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Biological Markers of Fertility

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SFOG

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<http://www.diva-portal.org/smash/get/diva2:756869/FULLTEXT01.pdf>



Factors Not Included in Screening

- Angiogenic
- Immunological
- Coagulation/fibrinolysis
- Genetic
- Endometrial receptivity
- Implantation defects



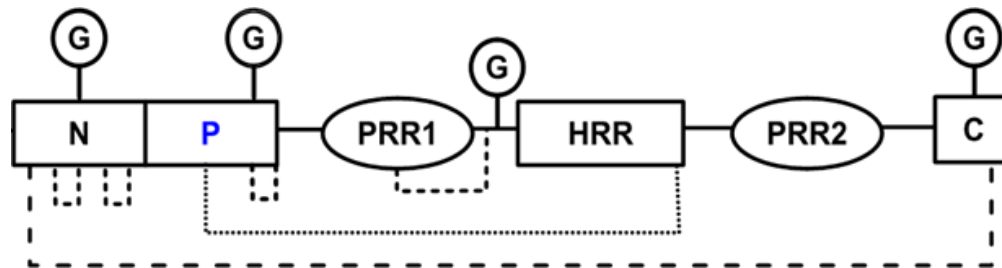
Polymorphisms Associated with IVF

- Hormones and Receptors
 - FSH, LH, Estrogen, Progesterone, AMH (Altmäe, 2011)
- Angiogenic
 - Vascular endothelial growth factor (VEGF)
 - Fibroblast growth factor (FGF) (Chaves, 2012; McFee, 2009)
- Immune System
 - Interleukin-1 receptor antagonist (Gremlich, 2008)
- Coagulation/Fibrinolysis
 - Thrombin-activatable fibrinolysis inhibitor (TAFI)
(Sticchi, 2012)



Histidine-Rich Glycoprotein (HRG)

- Abundant plasma protein
- Many ligands
 - Angiogenesis
 - Immune System
 - Coagulation/Fibrinolysis
 - Apoptosis



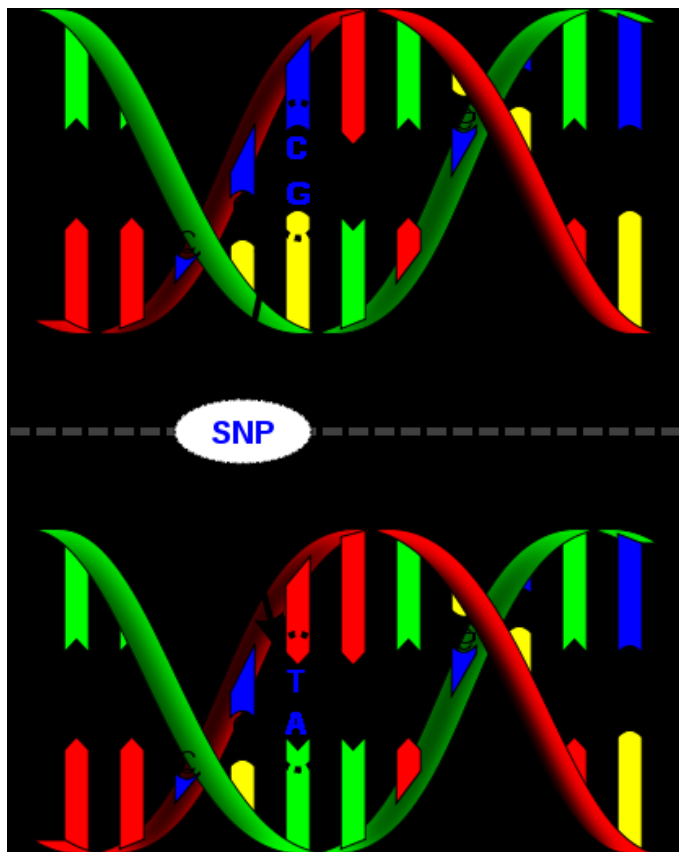


HRG C633T SNP/Isoform

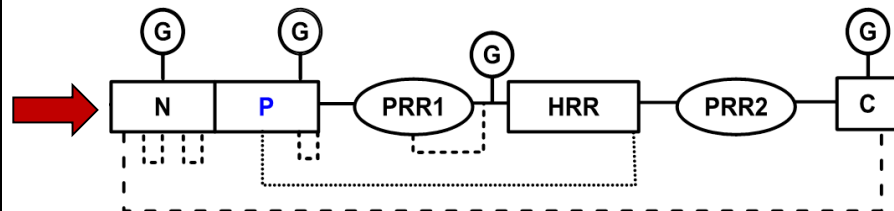
Gene
C = Cytosine



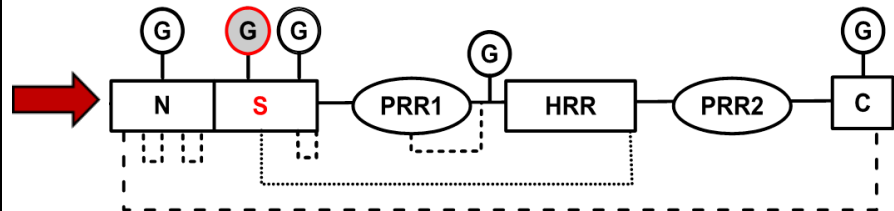
Protein
P = Proline



T = Thymine



----- 2 Isoforms -----



S = Serine



HRG in Reproduction

- **Estrogen lowers concentration**
(Hennis BC, et al, 1995)
- **50% of normal levels 3rd trimester**
(Haukkamaa M, et al, 1983)
- **Preeclampsia imbalance**
(Kårehed K, et al, 2010; Bolin M, et al, 2011)
- ***HRG* 633T SNP linked with recurrent miscarriage** (Lindgren K, et al, 2013)



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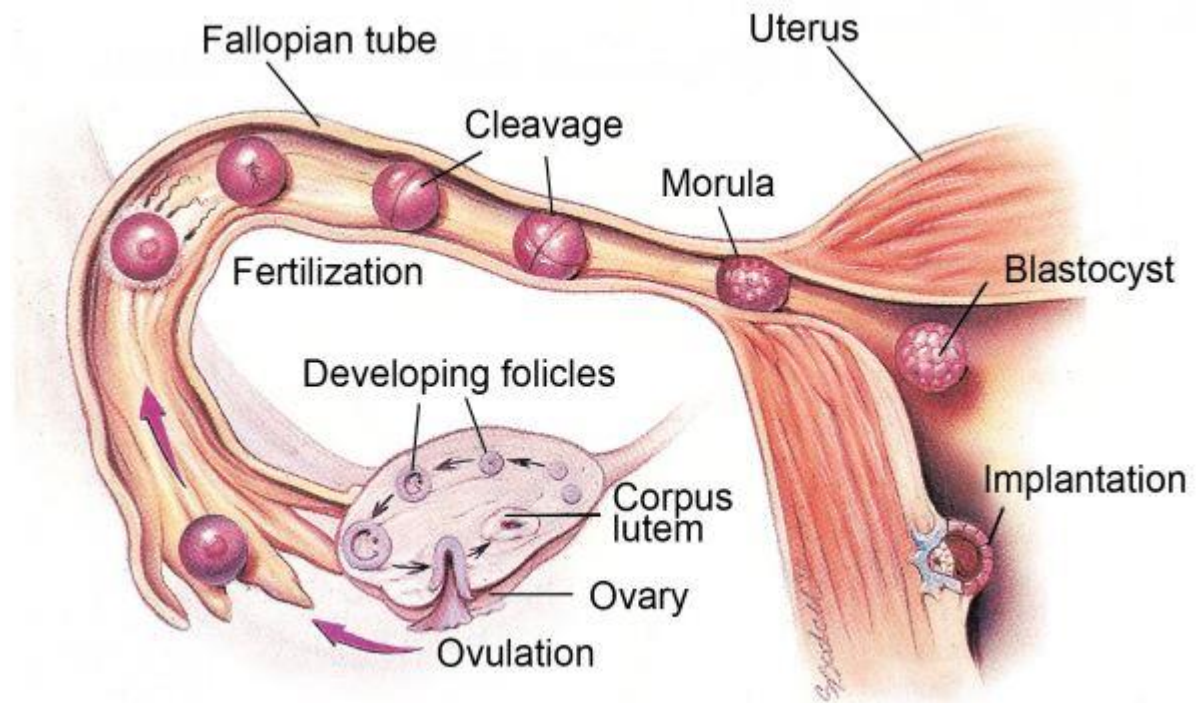
Papers I-III

Aim

To investigate the impact of HRG on
human female fertility

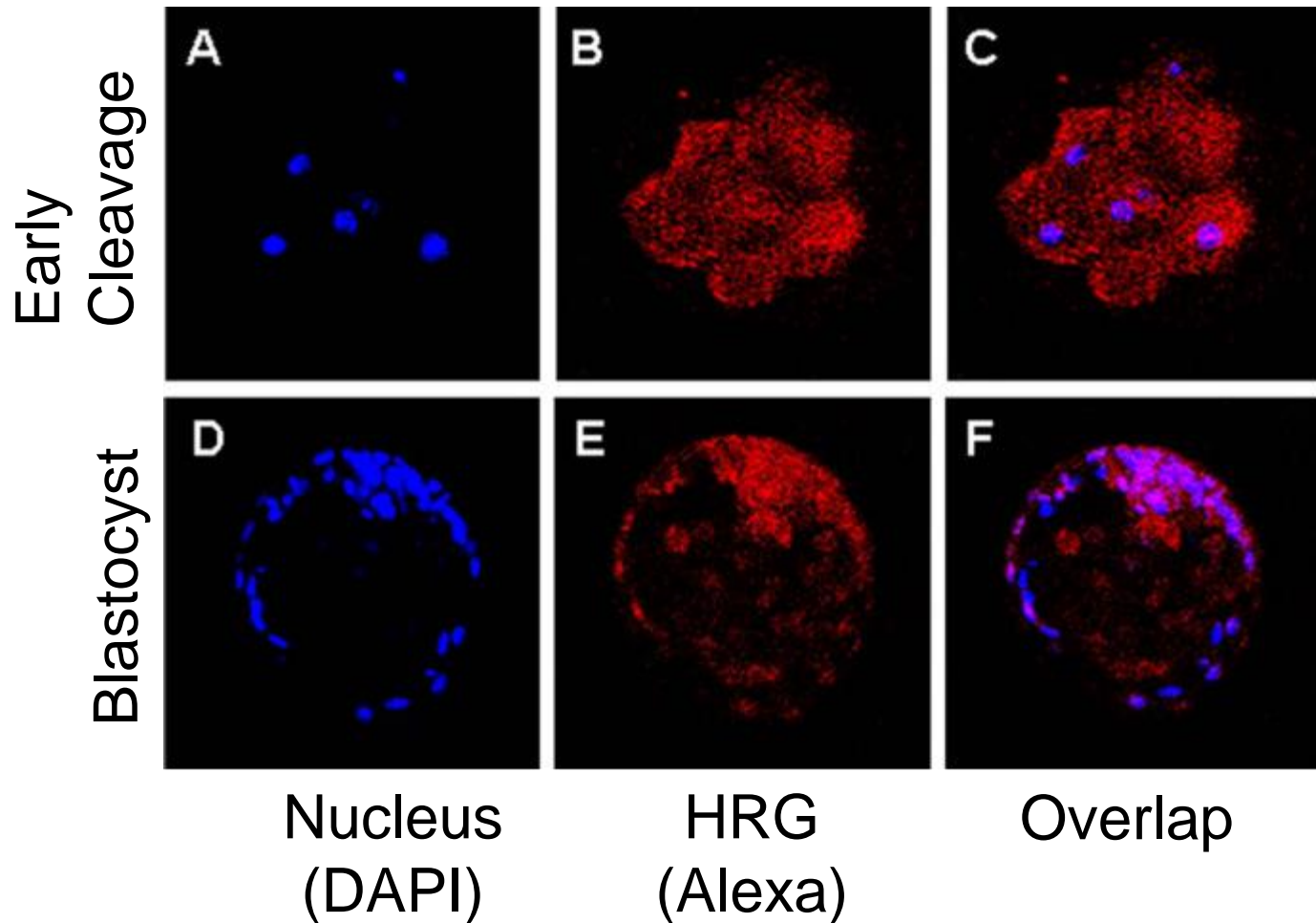


HRG Exists from Follicle to Implantation





Embryos Contain and Produce HRG





HRG Affects Pregnancy in IVF

HRG SNP	C/C	C/T	T/T
Total n (%)	32 (55.2)	20 (34.5)	6 (10.3)
Pregnant (%)	80.8	19.2	0

C/C = Homozygous major allele

C/T = Heterozygous

T/T = Homozygous minor allele



HRG Affects IVF Variables

HRG SNP	C/C	C/T	T/T
n (%)	39 (58.2)	23 (34.3)	5 (7.5)
FSH (IU/L)	1875	1650	3150
Oocytes	8	8	5
Fert. Oocytes	6	5	2
Fert. Rate (%)	64.3	64.3	33.3
No ET (%)	5.1	17.4	40.0

C/C = Homozygous major allele

C/T = Heterozygous

T/T = Homozygous minor allele



Src Homology 2 Domain-Containing Adapter Protein B (SHB)

- Intracellular signaling complexes
- Many ligands
 - Angiogenesis
 - Immune System
 - Apoptosis





SHB in Reproduction

- Oocyte development
 - pre- and postnatal
- Synchronization of meiosis
- Embryo development
- Birth defects/resorption of pups
- Stem cell differentiation
 - mesodermal and endodermal



Aim

To investigate the association between *SHB* polymorphisms and prognostic markers associated with pregnancy outcome for women undergoing IVF



SHB Affects IVF Variables

	SNP	1/1	1/2	2/2
FSH (IU/L)	rs13298451	1575	1750	1500
	rs7873102	1875	1687	1500
Fertilized	rs2025439	5.5	4.0	2.0
	rs13298451	5.0	4.0	1.0
Immature (%)	rs7873102	0.0	12.5	0.0
GQE (%)	rs13298451	25.0	33.3	8.3
ET d 2-3 (%) d 4-5	rs7873102	80.5	94.6	100.0
	rs7873102	19.5	5.4	0

1/1 = Homozygous major allele

1/2 = Heterozygous

2/2 = Homozygous minor allele



Conclusion

HRG and SHB may affect female fertility

Potential biomarkers of fertility



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Thank you

