

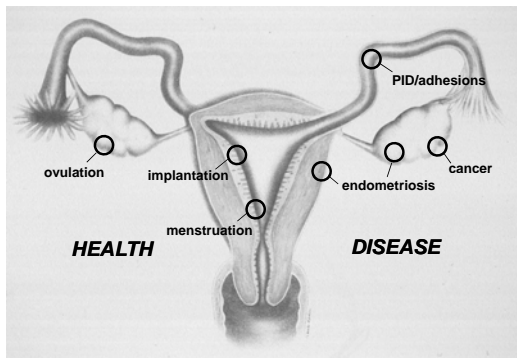
Control of Ovulation

Stephen G. Hillier

University of Edinburgh
Centre for Reproductive Biology
Edinburgh, UK

s.hillier@ed.ac.uk

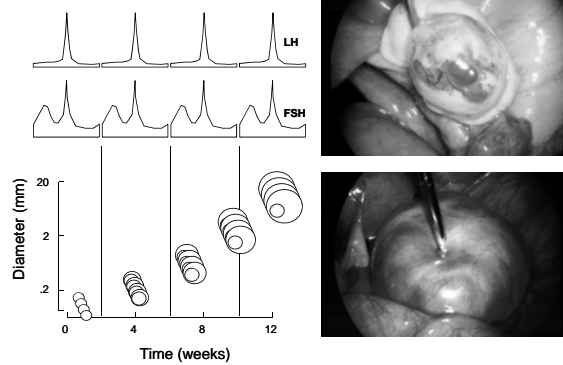
Inflammation in reproductive health and disease

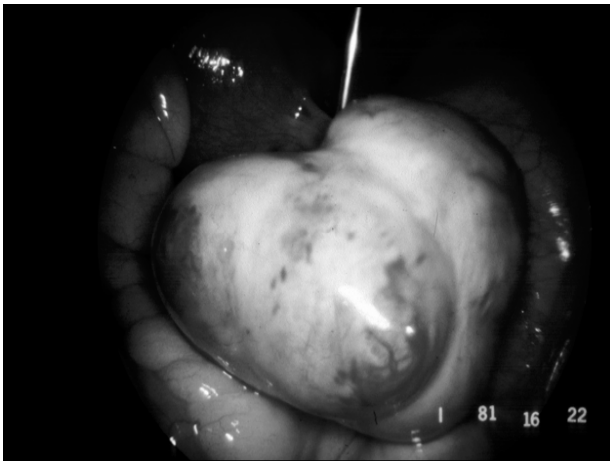


Control of Ovulation

- Ovulation up close
- Ovulation as injury
- Postovulatory repair

The Follicular Lifespan



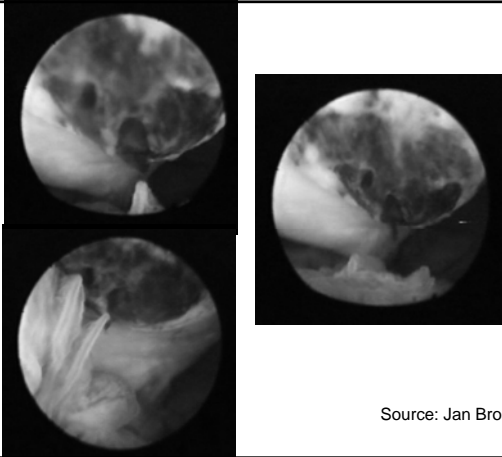


Control of Ovulation

- Ovulation up close
- Ovulation as injury
- Postovulatory repair

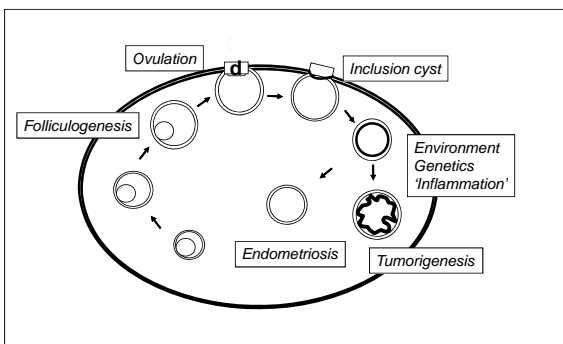
QuickTime™ and a
YUV420 codec decompressor
are needed to see this picture.

Source: Jan Brosens



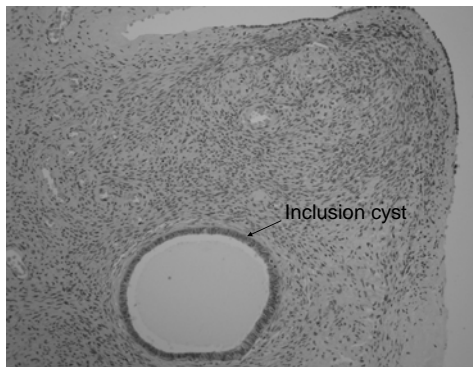
Source: Jan Brosens

Ovulation and ovarian disease



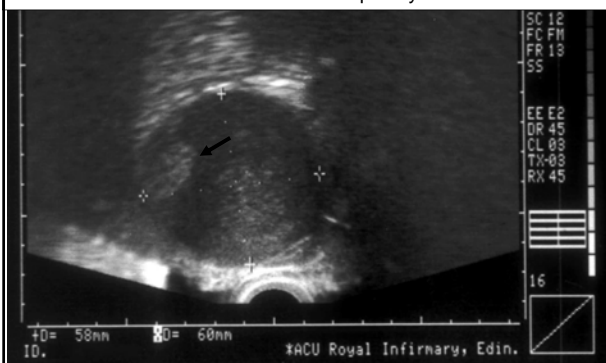
Okamura et al 2003

Intra-ovarian inclusion cyst

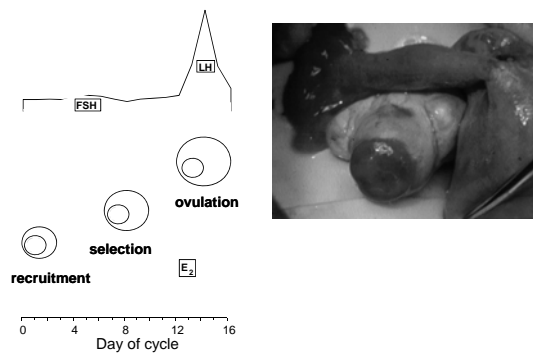


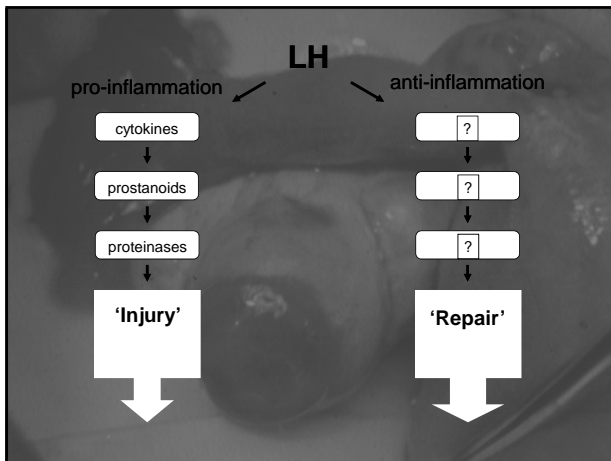
Ovarian Cancer

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



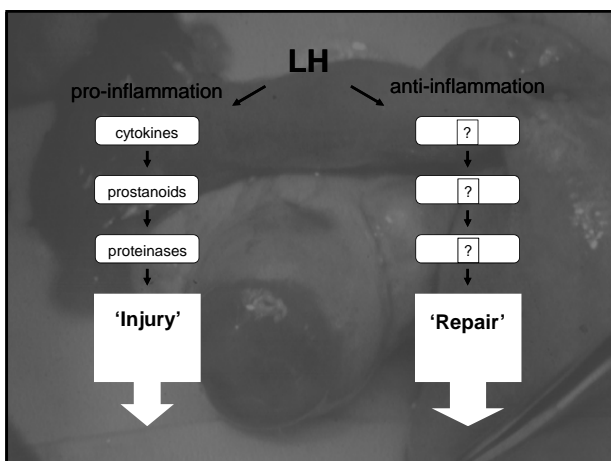
Ovulation = Inflammation

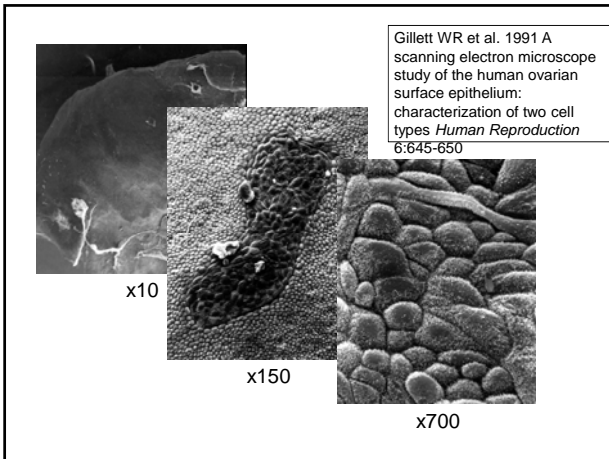


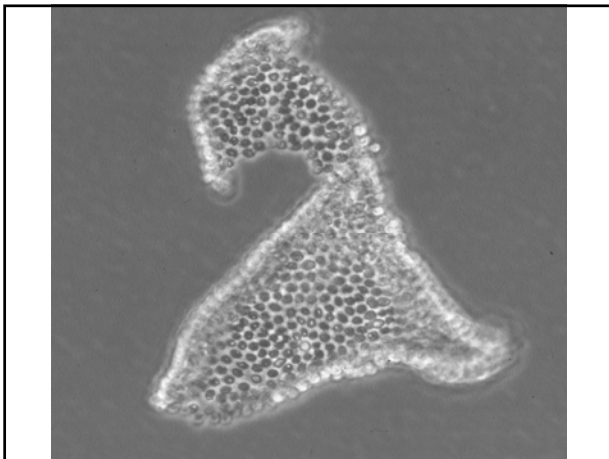


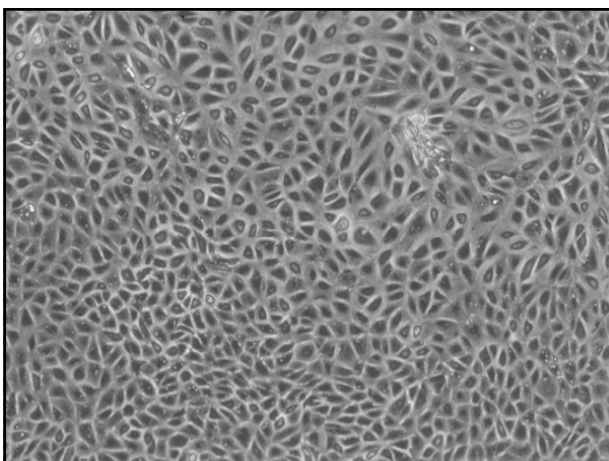
Control of Ovulation

- Ovulation up close
- Ovulation as injury
- Postovulatory repair







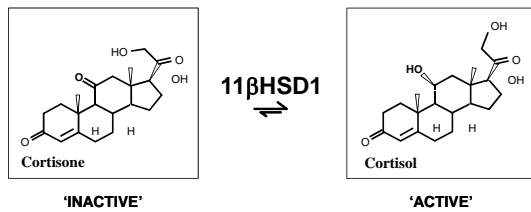


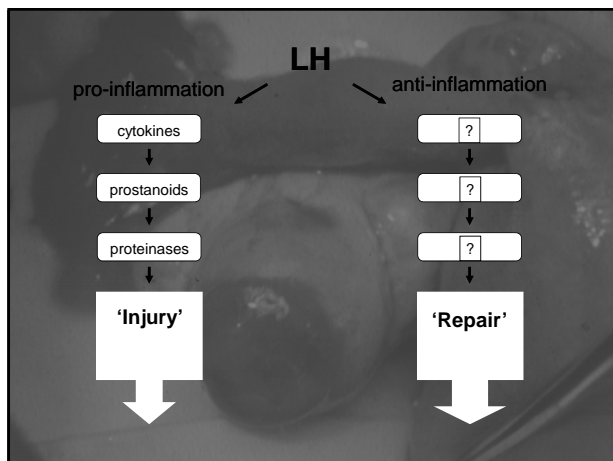
Gene expression in experimentally inflamed* OSE cells

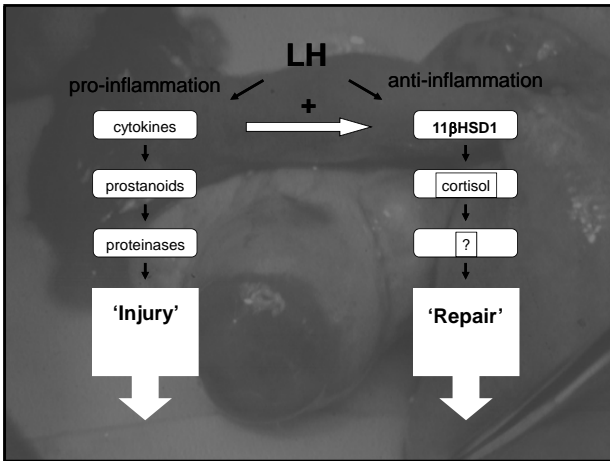
* Treatment with Interleukin-1

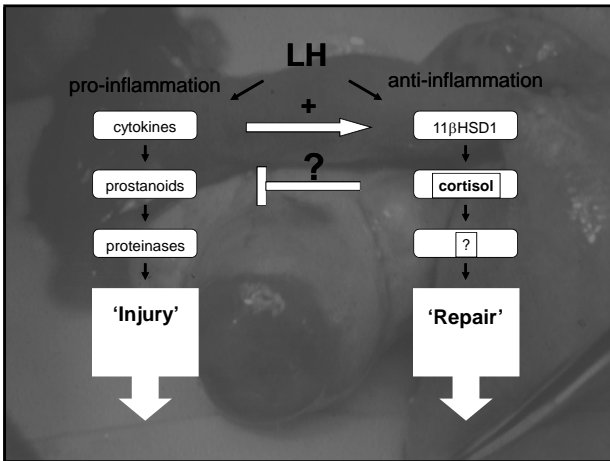


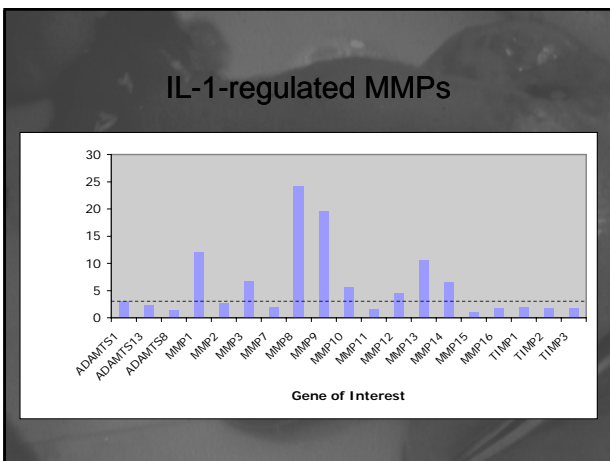
The Cortisone-Cortisol Shuttle



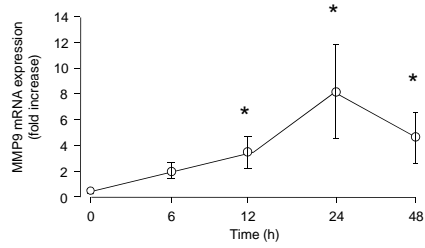




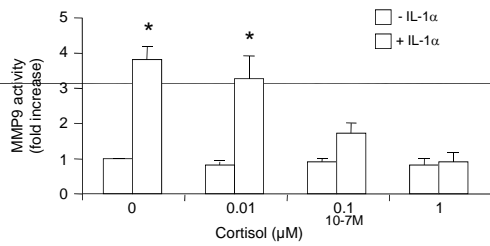




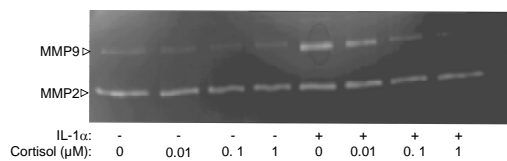
IL1-regulated MMP9



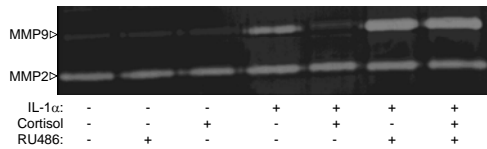
IL-1-regulated MMP9



IL-1-regulated MMP9

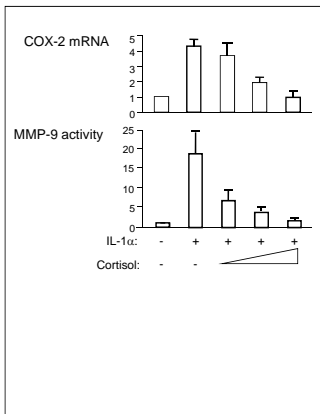


GR-regulated MMP9



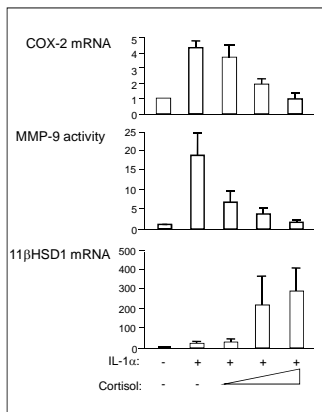
Anti-inflammatory cortisol action in OSE cells

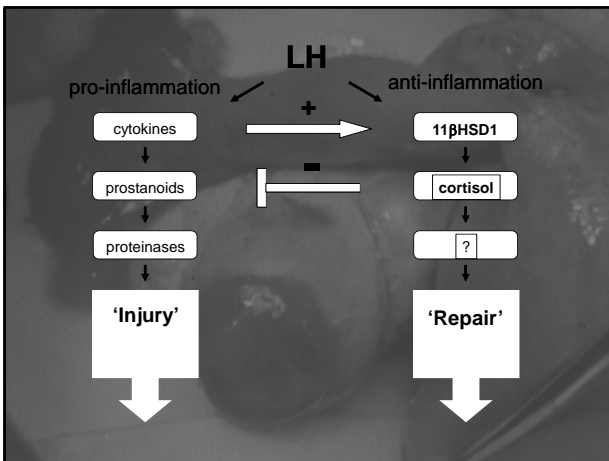
Rae et al. *JCEM* 2004
Rae et al. *Fertil Steril* 2008

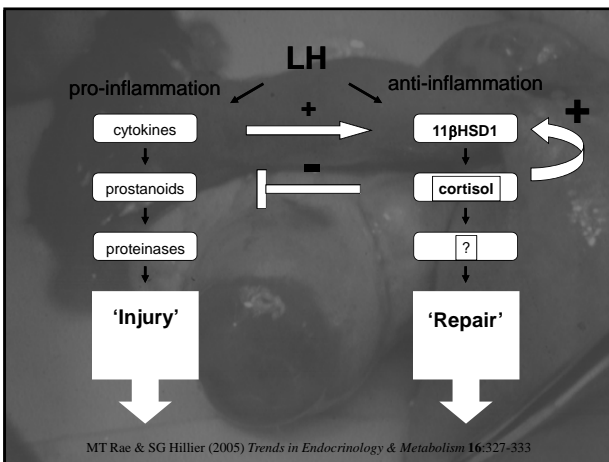


Anti-inflammatory cortisol action in OSE cells

Rae et al. *JCEM* 2004
Rae et al. *Fertil Steril* 2008

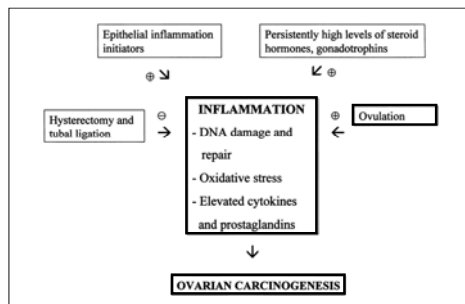




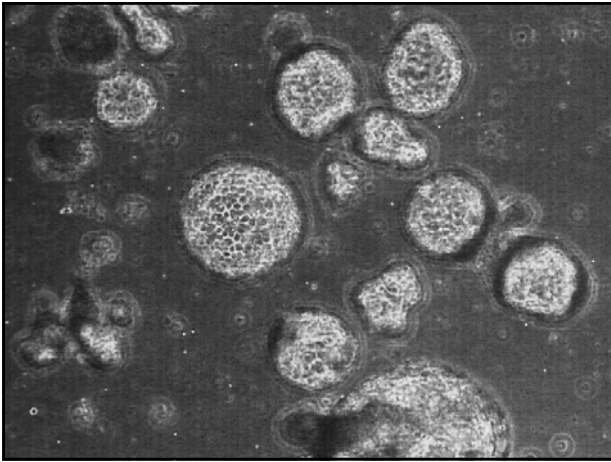


MT Rae & SG Hillier (2005) *Trends in Endocrinology & Metabolism* 16:327-333

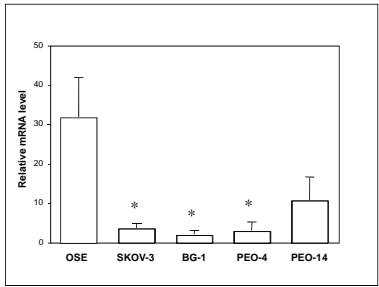
Hypothetical link between inflammation and ovarian cancer



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

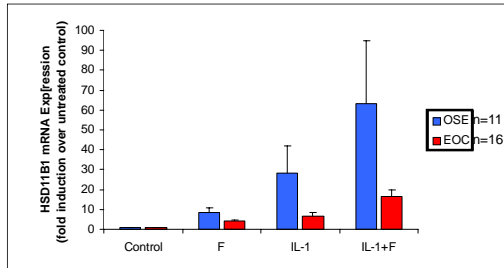


Abnormal *HSD11B1* gene expression in human ovarian cancer cell lines

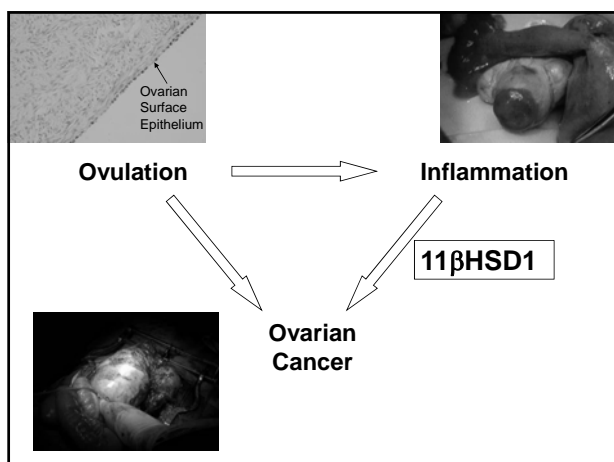


O Gubbay et al. Br J Cancer. 2005

Abnormal *HSD11B1* gene expression in epithelial ovarian cancer

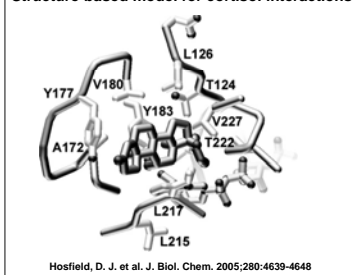


KS Fegan, MT Rae & SG Hillier *Endocrine Abstracts* (2006) 11 P498



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

Mick Rae	Hilary Critchley	Peter Ghazal
Scott Fegan	Ian Mason	Jan Brosens
Deborah Price	Alistair Williams	
Chris Harlow	Catherine Murray	
Oliver Gubbay	Sharon Macpherson	
Wei Guo	Joo Thong	

Grant support:
Medical Research Council
European Commission FPV
