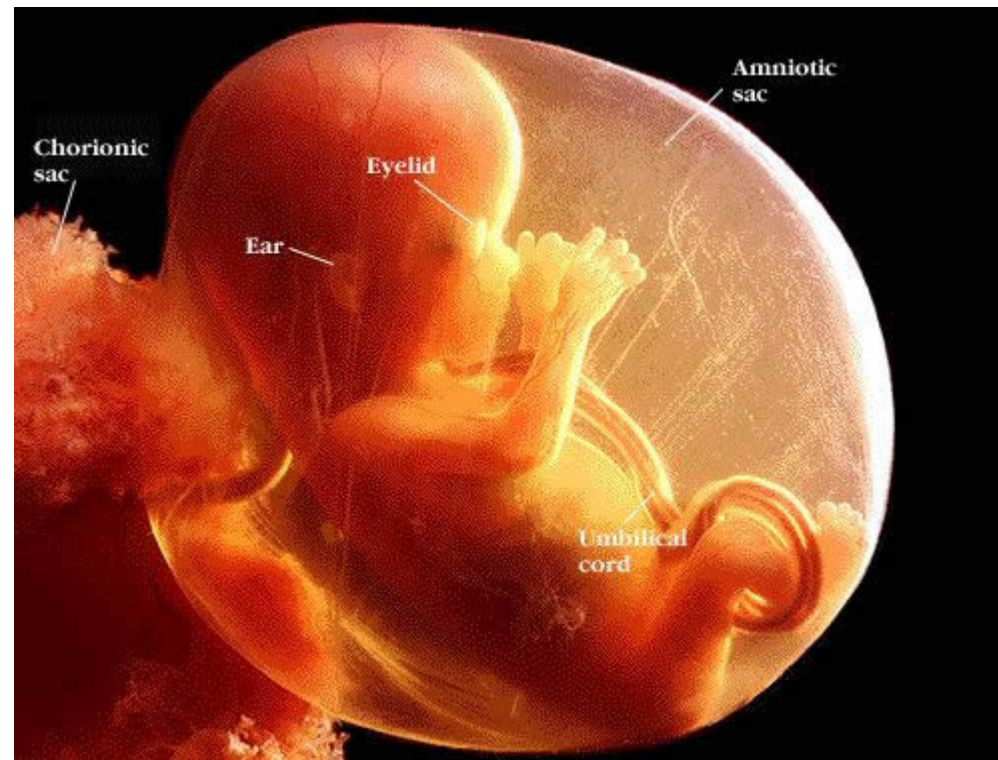


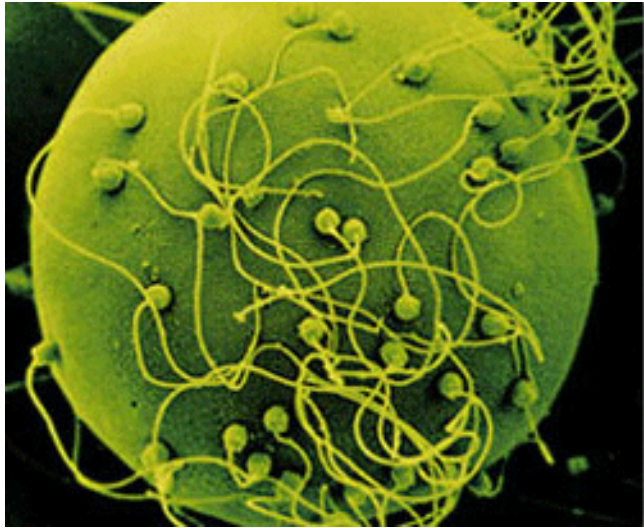
Modul k8

Immunisering i svangerskabet

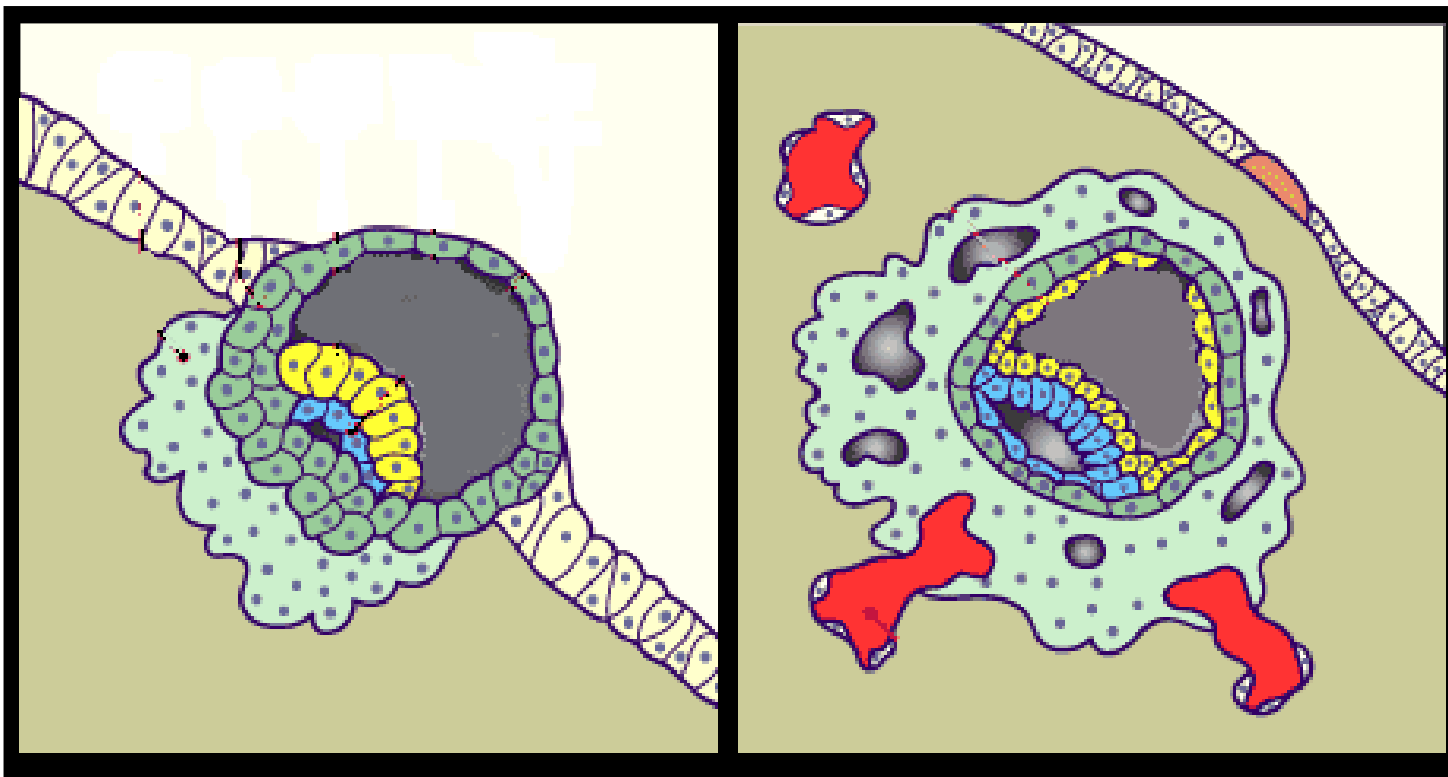
Torben Barington, KIA

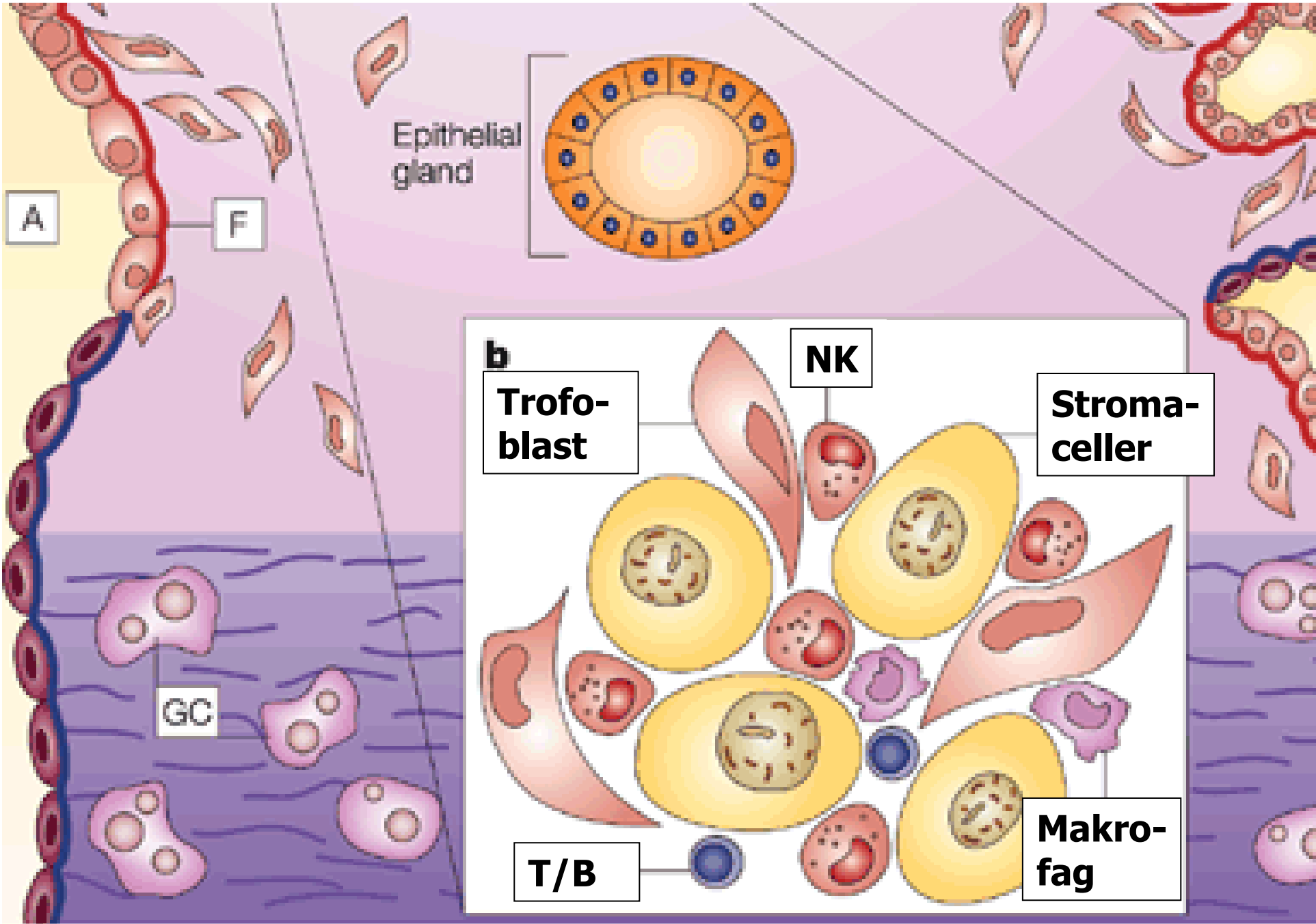


Fosteret er et allotransplantat!



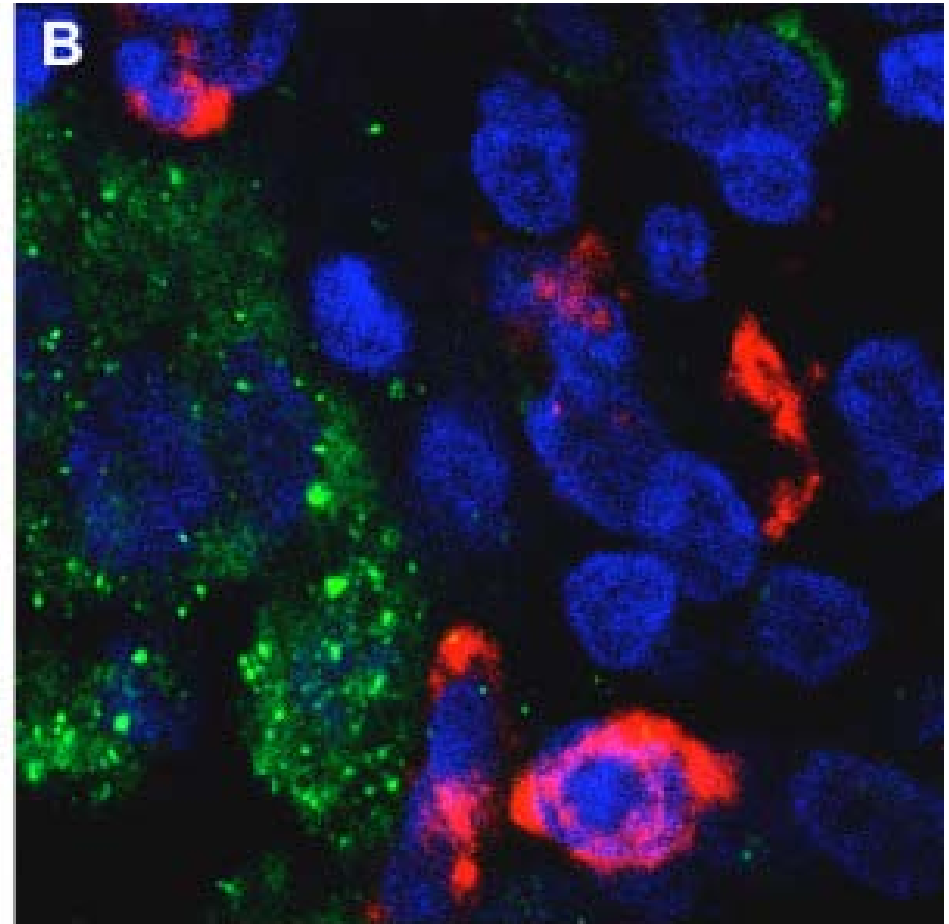
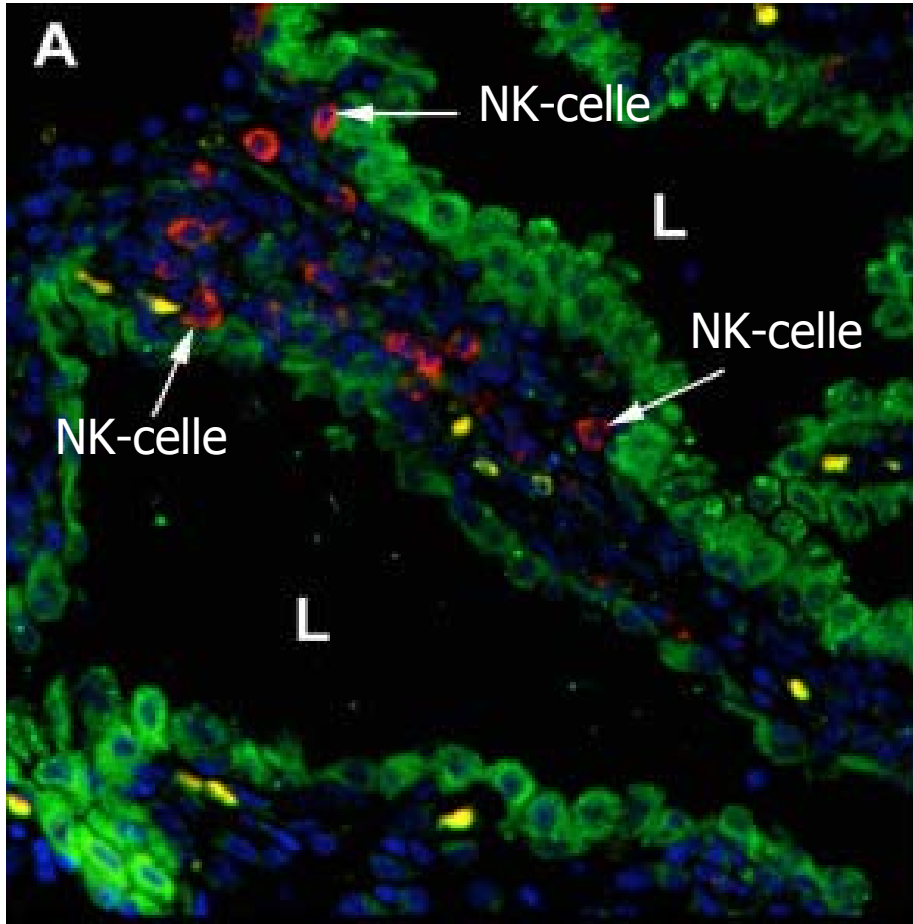
Fosteret som allotransplantat





Leukocytter i decidua

NK-celler		70 %
Makrofager	knap	30 %
T-lymfocytter	få	%
B-lymfocytter		0 %



Decidua, 12. uge. L: lumen i gl. epitel

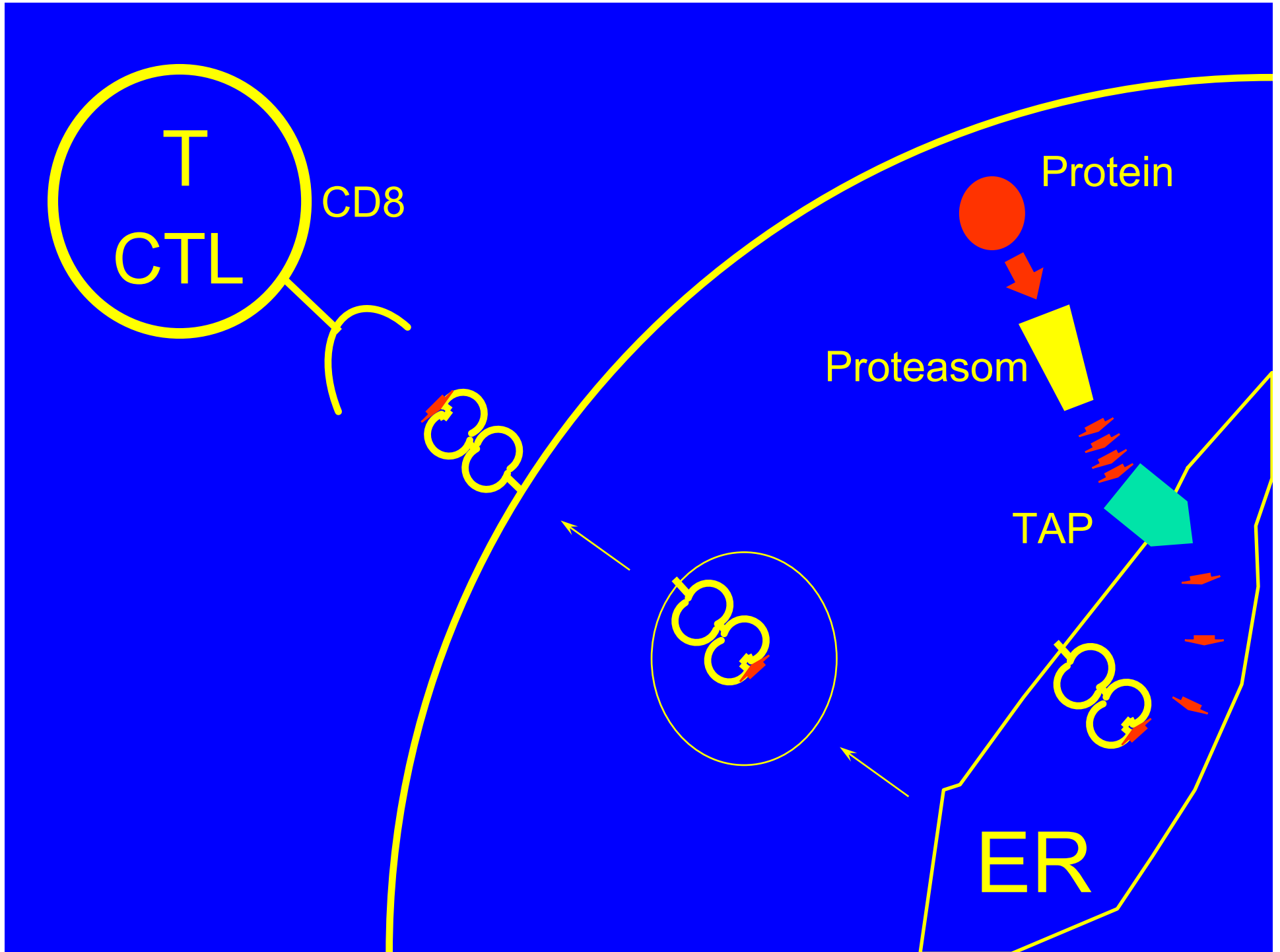
(CD56; tocopherol transfer protein; DAPI)

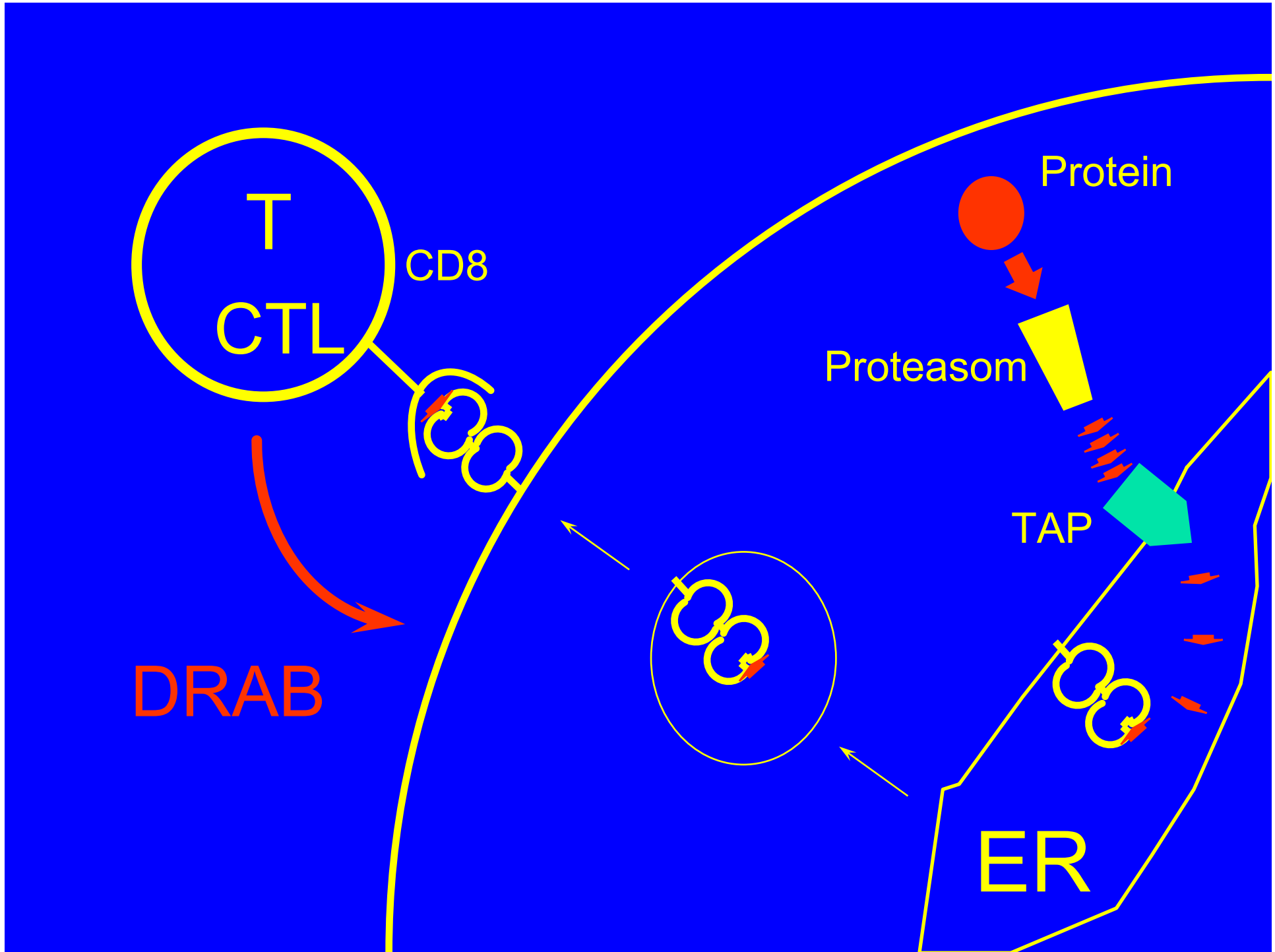
Villøs trofoblast

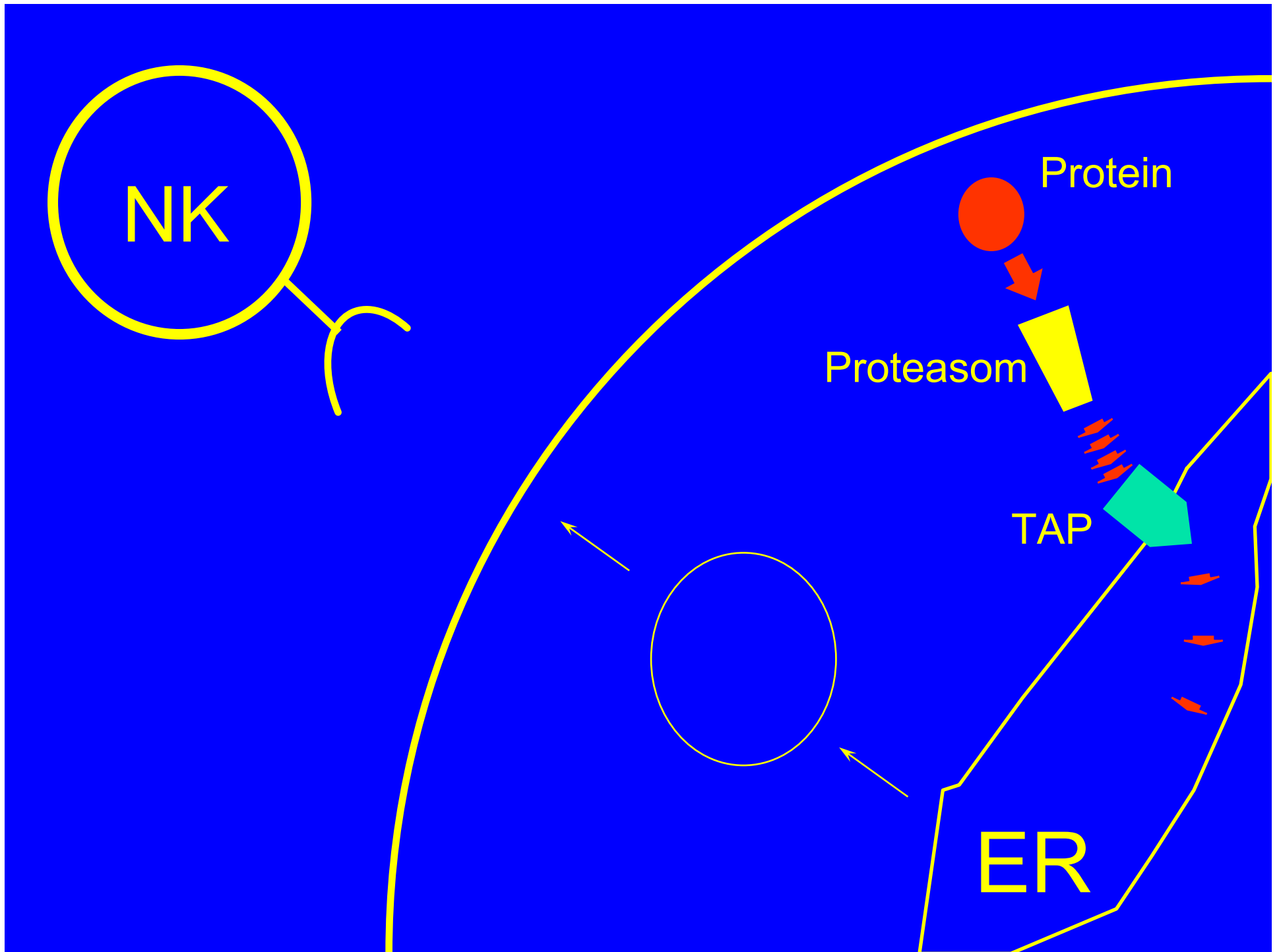
1. Mangler HLA-klasse I
2. Mangler HLA-klasse II

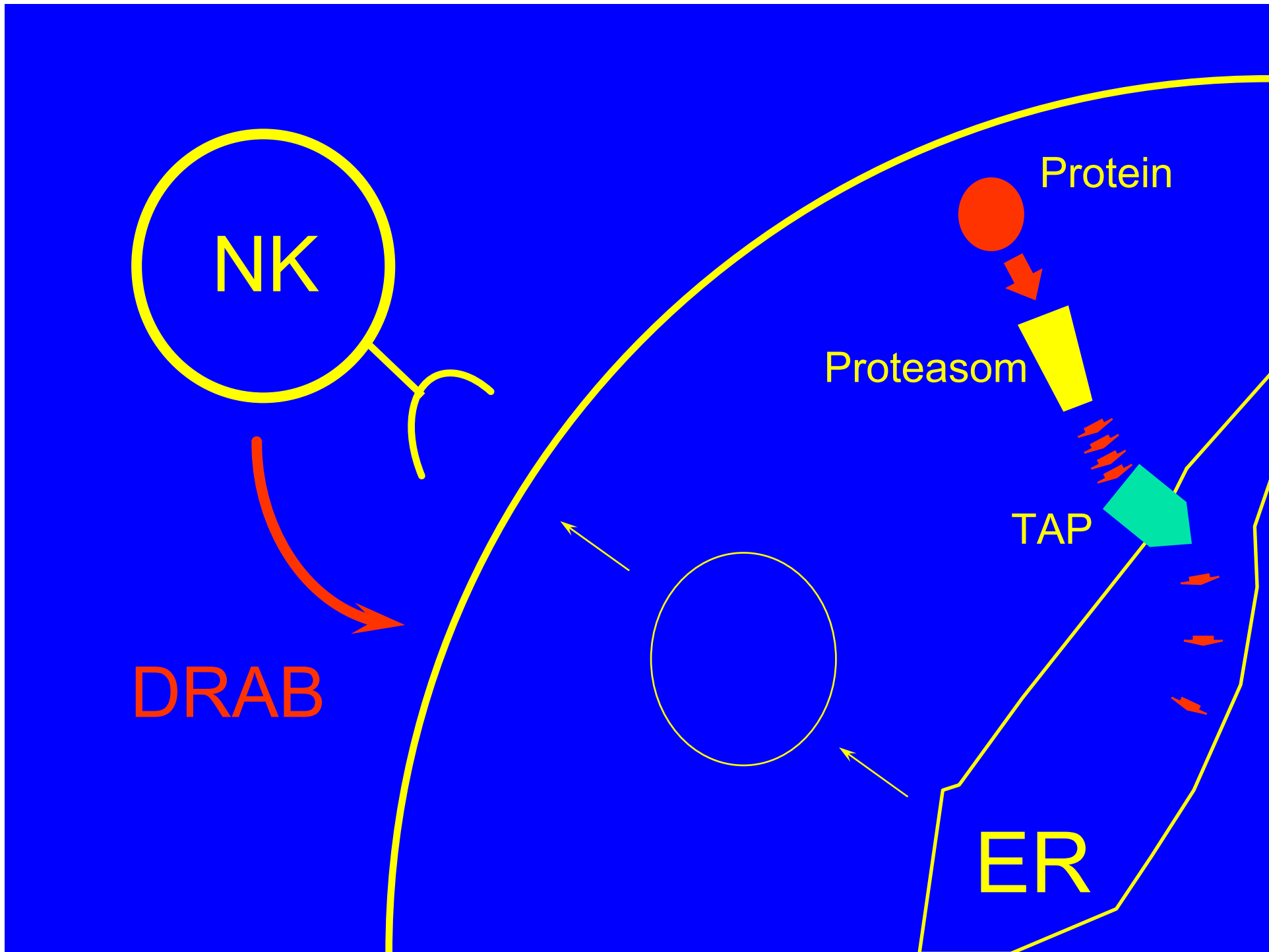
Ekstravilløs trofoblast

1. Mangler HLA-A og -B, men ikke HLA-C
2. Mangler HLA-klasse II
3. Udtrykker HLA-E og -G









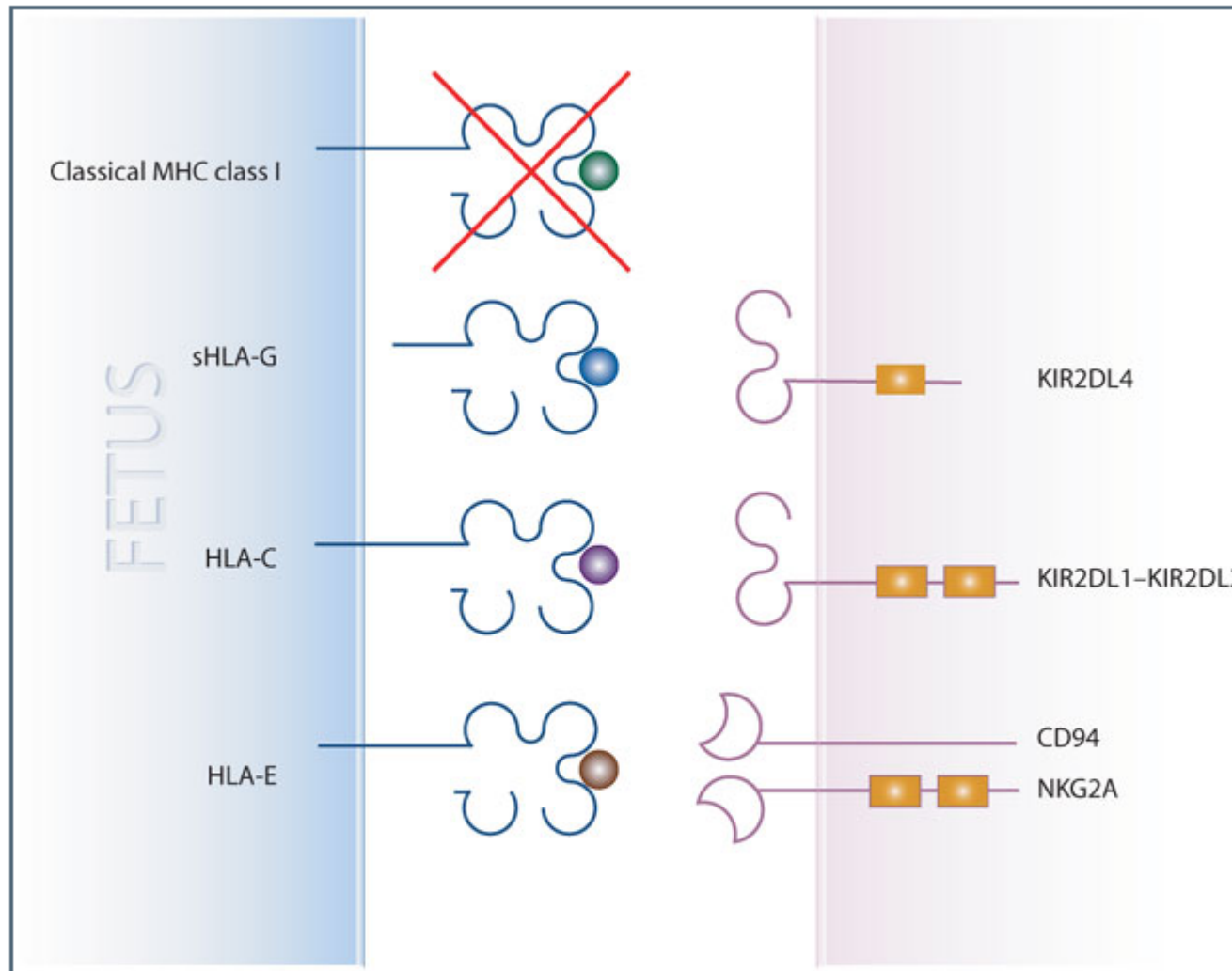
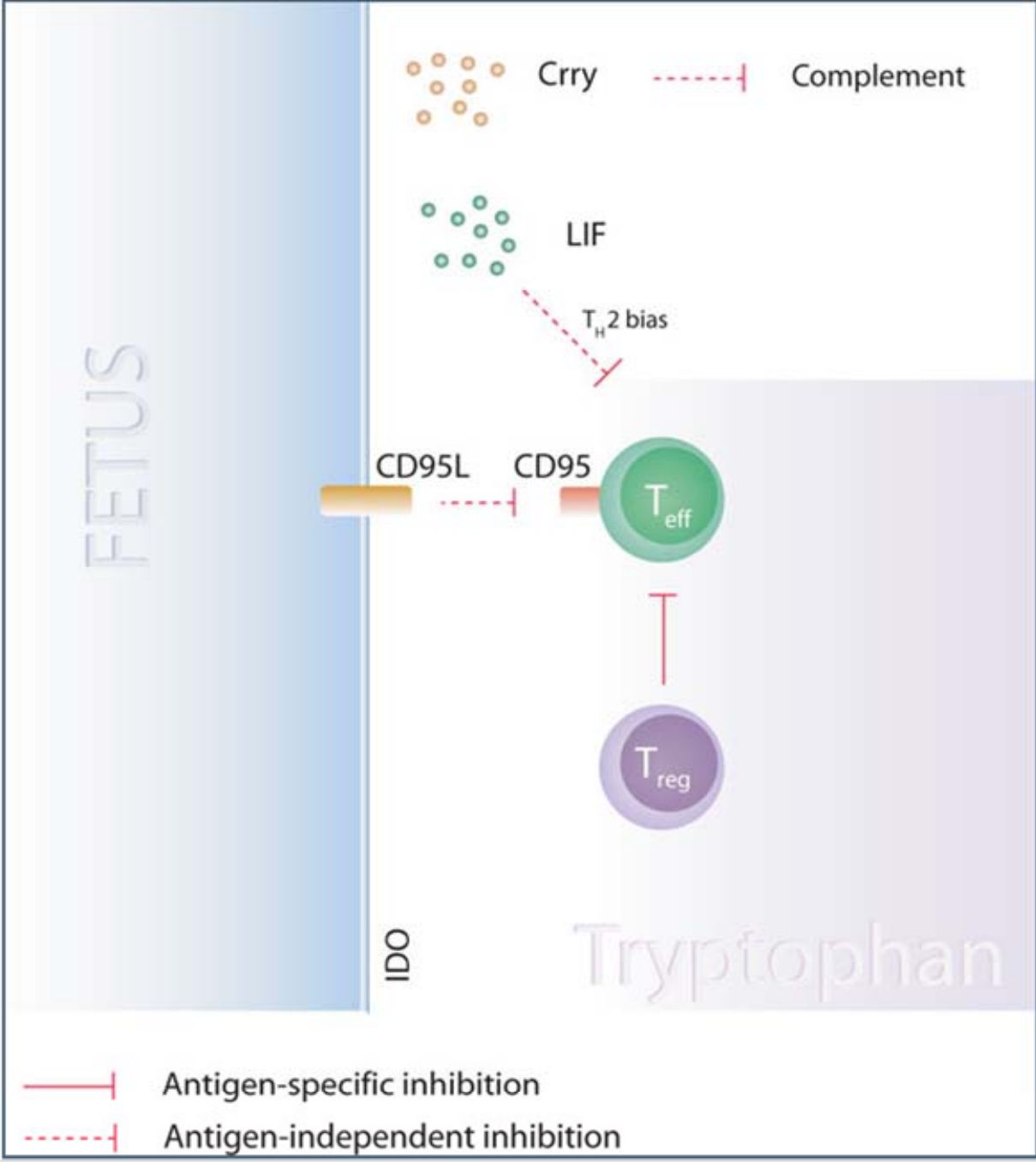
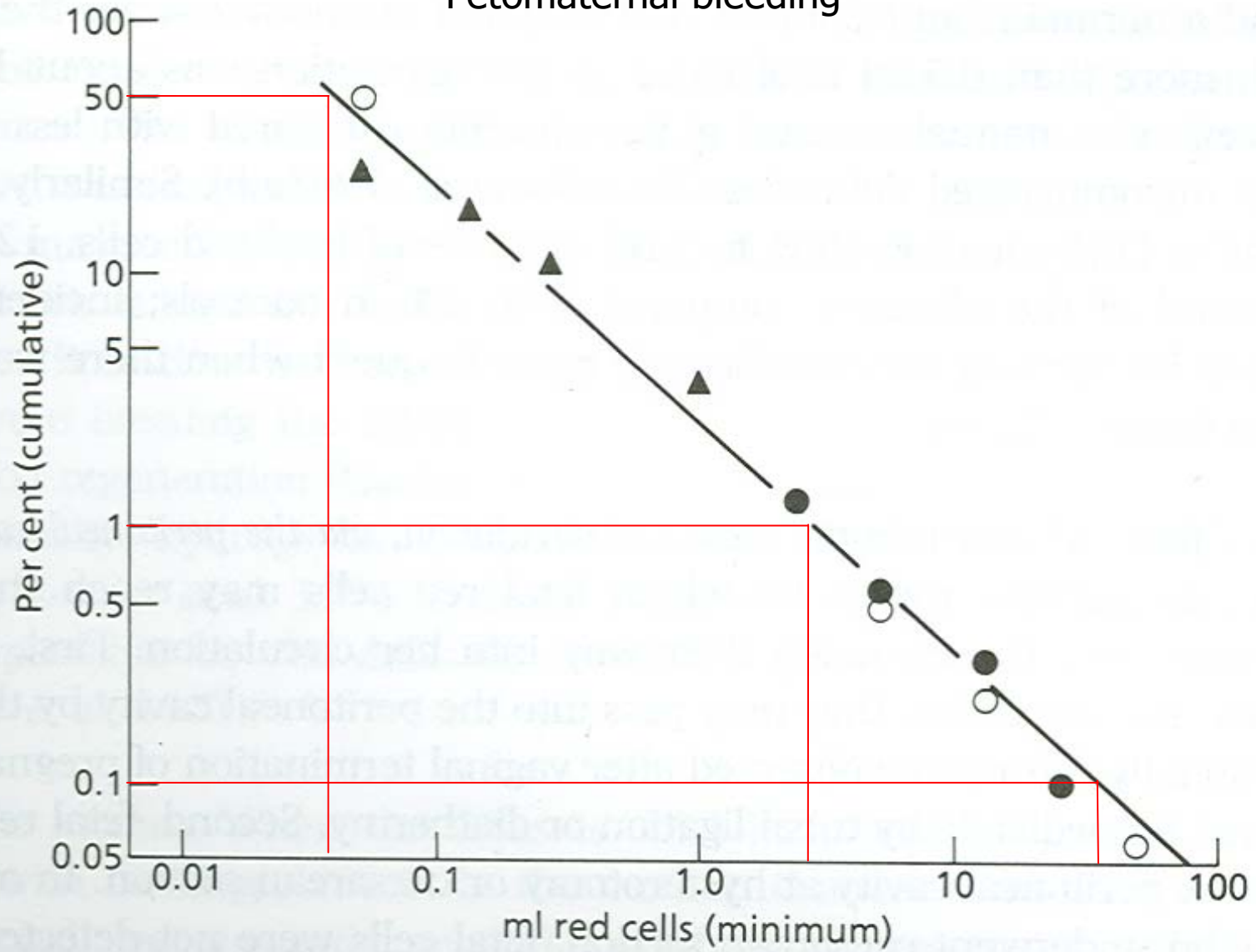


Figure 2. Some immune receptors proposed to regulate human maternal-fetal interaction.

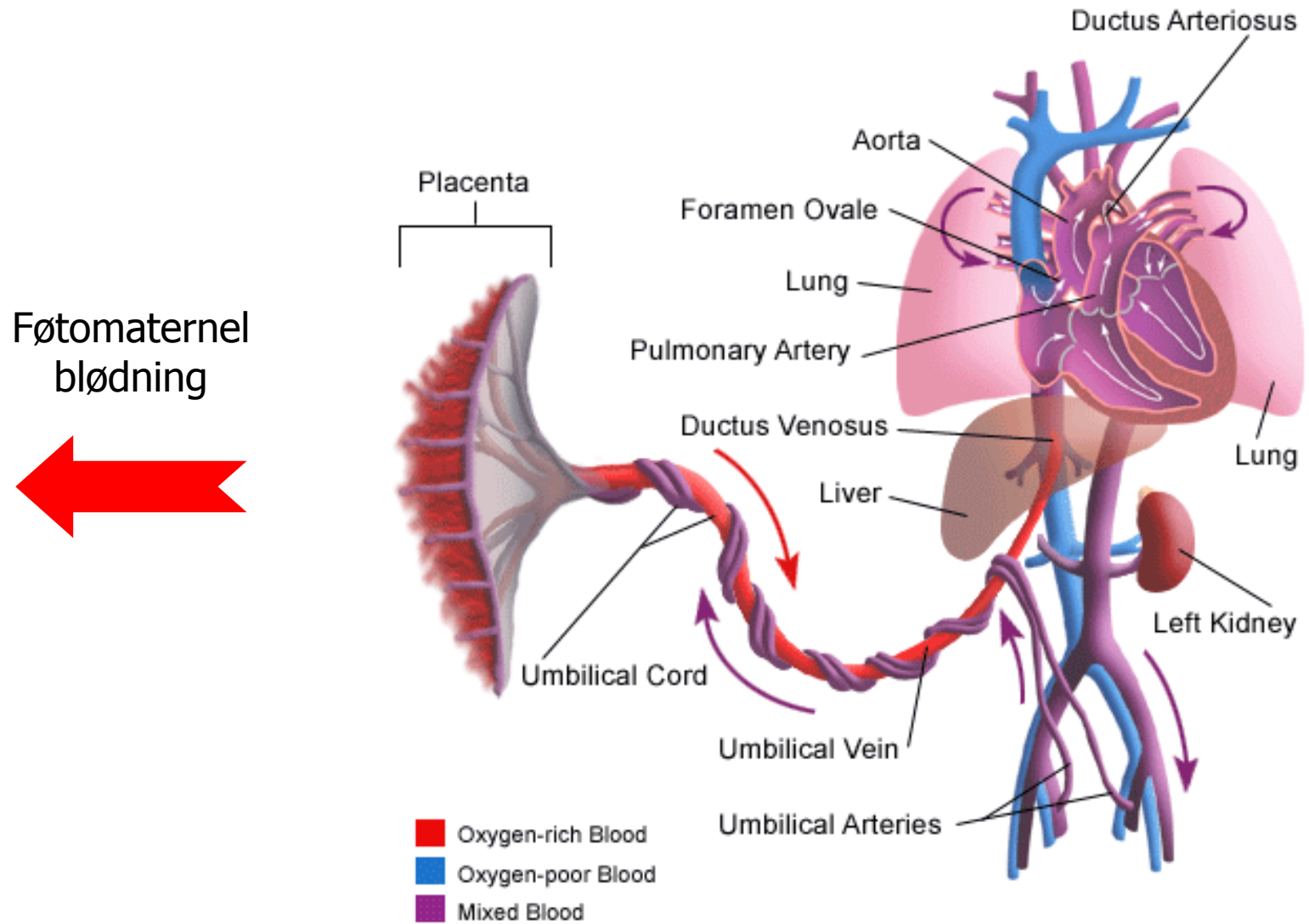
Classical MHC class I molecules are not expressed on trophoblasts. Nonclassical HLA-C and soluble HLA-G (sHLA-G) may interact with KIR2DL1-KIR2DL3 and KIR2DL4 receptors, respectively, to block NK cell recognition and to regulate vascularization.



Fetomaternal bleeding



Fetal Circulation



Immunisering

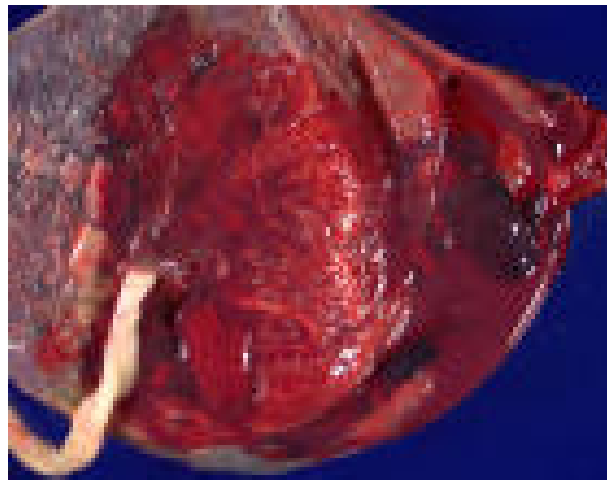
Mod erythrocytter,
leukocytter og
trombocytter

- Graviditet
- Blodtransfusion
- Transplantation



Immunisering i forbindelse med graviditet

- kræver blødning fra foster til moder
 - I forbindelse med fødsel
 - I forbindelse med indgreb
 - Spontant



Erythroblastosis fœtalis

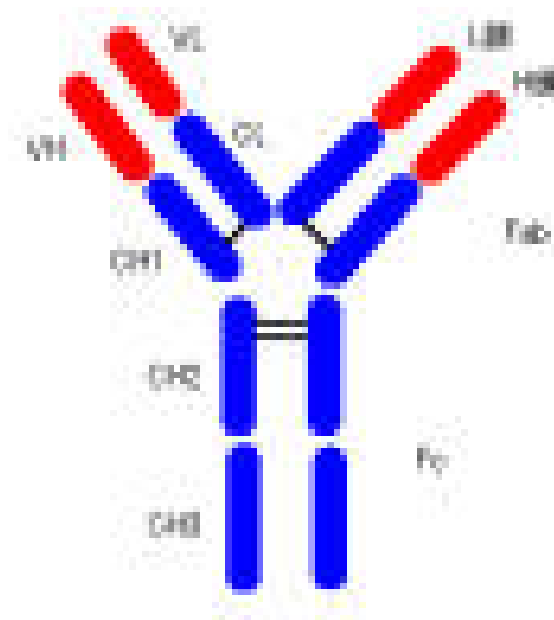
Transplacentær passage af erythrocytter

Hos

- 75% ses fœtale erythrocytter i maternelt blod i graviditeten eller ved fødsel
- 3% har 0,45 ml i 1. trimester
- 45% har 25 ml i 3. trimester
- a. spontaneus: < 1 % har < 0,17 ml
- a. provocatus: 20 - 25% har signifikant volumen

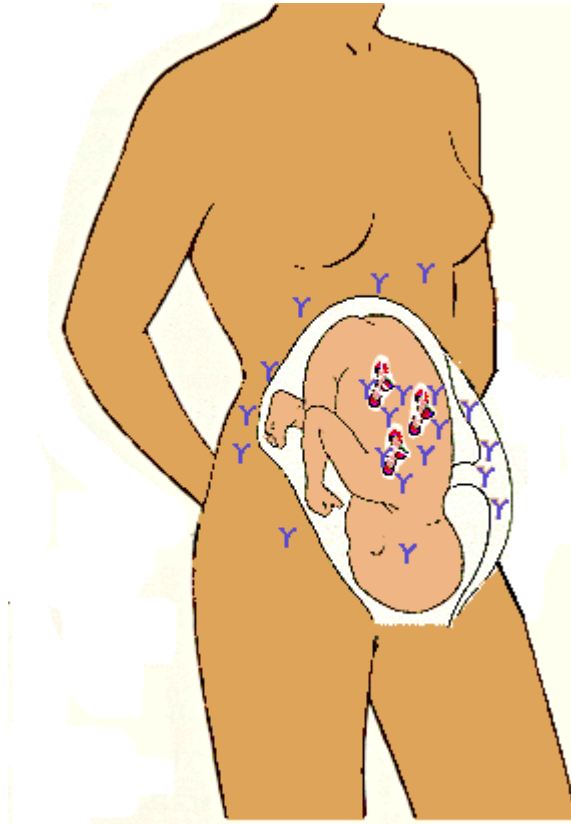
Immunisering

- Alloantistoffer rettet mod
 - Røde blodlegemer
 - Hvide blodlegemer
 - Blodplader
- Autoantistoffer rettet mod
 - Blodplader
 - Neuromusk. endeplade

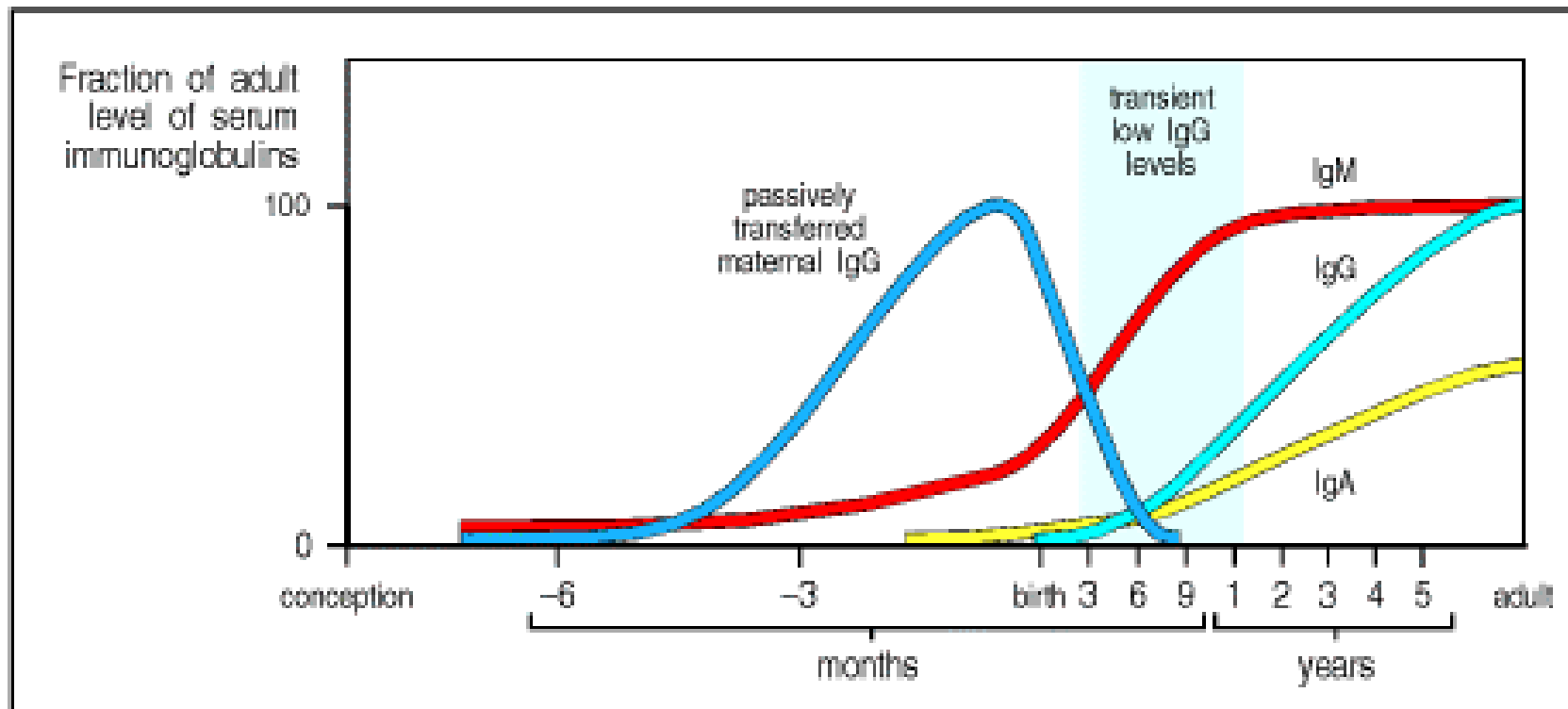


Transport af maternelle antistoffer

- IgG antistoffer transporteres aktivt over placentabarrieren fra moderens kredsløb til barnets
- Antistofferne indgår som en vigtig del af barnets immunforsvar i månederne efter fødslen



Transplacentært IgG beskytter det nyfødte barn



Erythroblastose

- Morens antistoffer af IgG klassen rettet mod antigener på erythrocytter kan passere placenta og optræde i barnets cirkulation
- Antistofferne kan binde sig til erythrocytterne og ødelægge disse

Hvilke antistoffer?

- Meget stor risiko: anti-D
- Stor risiko: anti-c, anti-e, anti-C, anti-e, anti-K
- Middels risiko: anti-Fy^a, anti-Fy^b, anti-Jk^a, anti-Jk^b, anti-k
- Lav risiko: anti-A, anti-B, anti-M
- Ingen risiko: anti-Le^a, anti-Le^b, anti-N

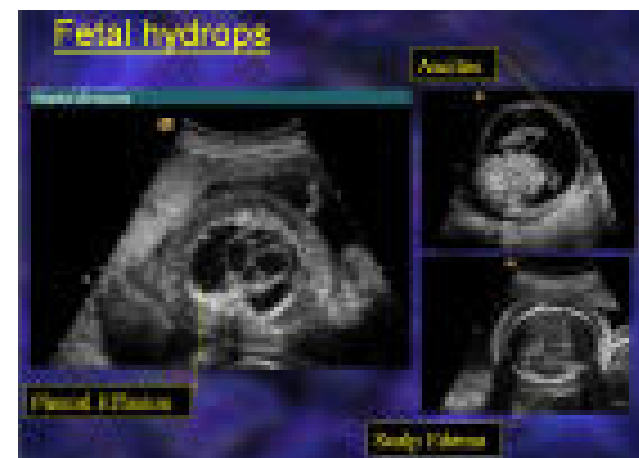
Hvilke kombinationer?

- Hyppigst RhD negativ kvinde, RhD positiv mand og RhD positivt foster
- "Rhesusbørn"

- (Generelt: Ag negativ kvinde, Ag positiv mand og Ag positivt foster)

Erythroblastose: symptomer

- Anæmi
- Lever og miltforstørrelse
- Ødemer ("hydrops")
- Hjerneskader (iltmangel, kernikterus)
- Ikterus

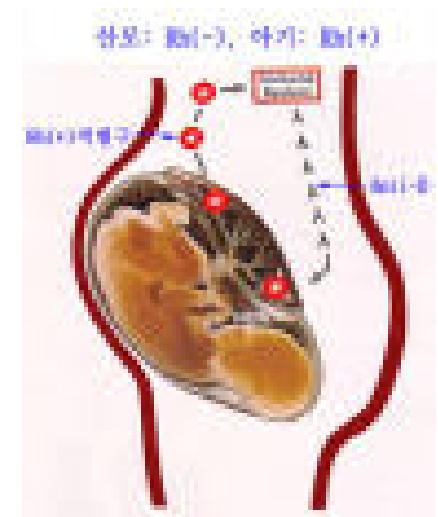


Erythroblastose: profylakse

- 1. graviditetsundersøgelse
 - RhD typebestemmelse
 - Screening for irregulære antistoffer
- RhD negative
 - Screening gentages i 35. uge
- Alle med irregulære antistoffer, der kan medføre erythroblastose
 - Følges på obstetriske afdelinger
 - Henvisning til fødsel RH, OUH, Århus, Aalborg

Erythroblastose: profylakse

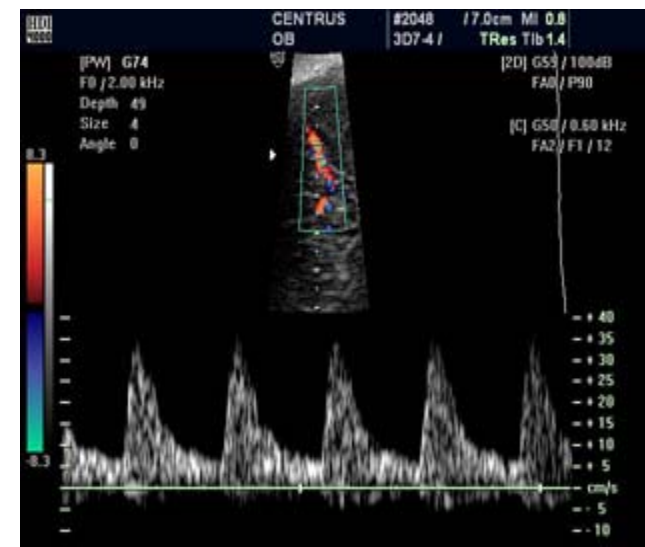
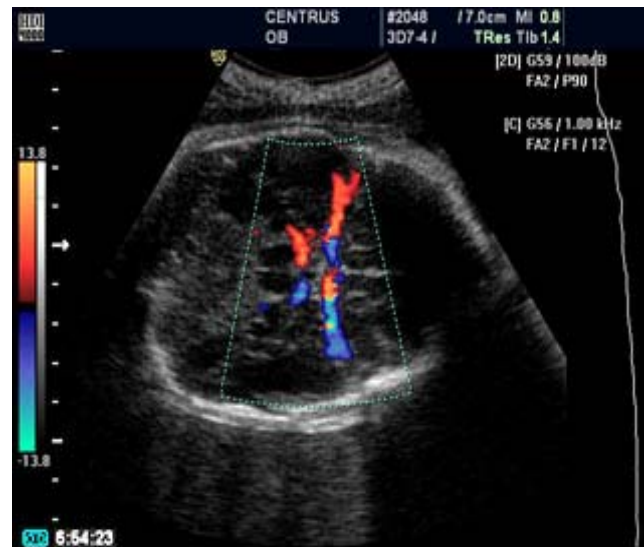
- Indgift af 300 µg anti-D til RhD neg kvinder ved
 - Fødsel af RhD pos barn
 - Indgreb i graviditeten (vending, fostervandsprøve etc.)
 - Spontan eller provokeret abort



Erythroblastosis fœtalis

Klinisk diagnose

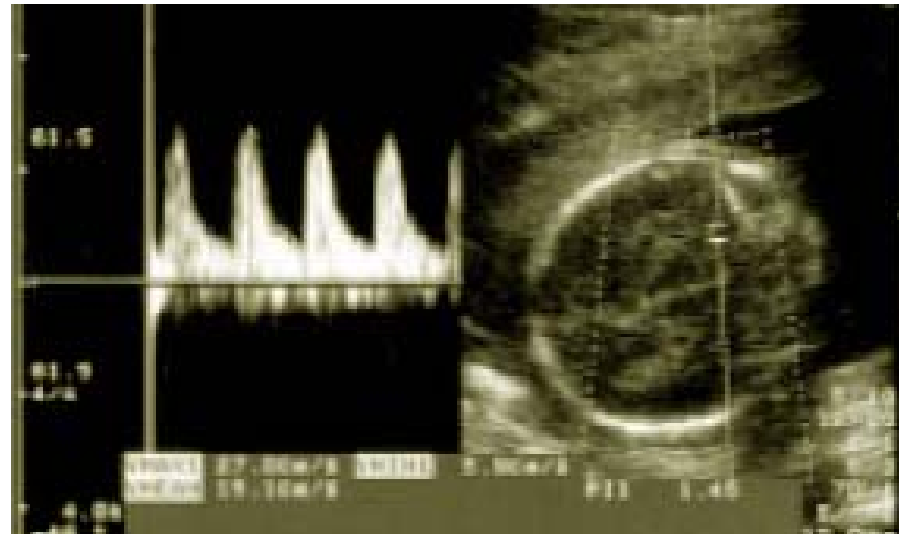
Flow i a. cerebri media



Normalt flow med normal peak systolic velocity (PSV)

Erythroblastosis fœtalis

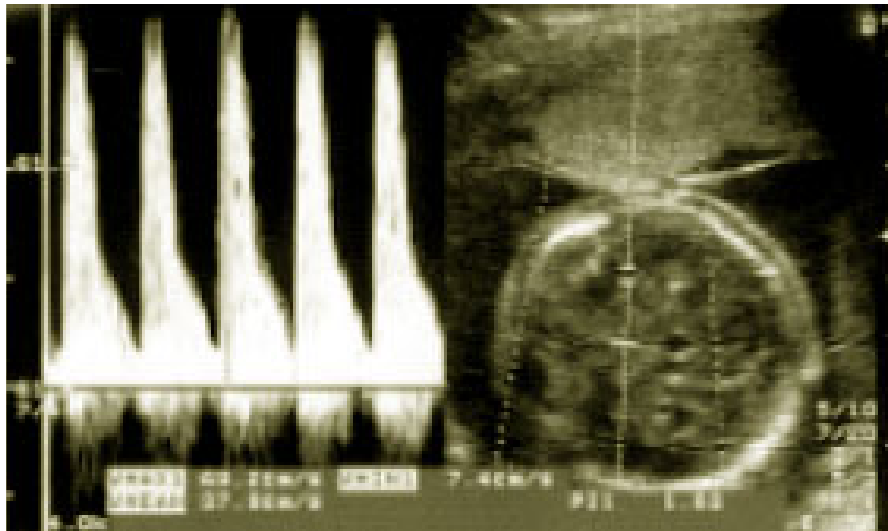
Flow i a. cerebri media



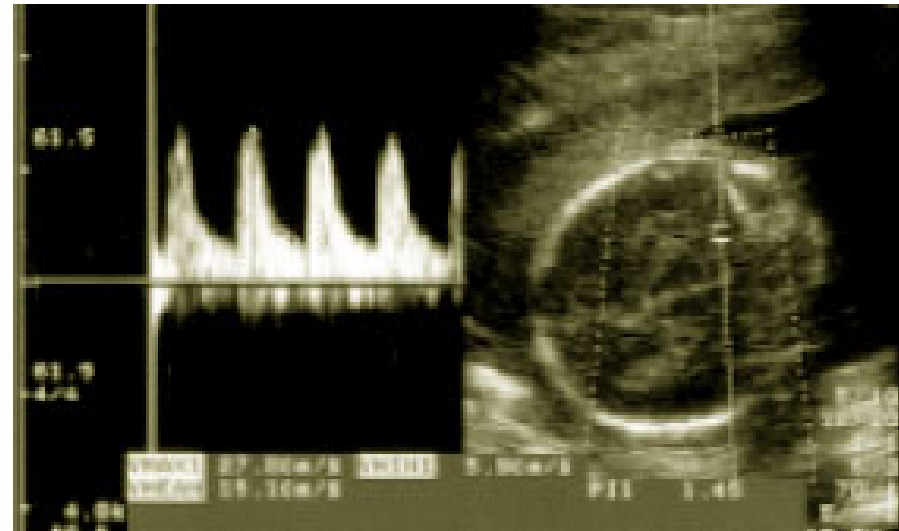
Normal PSV

Erythroblastosis fœtalis

Flow i a. cerebri media



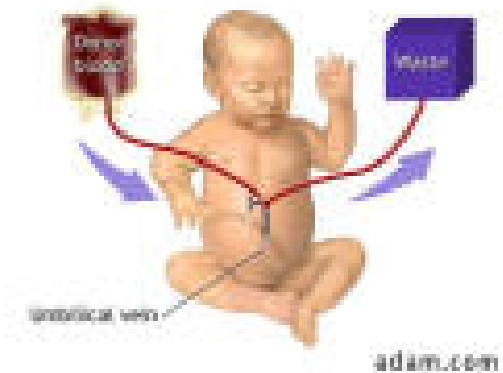
Forhøjet PSV



Normal PSV

Erythroblastose: behandling

- Antistoftiter
- Ultralydsus. af flow
- Tidlig fødsel/sektio
- Lysterapi
- Intrauterin transfusion
- Udskiftningstransfusion



Neonatal alloimmun granulocytopeni

- Sjældent
- Antistoffer mod neutrofilocyt-specifikke antigener (NA-1 og NA-2 på CD16 molekylet)
- Infektionstendens hos den nyfødte

Neonatal alloimmun trombocytopeni

- Hyppigst antistof mod HPA-1a (tidligere anti-Zw^a eller anti-P1^{a1})
- Ca. 2% er HPA-1a negative
- Moren skal have en speciel vævstype (DRw52a = DRB3*0101)
- Sjældnere antistof mod HPA-5b

NAIT: Symptomer

- Ofte første fødsel
- Blødninger, specielt intrakranielt

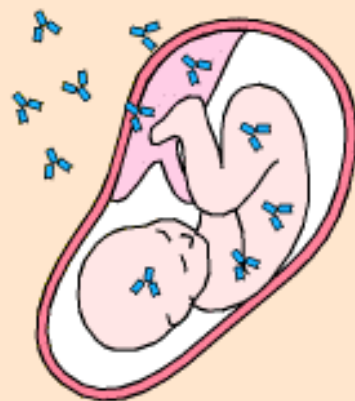
NAIT: Behandling

- Evt. IVIG til moderen fra 20.-22. uge
- Evt. steroid til moderen
- Evt. intrauterin trombocyttransfusion
- Trombocytal >50 : normal fødsel
- Trombocytal <50 : sectio, trombocytter (HPA-1a neg) i beredskab

Patient with Graves' disease makes anti-TSHR antibodies



Transfer of antibodies across placenta into the fetus



Newborn infant also suffers from Graves' disease

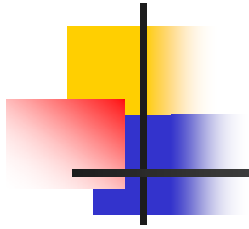


Plasmapheresis removes maternal anti-TSHR antibodies and cures the disease

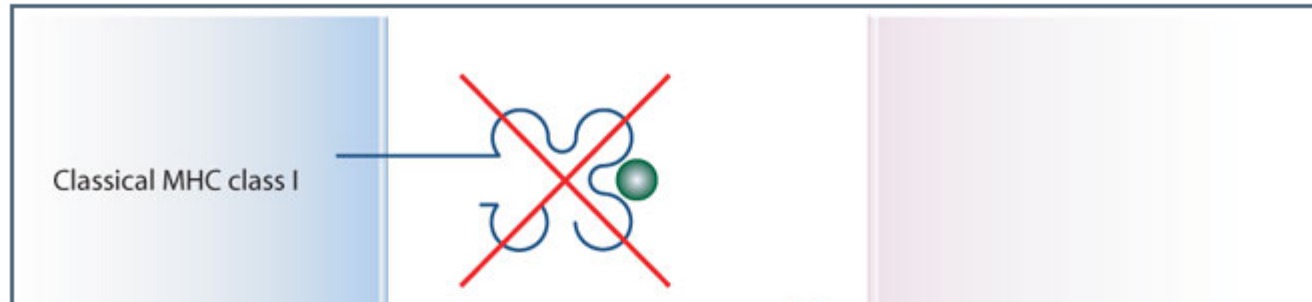


Autoimmune diseases transferred across the placenta to the fetus and newborn infant

Disease	Autoantibody	Symptom
Myasthenia gravis	Anti-acetylcholine receptor	Muscle weakness
Graves' disease	Anti-thyroid-stimulating hormone (TSH) receptor	Hyperthyroidism
Thrombocytopenic purpura	Anti-platelet antibodies	Bruising and hemorrhage
Neonatal lupus rash and/or congenital heart block	Anti-Ro antibodies Anti-La antibodies	Photosensitive rash and/or bradycardia
Pemphigus vulgaris	Anti-desmoglein-3	Blistering rash



John Trowsdale & Alexander G Betz



Foster
syncytotrophoblast

Mor
immunsystem

