Implantation

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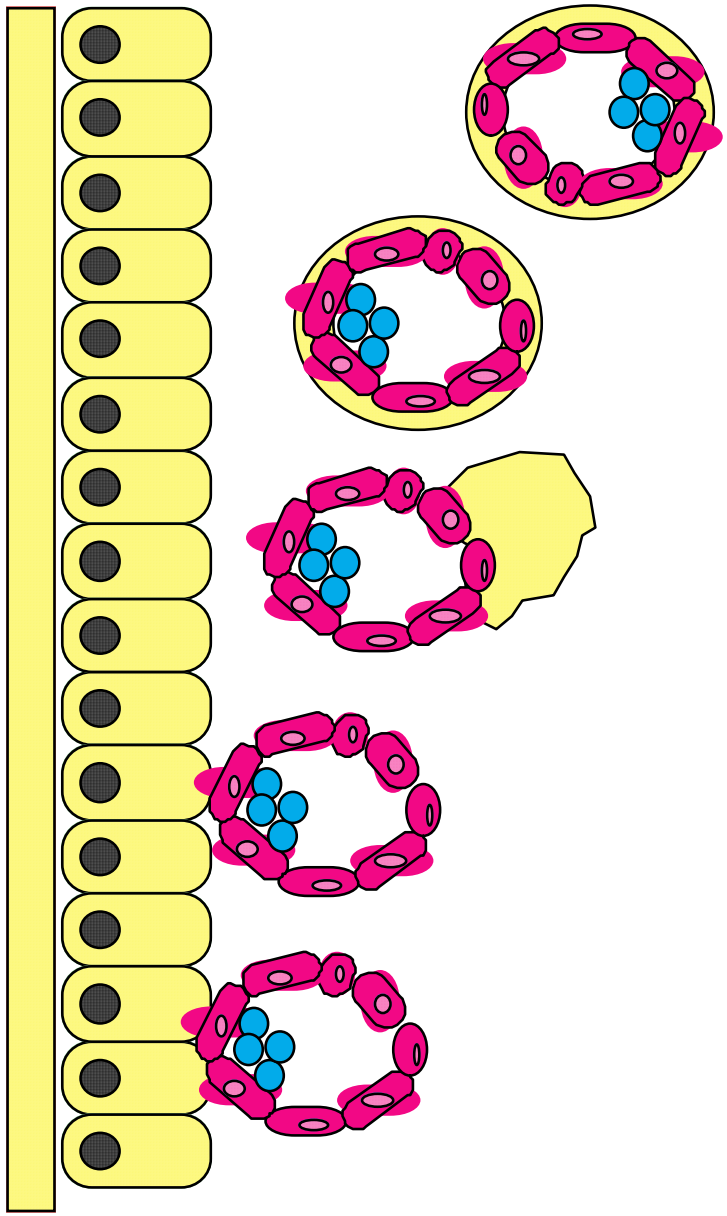
Geneva



1. TRANSPORT The blastocyst arrives in the uterus 132 to 144 hours after fetilization (Findlay 1984).

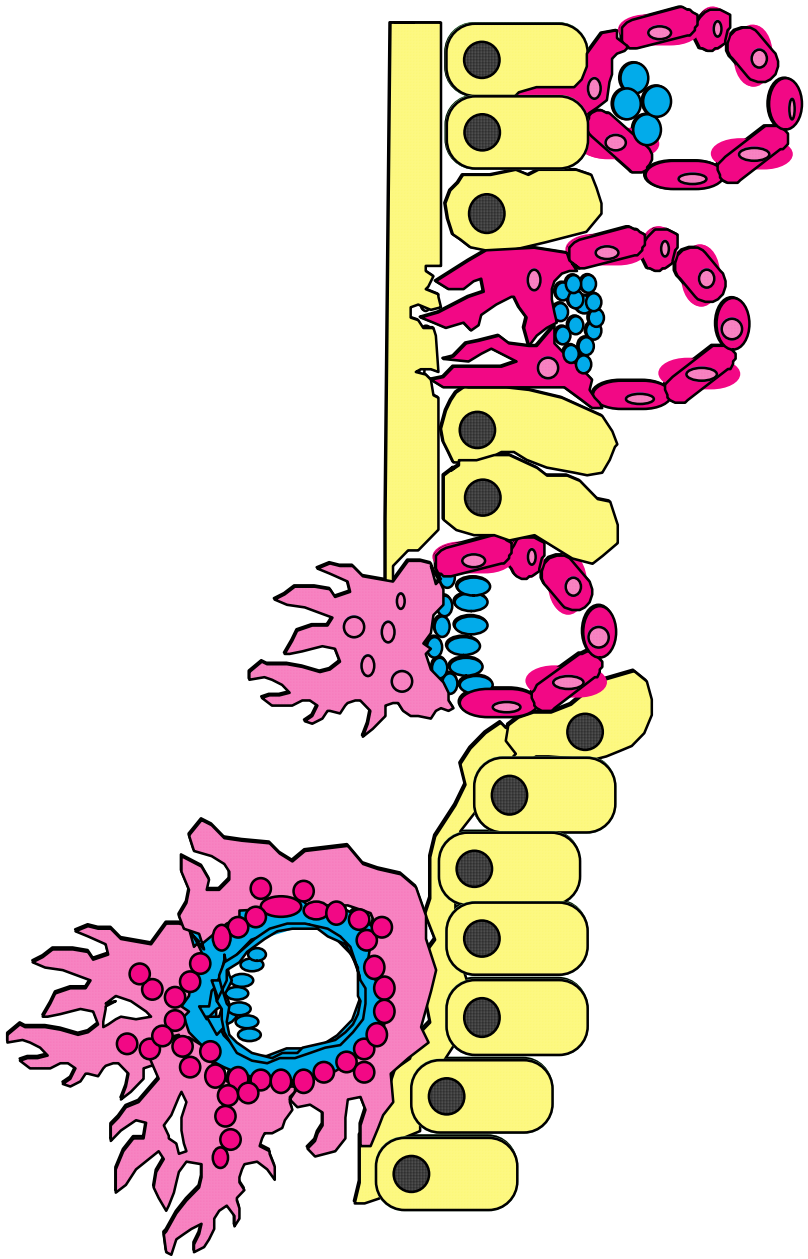
2. ORIENTATION The inner cell mass is oriented towards the endometrial epithelial lining.

3. HATCHING The zona pellucida dissolves possibly because of the secretion of proteases by trophectodermal cells.

4. APPOSITION The blastocyst is now in close contact with the endometrial lining but no connections have been established. The embryo can still be dislodged by washing.

5. ADHESION Connections of an unknown nature are established between the embryo and the endometrial epithelium. The embryo cannot be dislodged anymore.

Figure 1a



6. INVASION Thin folds of trophectodermal cells intrude inbetween the endometrial epithelial cells.

7. DIGESTION At the tips of the invadopodia, integrins (fig) anchor the trophoblast to the basement membrane. This binding triggers the secretion of proteases which digest the basement membrane.

8. SYNCYTIALISATION Some trophectodermal cells fuse to form syncytia. These syncytia proliferate and invade the endometrial extracellula matrix.

9. VILLOUS FORMATION The former trophectodermal cells, now called cytotrophoblastic cells migrate inbetween the syncytia followed by the fetal stoma. This will lead to the formation of the placental villi.

Figure 1b

PLACENTAL CELLS

Syncytiotrophoblast ← **Cytotrophoblast**

STB — **CTB**

- **Villous STB**
- **Extravillous STB**
- **Villous CTB**
- **Extavillous CTB**
  - **Intravascular**
  - **Chorionic plate**
  - **Fetal memranes**
  - **Septum**
  - **Cell columns (Anch. villi)**
  - **Cell columns (Cell islands)**

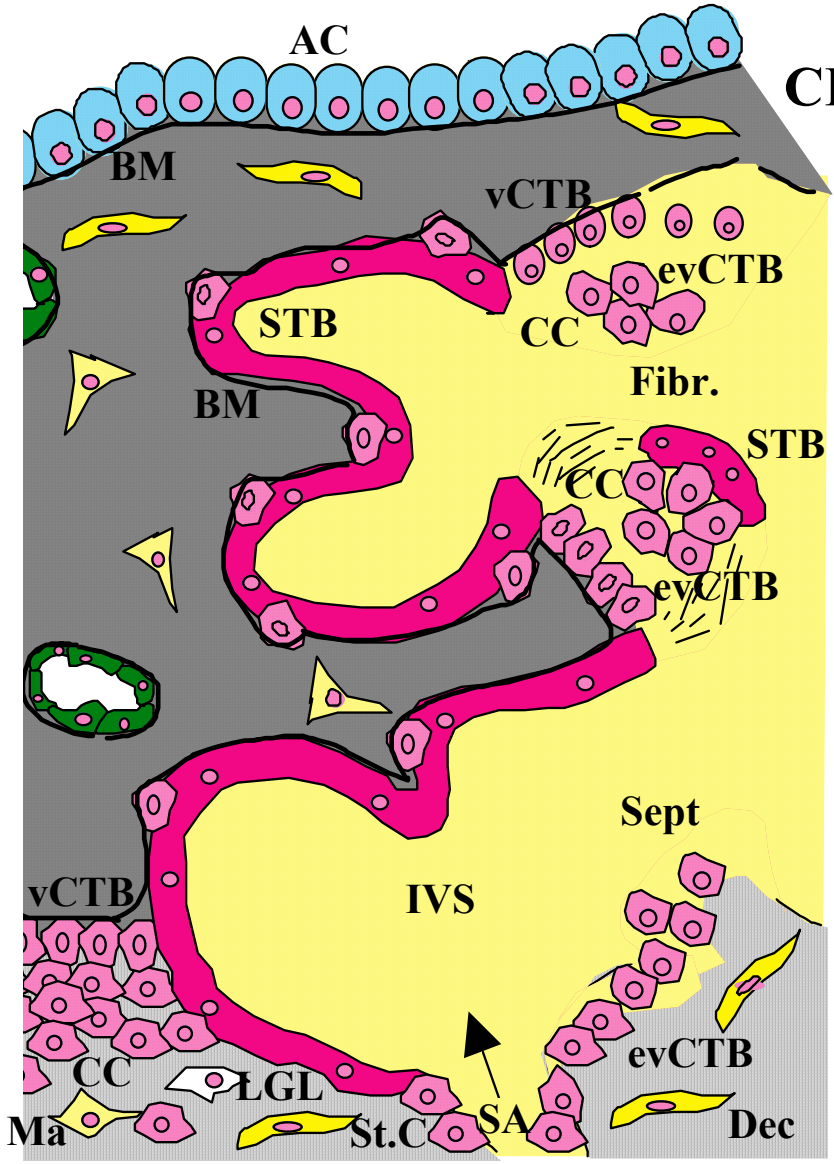


Figure 2

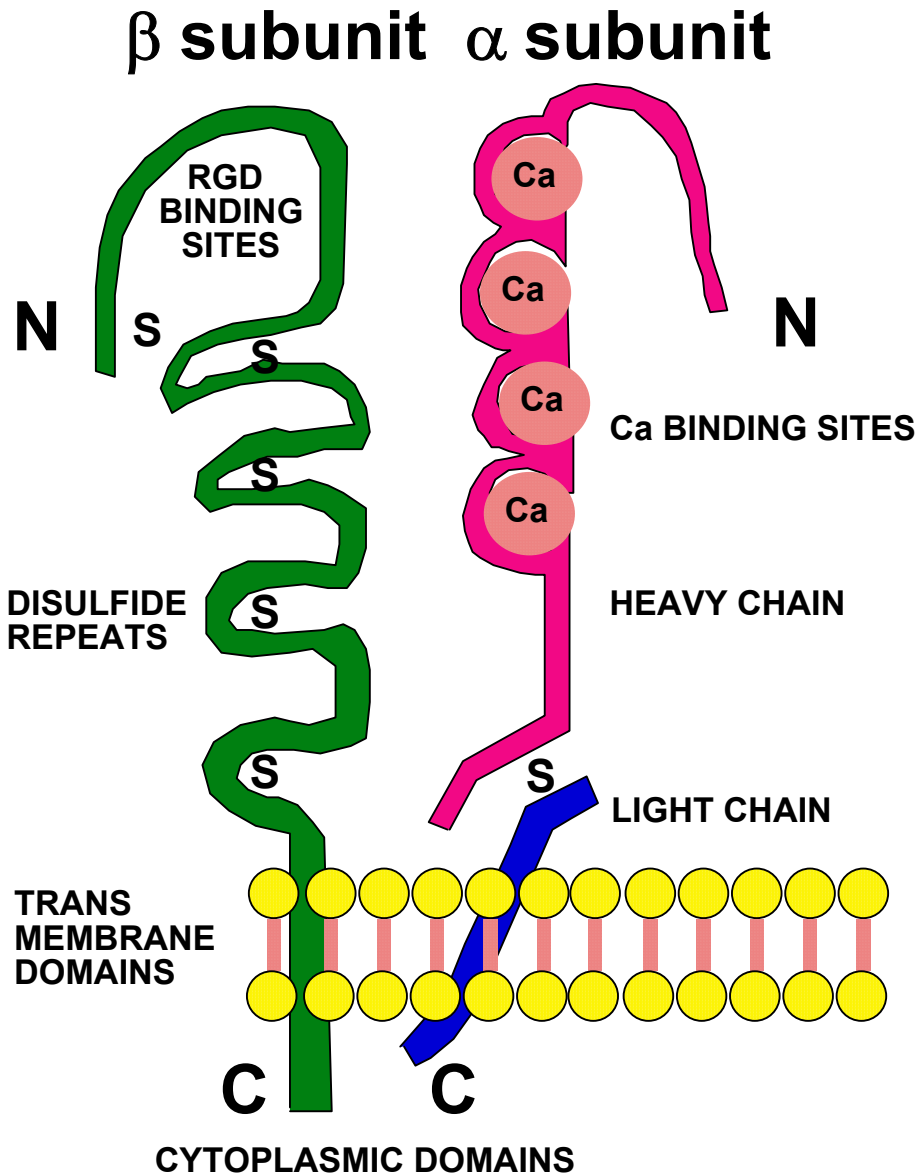

β subunit
α subunit
RGD
BINDING
SITES
N
S
S
S
S
S
DISULFIDE
REPEATS
Ca
Ca
Ca
Ca
N
Ca BINDING SITES
HEAVY CHAIN
S
S
LIGHT CHAIN
TRANS
MEMBRANE
DOMAINS
C
C
CYTOPLASMIC DOMAINS

Figure 3

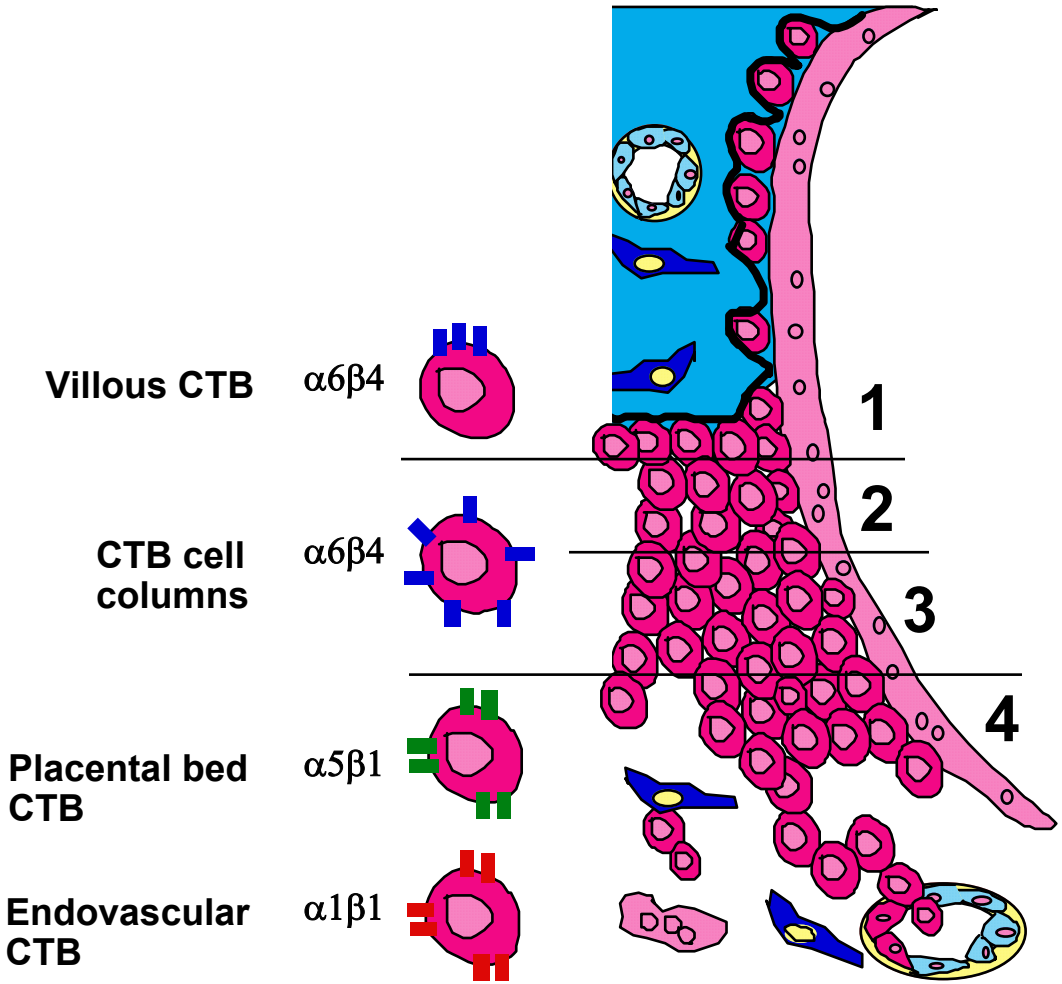

Villous CTB
α6β4
CTB cell columns
α6β4
Placental bed CTB
α5β1
Endovascular CTB
α1β1
1
2
3
4

Figure 4

	Other names	M.W.	# a.a.	Zinc at pos.	Substrates	Location of gene
MMP-1	Intersti.Collase	54007	469	218	Col I, II, III,VII, X	11q22-q23
	Fibrobl. Collase				MMP-5, Entactin	
MMP-2	Intersti.Collase	73882	660	403	Col IV, V, VII, X, Gelatin	16q13
	72kD gelatinase				Fibronectin, Elastin	
MMP-3	ST-1	53977	477	218	Col III, IV,IX, X, Gelatin, Laminin	11q23
	Transin-1				Fibronectin, Elastin, Casein	
MMP-7	PUMP-I	29677	267	214	Casein,Fibronectin, Gelatin	11q21-q22
	Matrilysin					
MMP-8	Neutophil Collase	53412	467	217	Col I, III	11q21-q22
	PMNL collase					
MMP-9	Gelatinase B	78427	707	401	Col IV, V, Gelatin	20q11.2-q13.1
	92 kD Gelatinase					
MMP-10	ST-2	54151	476	217	Col II, IV, V, Fibronectin, Gelatin	11q22.3-q23
	Transin-2					
MMP-11	ST-3	54595	488	215	Col IV	22q11.2
MMP-13	Collagenase-3	53819	471	222	Col I	11q22.3
MMP-14	MT1-MMP	65883	582	243	MMP-2	14 q11-q12
	MMP-X1					
MMP-15	MT2-MMP	75807	669	259	MMP-2	
MMP-16	MT3-MMP	69158	604	246	MMP-2	
	MMP-X2					

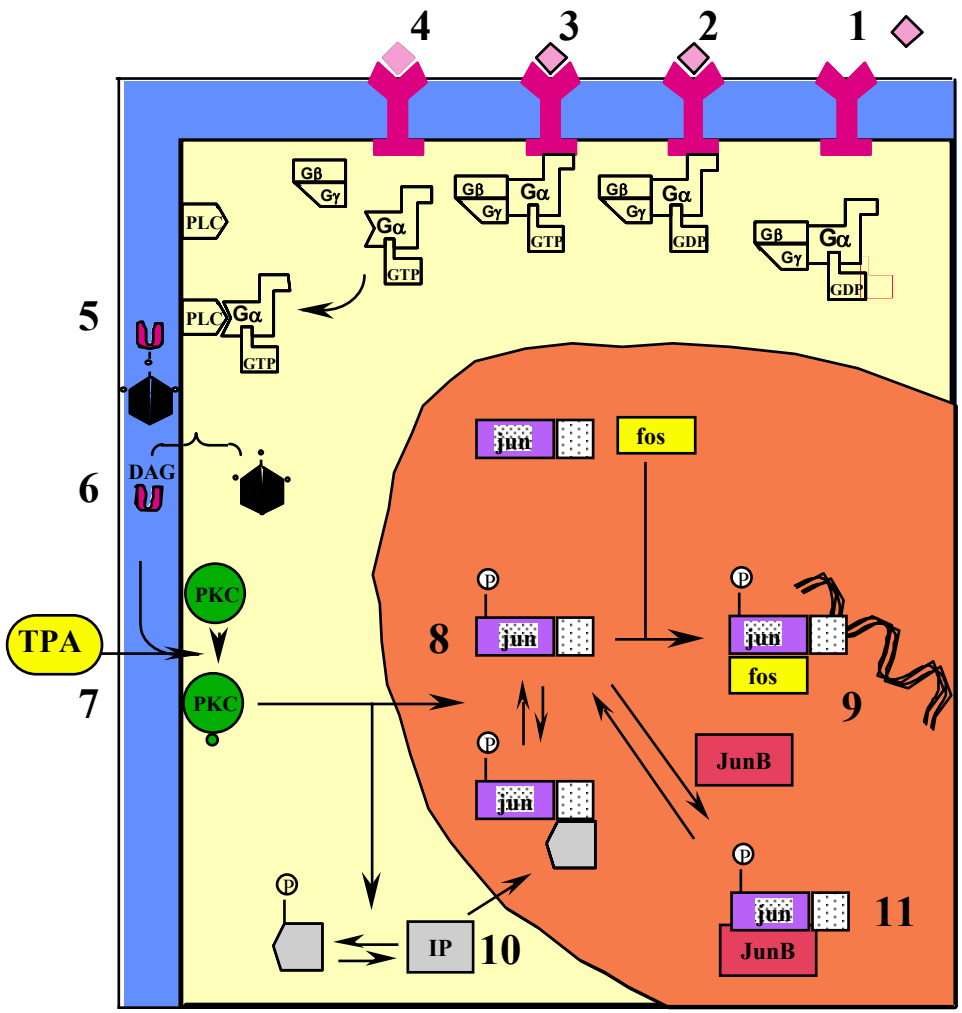
Figure 5

THE PROMOTER REGION OF THE HUMAN MMP-9 GENE

CIS - Regulatory Elements

NFkB binds p50-p65 complexes (products of REL oncogene family).
SP-1 binds the transcription factor SP-1.
ets binds ETS-1 or ETS-2 proteins (products of c-ets oncogene).
TRE TPA responsive element, binds Jun and Fos complexes the products of c-jun and c-fos oncogenes.
TIE TGF beta inhibitory elements binds TGF beta.
NIP binds NIP protein.
RCE Retinoblastoma control element binds $p105^{RB1}$ the product of RB1 oncogene.
TATA binds an octameric complex of transcription factors.

Figure 6



1. Membrane receptors are coupled to the G protein complex (ras oncogene products).

2. Upon binding of the ligand to the receptor, the G protein complex is activated.

3. GTP binds to protein G γ.

4. The G protein complex dissociates.

5. The Gγ protein activates phospholipase C (PLC).

6. Active PLC cleaves its substrate into inositol tri phosphate(IP_3) and diacyl glycerol (DAG).

7. DAG activates protein kinase C (PKC). This enzyme can be directly activated by TPA.

8. Active PKC phosphorylates Jun in its trans-activation domain (N terminus).

9. Phosphorylated jun binds Fos, this AP-1 complex binds a specific DNA sequence known as TRE.

10. Active PKC phosphorylates also an inhibitory protein (IP) which cannot inhibit anymore the binding of Jun to the DNA.

11. Jun can also bind Jun B (another oncogene product from the same gene family) and this complex is unable to bind to the DNA.

Figure 7