

Connexins in the Endometrium: Regulation Properties and Possible Functions

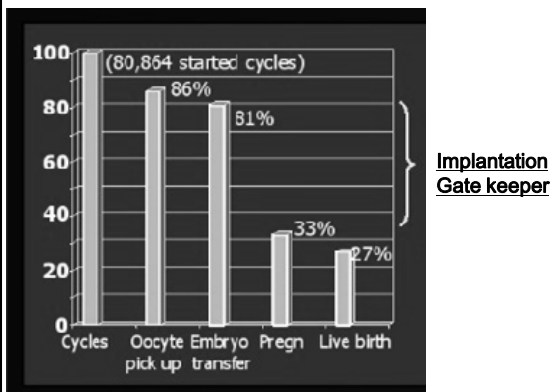
Elke Winterhager



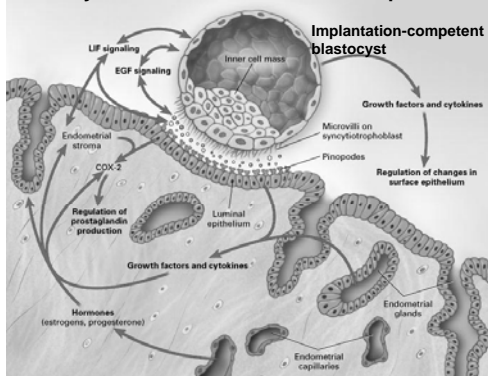
University Clinics, University of Essen
Institute of Molecular Biology

Glasgow, March 2009

IVF-register

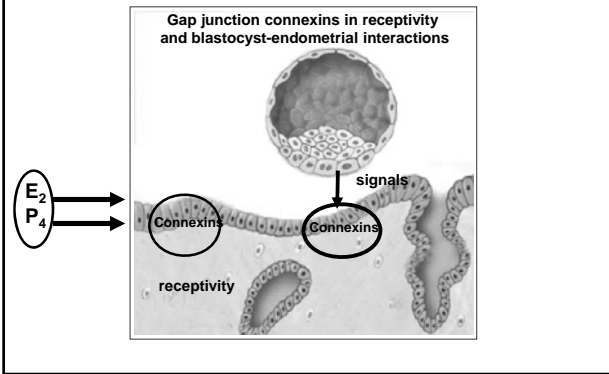


Embryo - Maternal Cross-Talk at Implantation

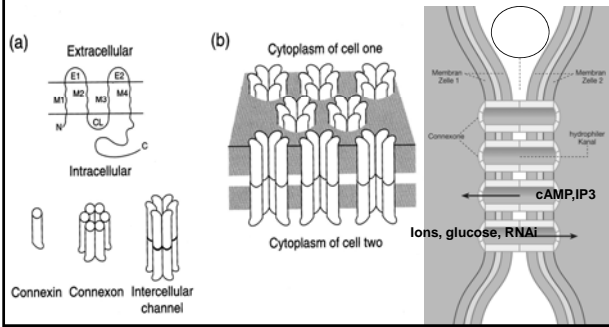


Norwitz ER, Schust DJ, Fisher SJ. (2001). N Engl J Med.345(19):1400-8.

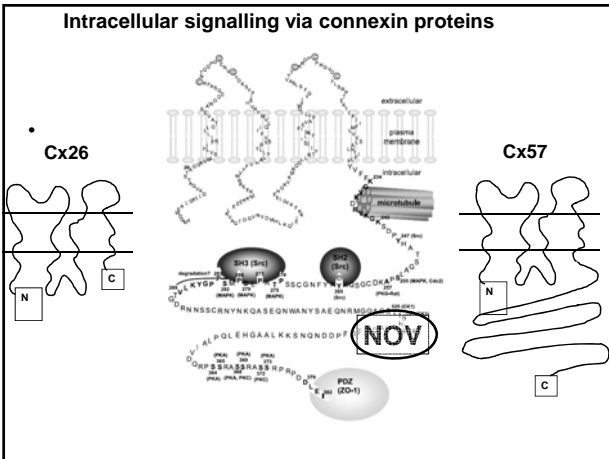
Genetic programming of the endometrium by steroid hormones and blastocyst signals



Connexins, connexons and gap junctions



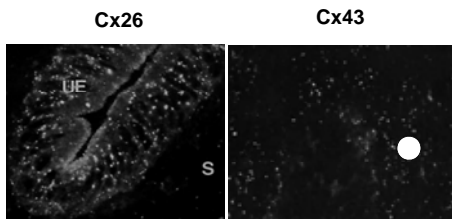
Intracellular signalling via connexin proteins



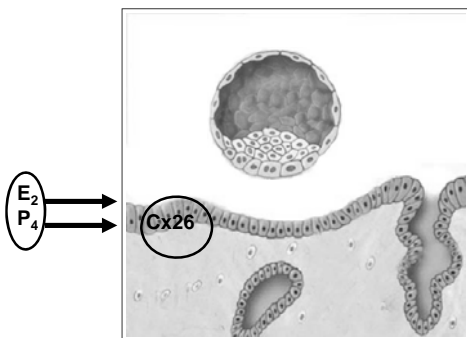
The mouse connexin multigene family

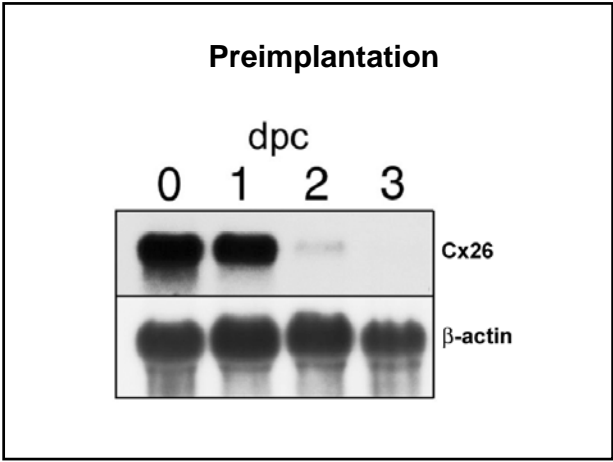
Connexin	prominent expression	prominent expression	
Cx23 (GJBE1)	lens	Cx37	vasculature, endothelium
Cx26 (GJB2)	liver, brain, placenta	Cx39 (GJD4)	musculature
	uterus	Cx40	heart, lung
Cx29	CNS, PNS	Cx43 (GJA1) ubiquitous	
Cx30	skin, cochlea	Cx45 (GJC1)	heart, vasculature
Cx30.2	n.a.	Cx46 (GJA3)	lens
Cx30.3	skin	Cx47	brain
Cx31 (GJB3)	skin, placenta	Cx50	lens
Cx31.1	skin, placenta	Cx57	skin, heart, kidney
Cx32	liver, kidney, PNS		
Cx33	testis		
Cx36	retina		

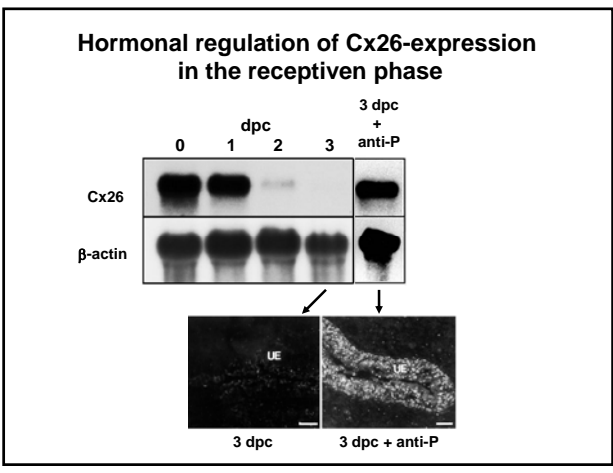
Connexin expression in the nonpregnant rodent endometrium

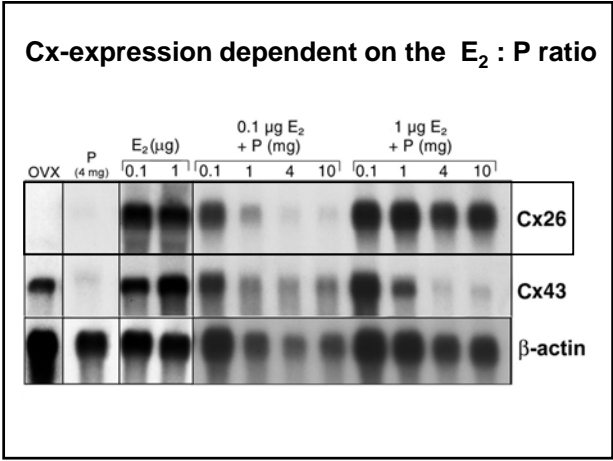


Connexins in receptivity

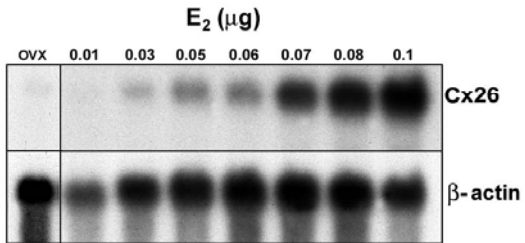


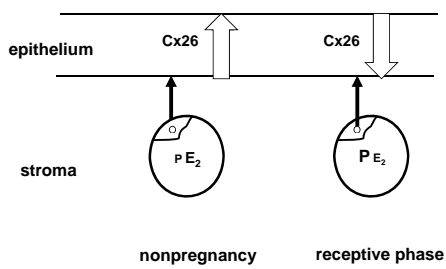




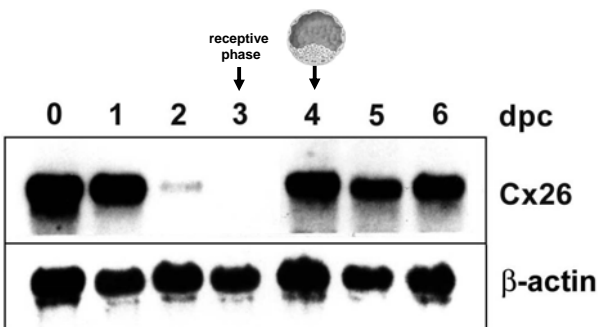


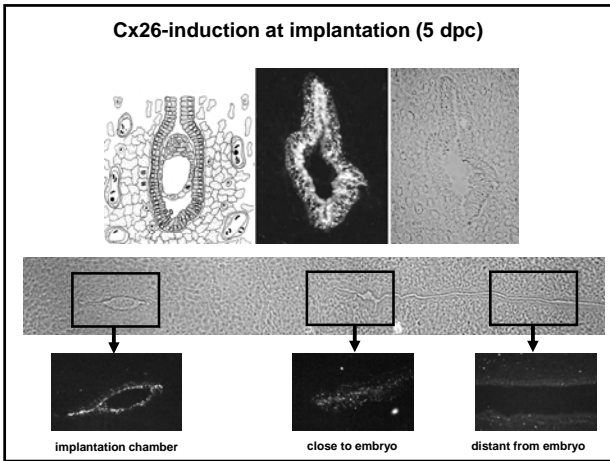
Cx26 gene response to E₂-concentrations

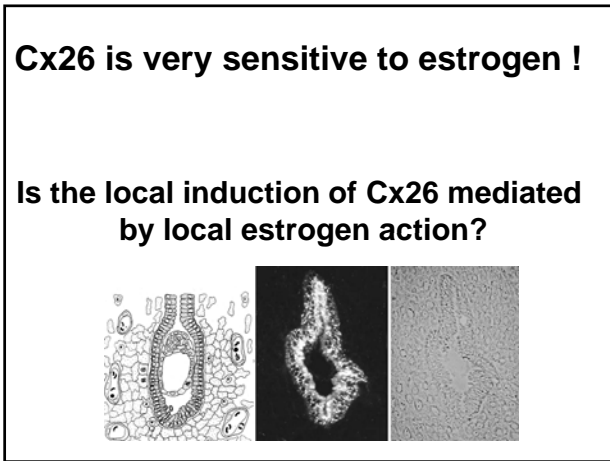


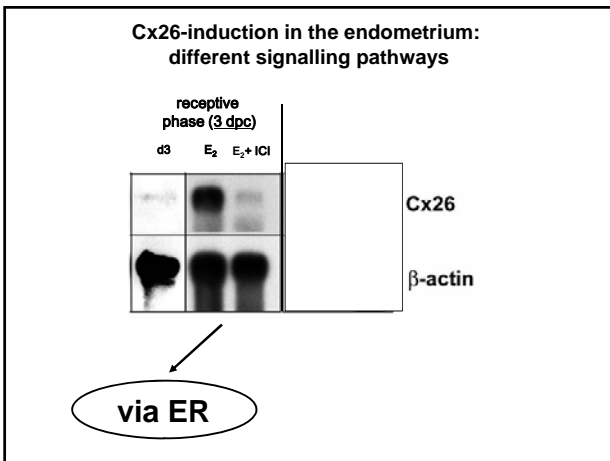


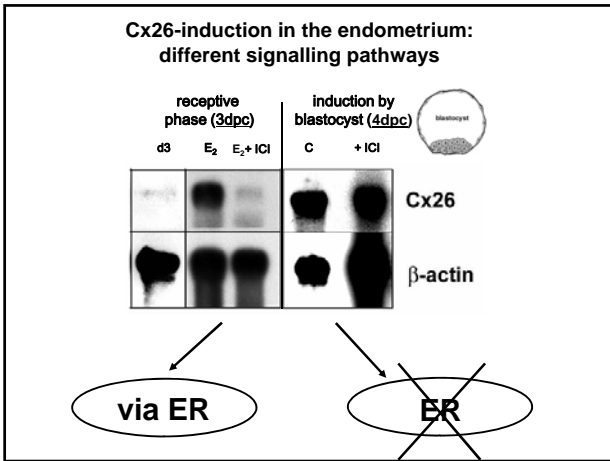
Cx26-transcripts in the endometrium









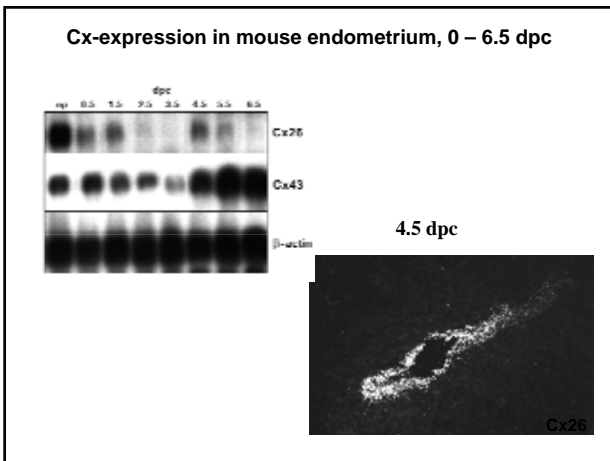


Cx26-induction in the endometrium upon E₂

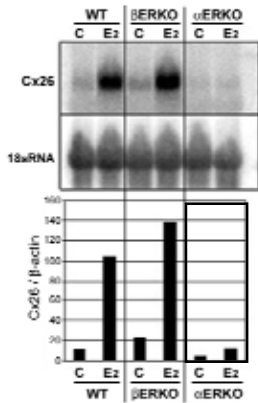
Which ER ?

ER-alpha knockout mouse
(Couse et al.1997)

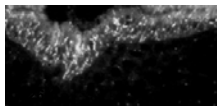
ER-beta knockout mouse
(Krege et al.1998)



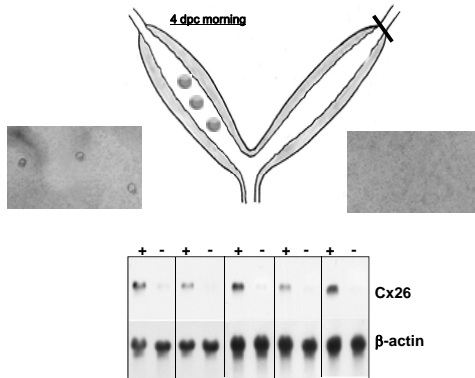
Expression of Cx26 in the ERKO and BERKO mouse

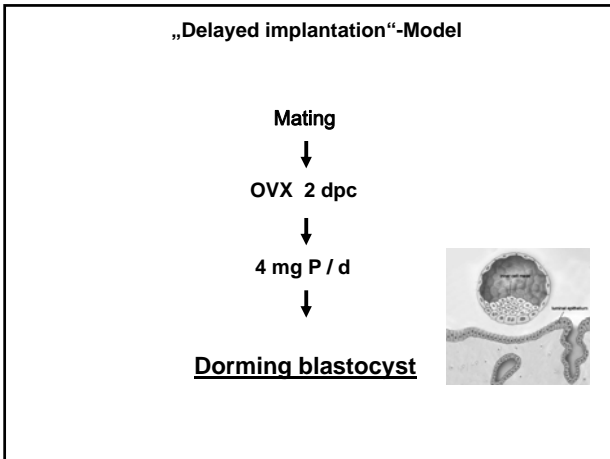


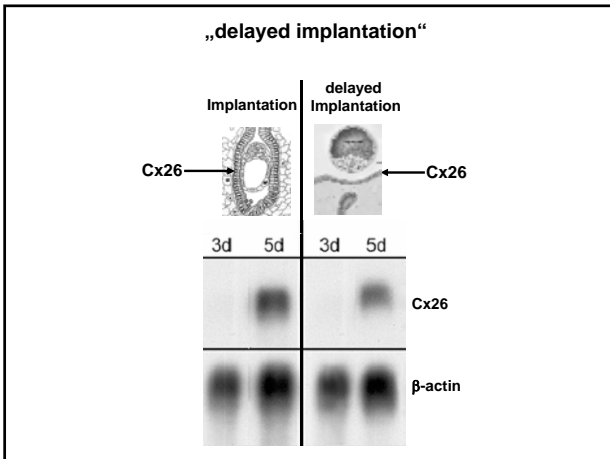
How early is Cx26 induced at implantation ?

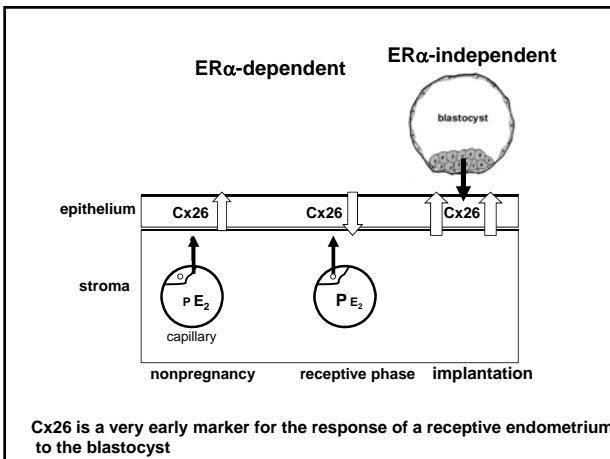


Tubal ligation experiments reveal already Cx26 expression only in the presence of a blastocyst at apposition/adhesion





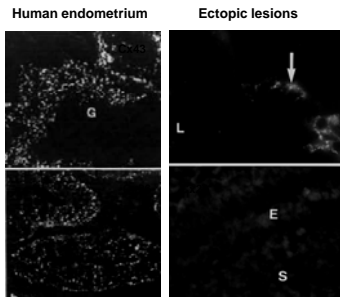




Cx26 is a very early marker for the response of a receptive endometrium to the blastocyst

Are connexins marker gene for a non-appropriate differentiated endometrium ?

Former publications on human endometrium has given hints that connexins are marker genes for inappropriate differentiation in endometriotic lesions



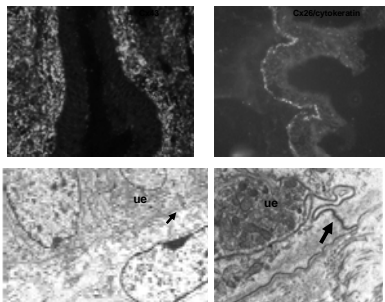


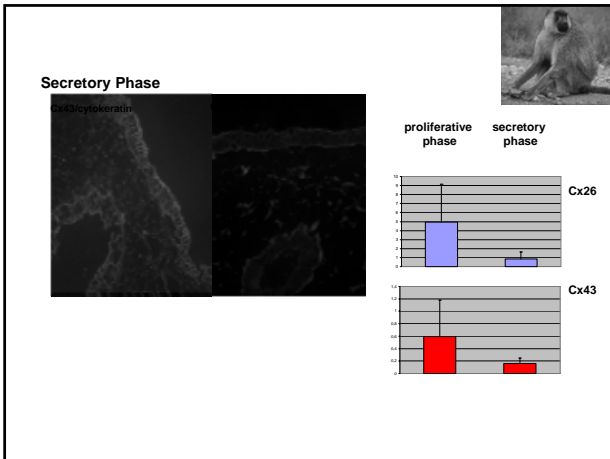
Connexin pattern in baboon menstrual cycle and endometriosis

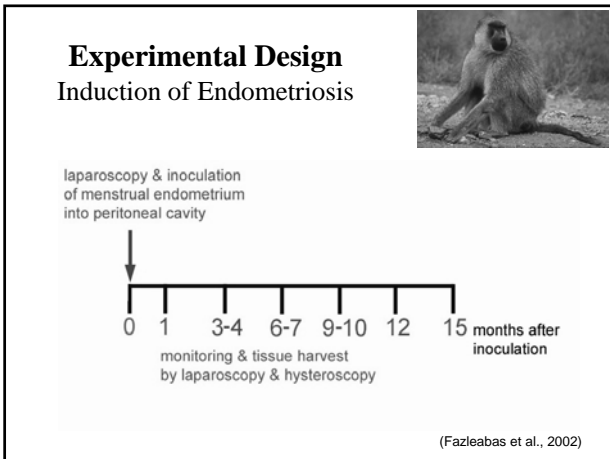
Pathological changes of the eutopic endometrium due to the presence of ectopic lesions?

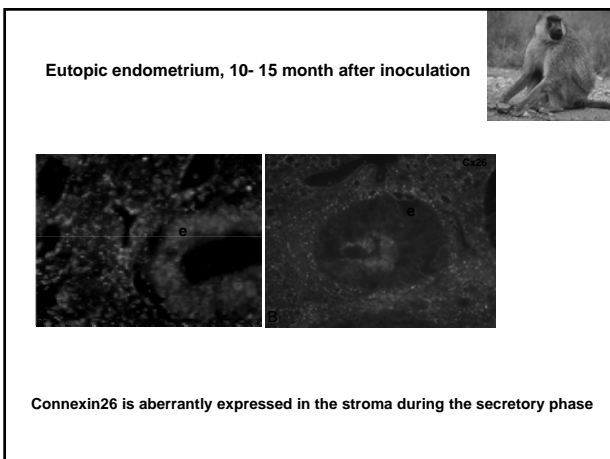
Connexin pattern in the menstrual cycle in baboon

Proliferative phase



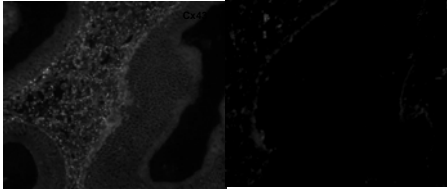




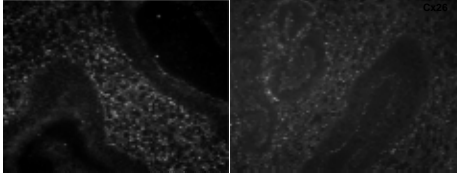


Does aberrant expression of Cx26 stay in pseudopregnancy with endometriosis?

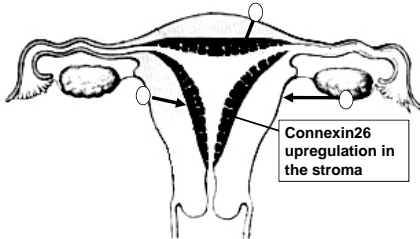
Pseudopregnancy (CG infusion on day 6-10 po)



Pseudopregnancy with endometriosis (10-15month after inoculation)



Cx26-deregulation in eutopic and pseudopregnant endometrium upon the presence of ectopic endometrium





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