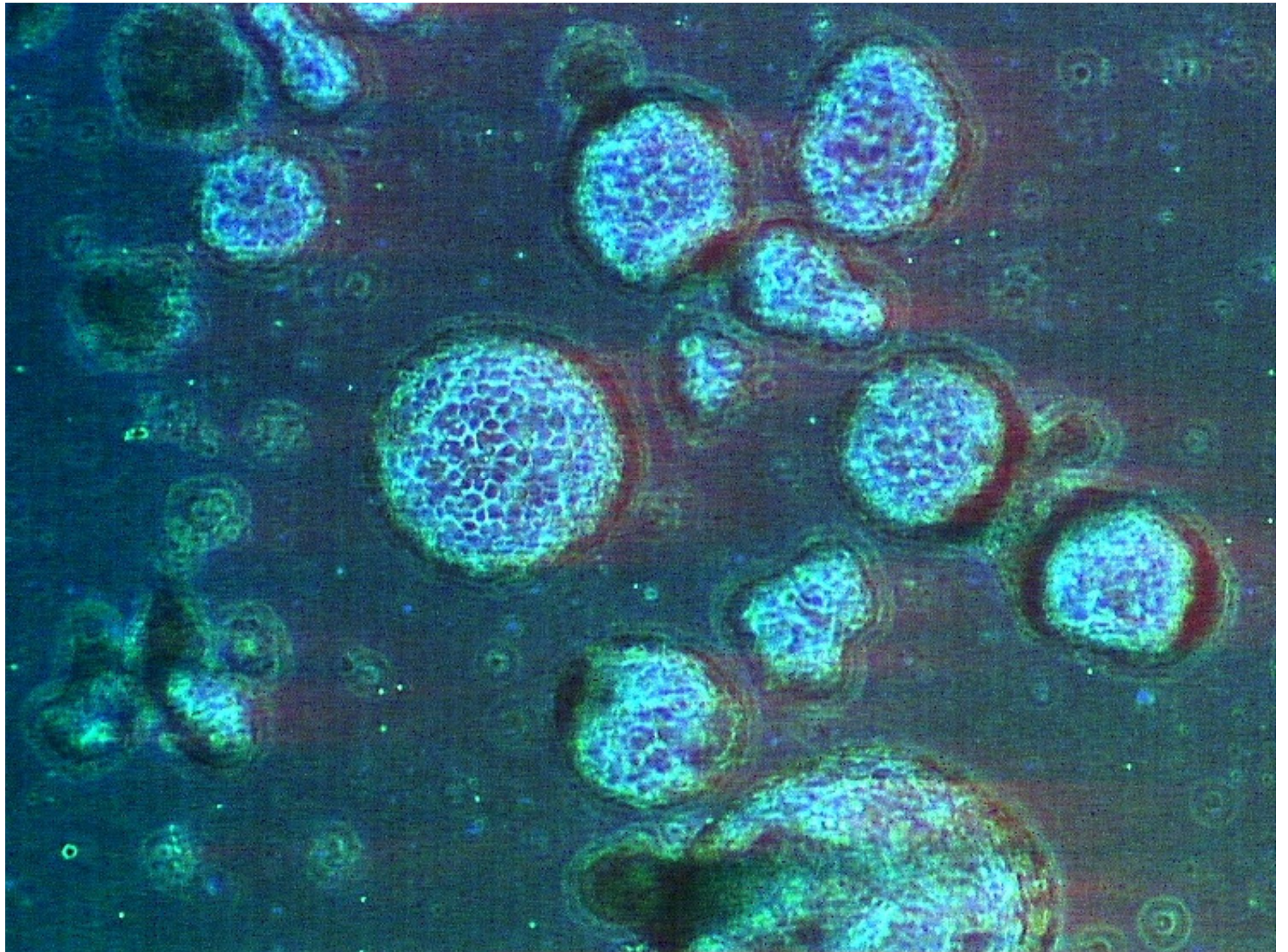




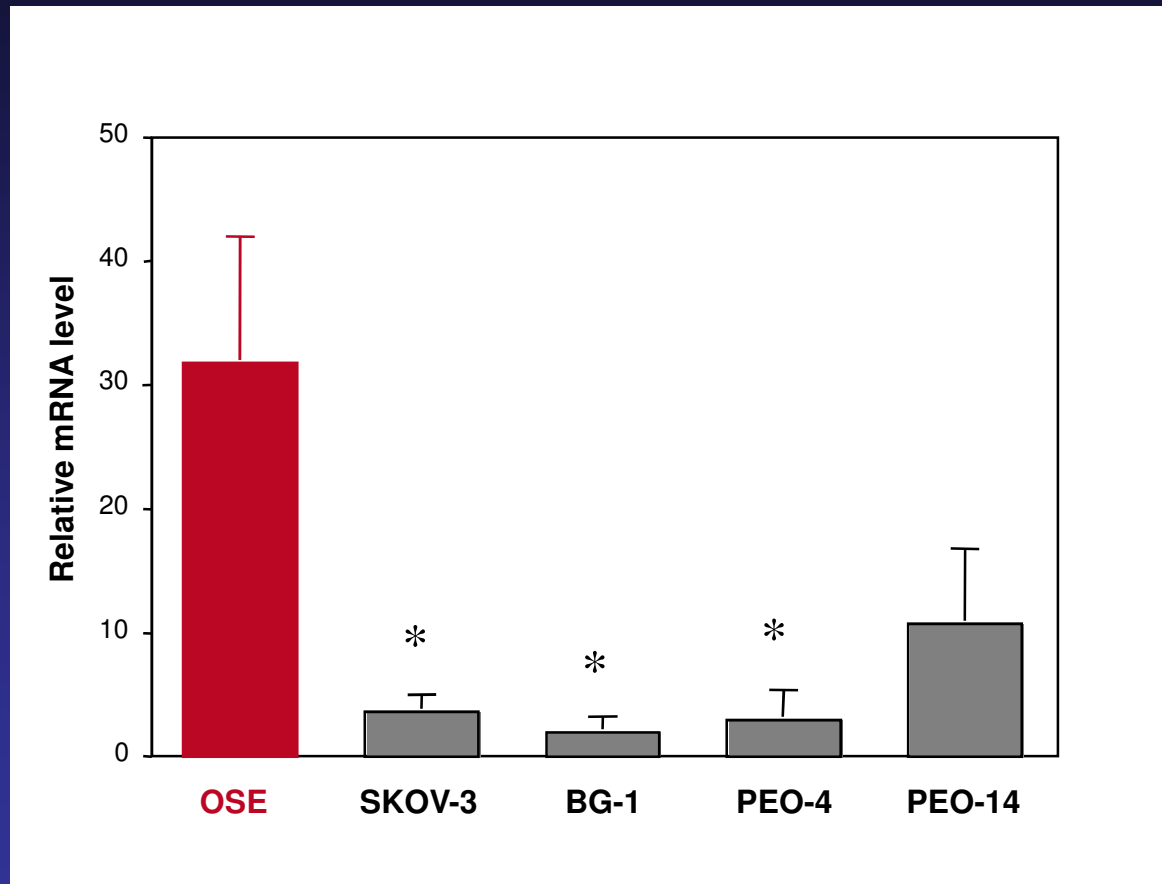
Hypothetical link between inflammation and ovarian cancer



Ness, R. B. et al. J. Natl. Cancer Inst. 1999 91:1459-1467

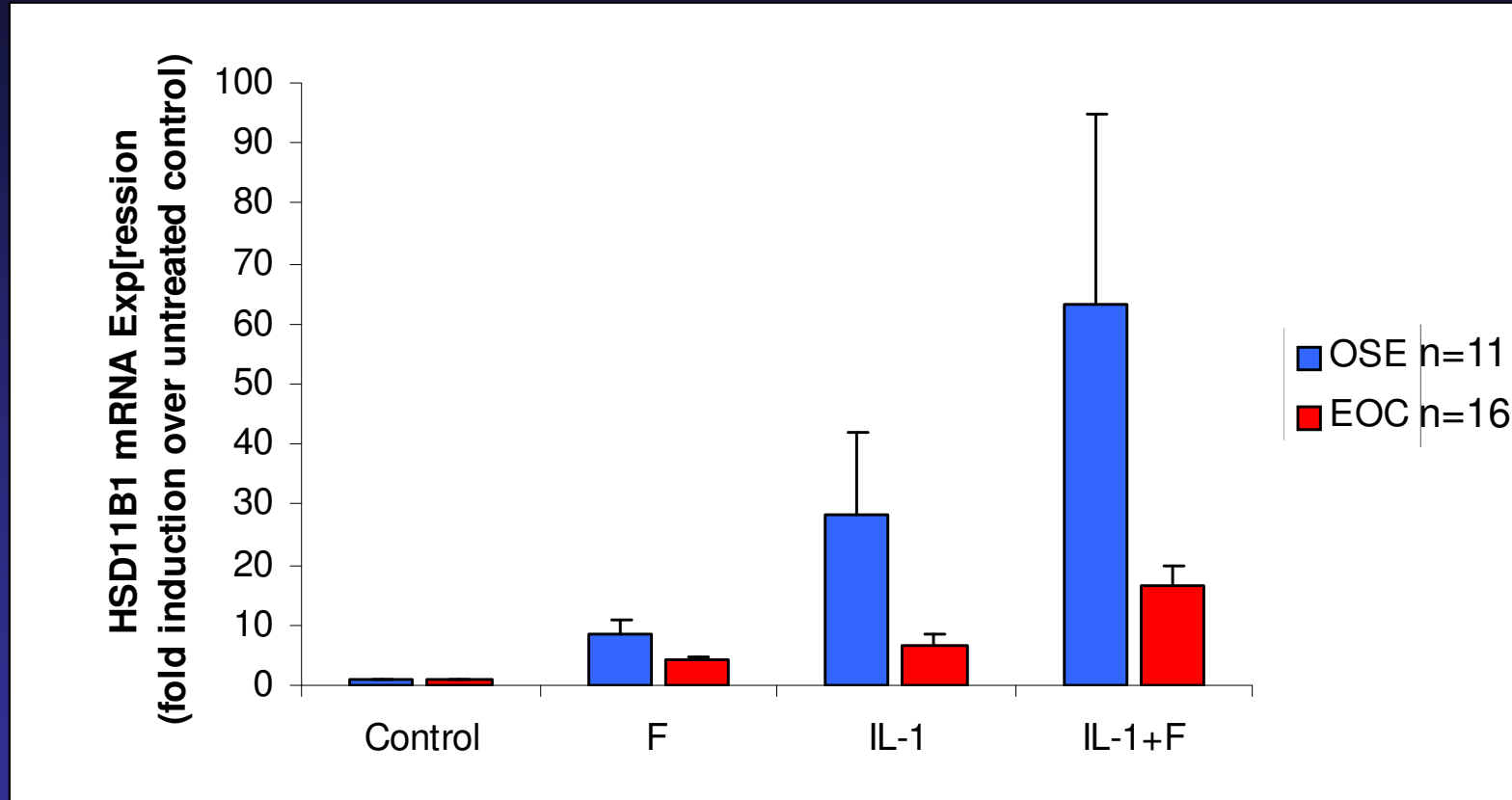


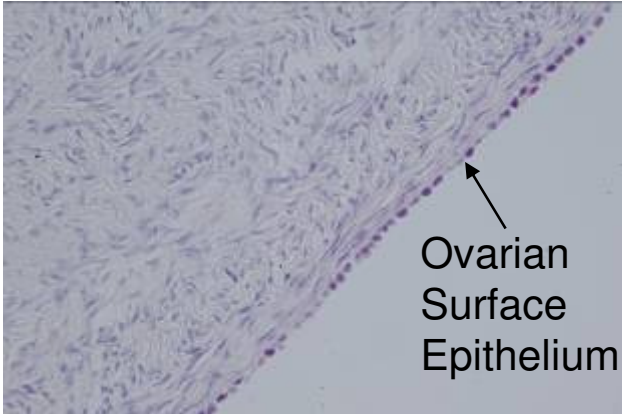
Abnormal *HSD11B1* gene expression in human ovarian cancer cell lines



O Gubbay et al. Br J Cancer. 2005

Abnormal *HSD11B1* gene expression in epithelial ovarian cancer

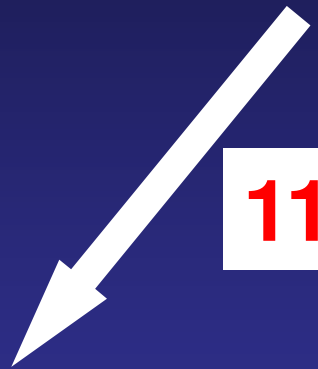




Ovulation



Inflammation



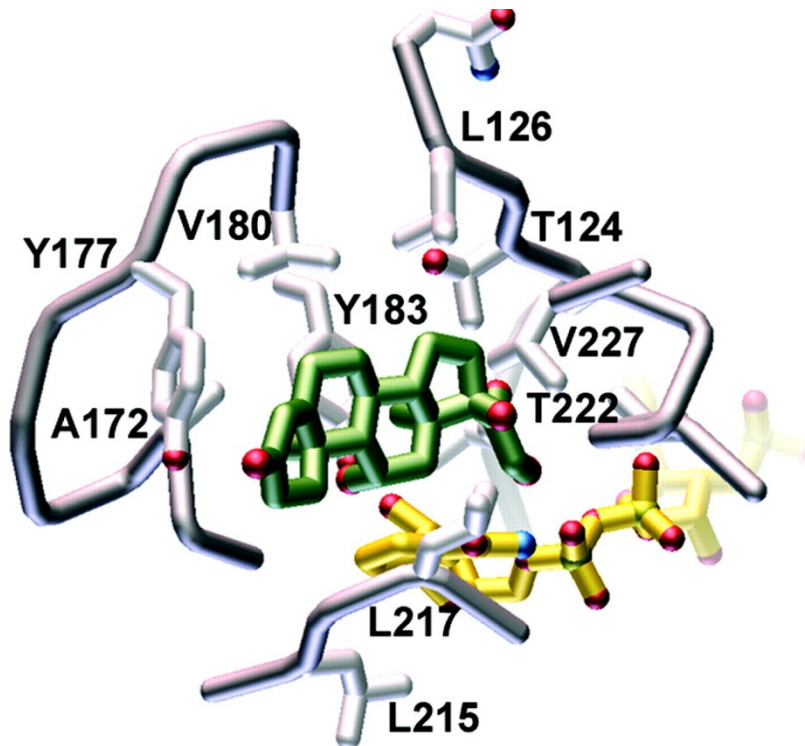
11 β HSD1

Ovarian Cancer



Conclusion: *HSD11B* gene expression is a potential marker or mediator of epithelial ovarian cancer

Structure-based model for cortisol interactions



Hosfield, D. J. et al. J. Biol. Chem. 2005;280:4639-4648

Acknowledgements

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