

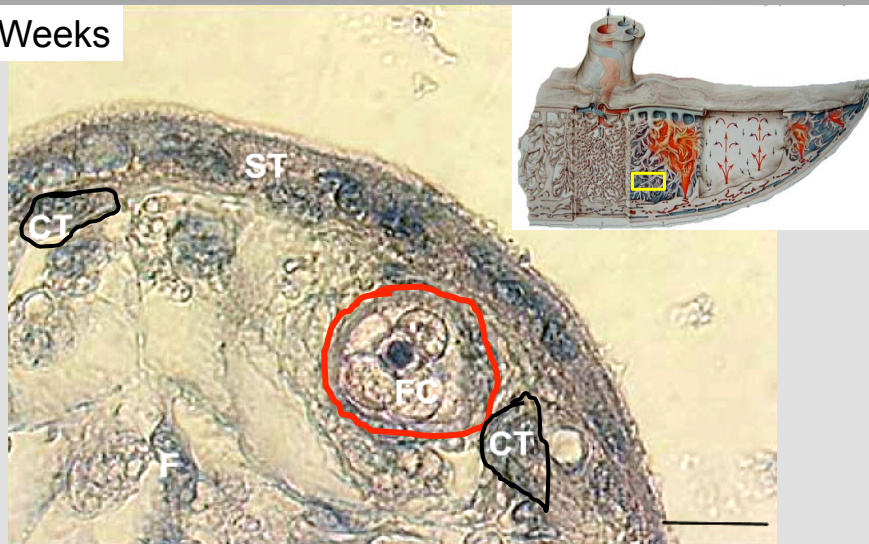
# New biochemical markers of trisomy 21

*Paul Bischof, PhD*

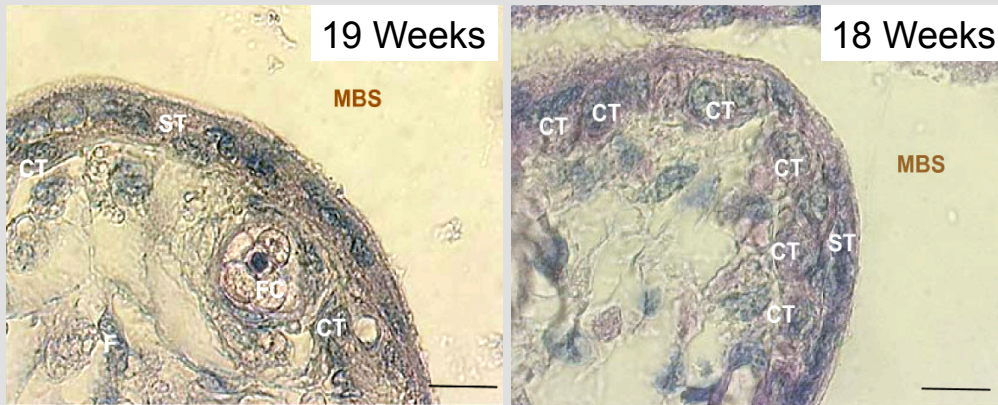


## PLACENTAL DIFFERENTIATION

19 Weeks



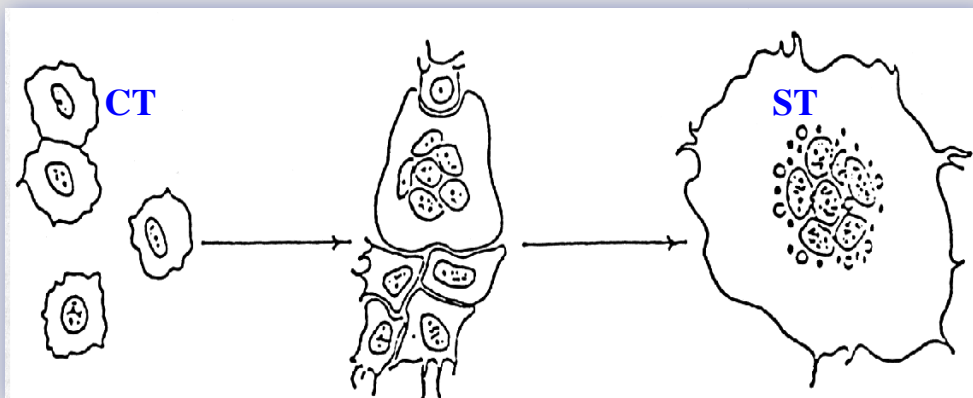
# PLACENTAL DIFFERENTIATION



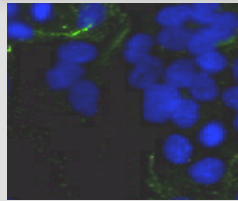
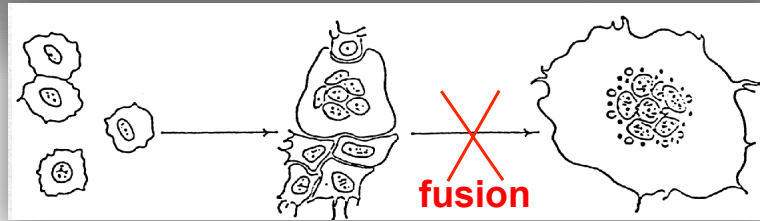
**NORMAL**

**TRISOMY 21**

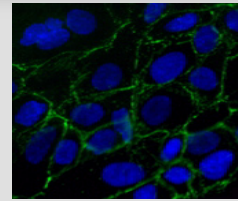
# PLACENTAL DIFFERENTIATION



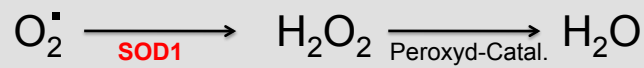
# PLACENTAL DIFFERENTIATION



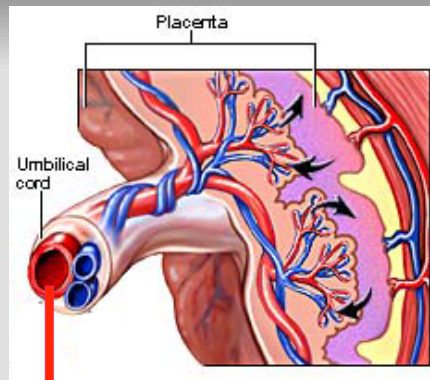
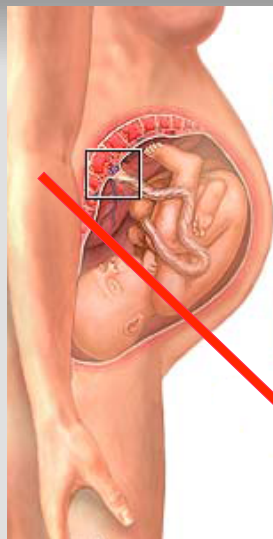
**Normoxia**



**Hypoxia**



# PLACENTAL DIFFERENTIATION



Markers must reflect the delayed differentiation of trophoblast

# DETECTING DOWN'S

**THE RISK OF CARRYING A  
TRISOMY 21 CHILD CAN BE EVALUATED  
INDIVIDUALLY  
BETWEEN 10 3/7 AND 18 6/7 WEEKS  
OF PREGNANCY BY COMBINING  
SERUM ASSAYS AND  
ULTRASONOGRAPHIC MEASUREMENTS**

# DETECTING DOWN'S

FIRST TRIMESTER 10 3/7 TO 13 6/7 WEEKS	SECOND TRIMESTER 14 0/7 TO 18 6/7 WEEKS
PAPP-A + free Beta hCG NT CRL Maternal Age Maternal Weight Obstet. History	AFP + free Beta hCG, AFP + hCG + uOestriol BPD Maternal Age Maternal Weight Obstet. History

# DETECTING DOWN'S

*In first trimester*

1.00 MoM controls

## In use

2.19 MoM for Free Beta hCG  
0.45 MoM for PAPP-A  
2.40 MoM Nuchal Translucency

## Already known

1.17 MoM for hCG  
0.97 MoM for free alpha hCG  
0.66 MoM for uE<sub>3</sub>  
0.71 MoM for SP<sub>1</sub>  
0.87 MoM for CA125  
0.97 MoM for Alk. Phos  
0.77 MoM for AFP

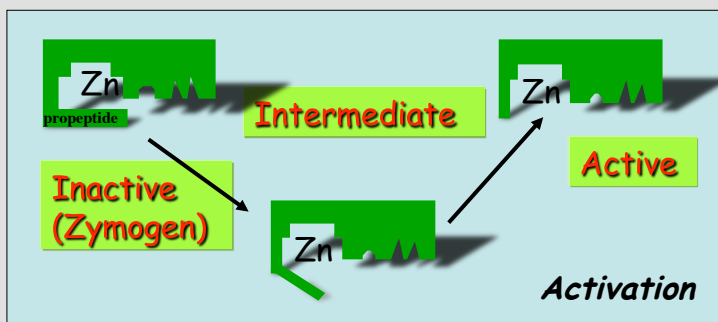
## New

0.91 MoM for PP<sub>13</sub>  
0.93 MoM for hPGH  
0.76 MoM for hPGF  
0.80 MoM for Lept.  
0.63 MoM for hPL  
1.28 MoM for DIA  
0.68 MoM for ADAM12

# ADAM 12 A Disintegrin And Metalloprotease



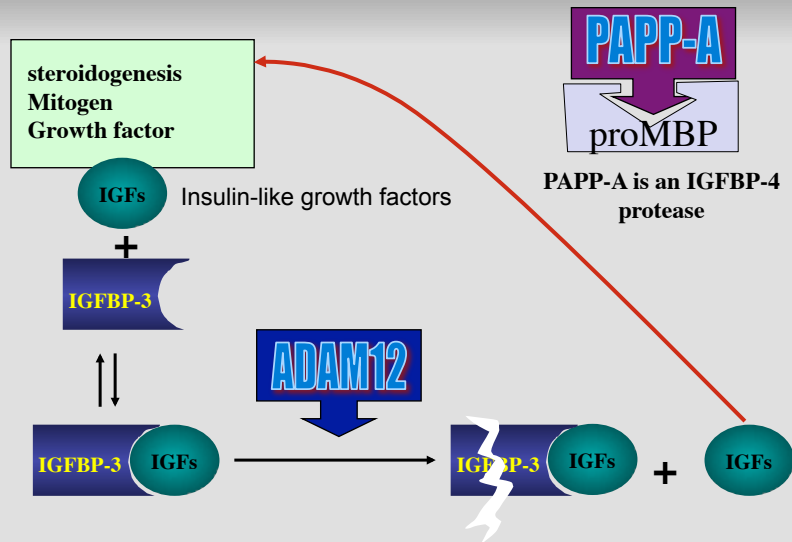
Disintegrin:  
Snake venom peptides  
Inhib. Platelet agreg.  
and cell adhesion



92 and 68 kDa MMP  
Degrades gelatin,  
type IV coll.

Involved in cell-cell  
and cell-matrix  
interactions.

## ADAM 12 A Disintegrin And Metalloprotease



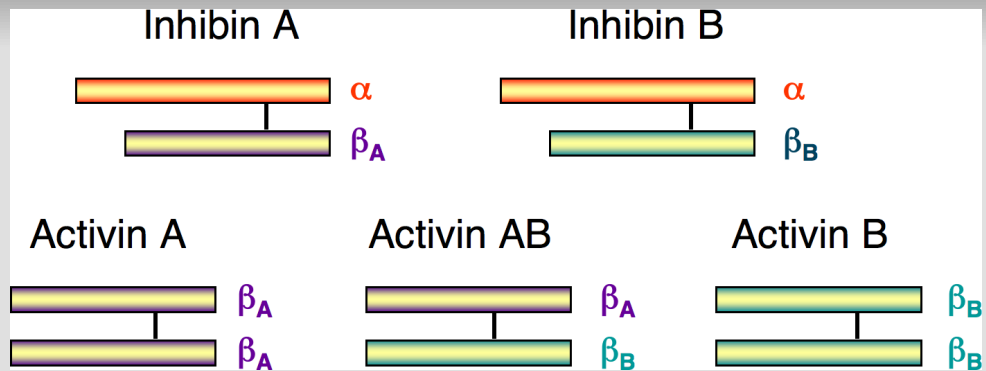
## ADAM 12 A Disintegrin And Metalloprotease

0.45 MoM for ADAM12 in DS at week 8  
 0.73 MoM for ADAM12 in DS at week 9  
 0.74 MoM for ADAM12 in DS at week 10  
 0.85 MoM for ADAM12 in DS at week 11  
 0.92 MoM for ADAM12 in DS at week 12  
 1.06 MoM for ADAM12 in DS at week 13

**ADAM 12 in *VERY* early pregnancy is an efficient marker for DS (8-9 weeks).**

**Combined with NT & 12Weeks fbeta :detection rate 92 % DS at 1% FP.** 11 studies between 2006-2010

## DIA DIMERIC INHIBIN A



14-18 kDa peptides produced by the ovarian follicles that regulate pituitary FSH. Circulate bound to alpha2M. Massively produced by the placenta, function ?

## DIA DIMERIC INHIBIN A

1.28 MoM for DIA in DS at week 11  
1.30 MoM for DIA in DS at week 12  
1.67 MoM for DIA in DS at week 13  
1.92 MoM for DIA in DS at week 14-16  
1.46 MoM for DIA in DS at week 17-23

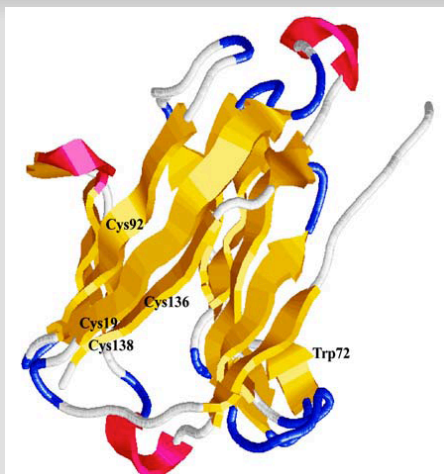
Age + NT + PAPP-A + fbeta 84%  
Age + NT + PAPP-A + hCG 83%  
Age + NT + PAPP-A + DIA 85%

## DIA DIMERIC INHIBIN A

Age + uE <sub>3</sub> + hCG	69%
Age + uE <sub>3</sub> + hCG + DIA	85%

- *DIA is not a marker for detecting DS in first trimester pregnancies.*
- *Adding DIA to the classical triple test significantly increases the detection rate in second trimester screening.* (8 Studies 2006-2010)

## PP 13 PLACENTAL PROTEIN 13



PP13 also named GALECTIN 13 is a placental protein binding lectins.

This 32kDa protein is involved in cell growth, cell adhesion and apoptosis.



## PP 13 PLACENTAL PROTEIN 13

0.92 MoM for PP 13 in T21 at week 11-13  
0.64 MoM for PP 13 in T18 at week 11-13  
0.46 MoM for PP 13 in T13 at week 11-13

BUT

PP13 is with PIGF the « Gold Standard » to predict preeclampsia.

## WHERE DO WE GO?

Circulating fetal DNA/RNA in maternal plasma (3 studies)

- Haplotype ratios
- Placental transcripts (fbeta)

Proteomics

- Several markers described that are modified in T21 sera (4 studies) only EGF has been validated clinically.

## WHERE DO WE GO?

Age, NT, and presence of nasal bone and/or blood flow in the ductus venosus to estimate the risk of T21.

Biochemistry (PAPP-A & fbeta hCG) only in cases with increased risk and re-calculation of the risk!

