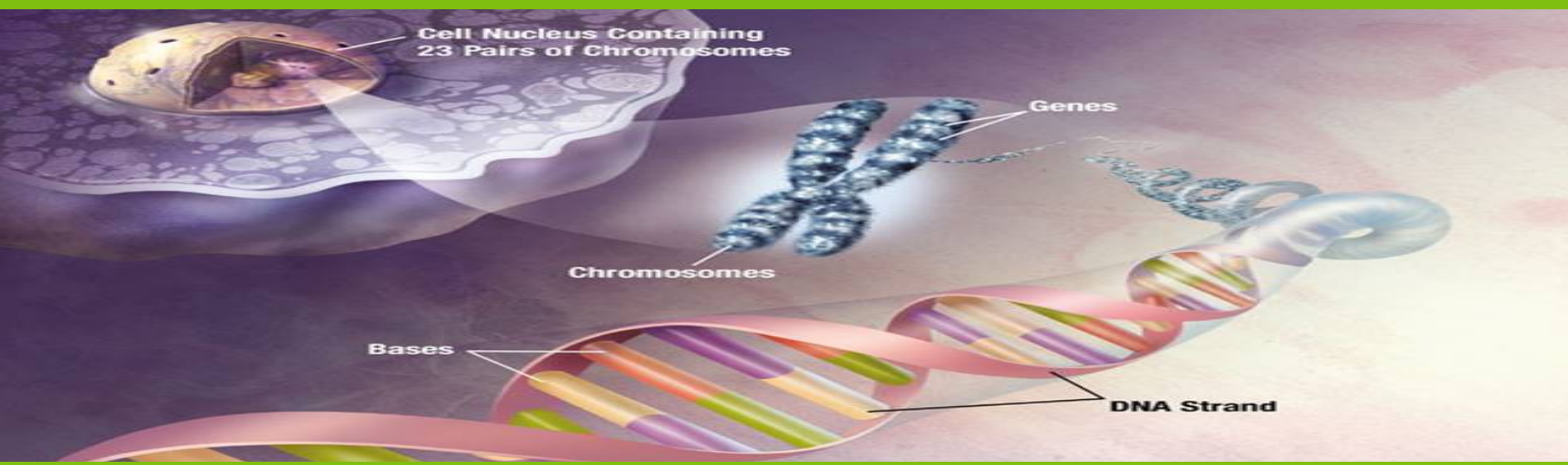


DNA Damage and Folate Nutrigenomics in Pregnancy

Denise Furness

Michael Fenech, Yee Khong, Bill Hague, Gus Dekker

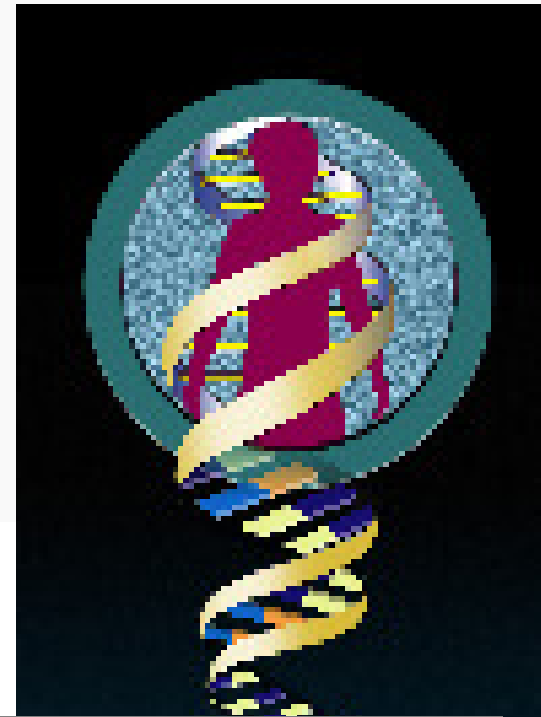


Research Centre
for Reproductive
Health

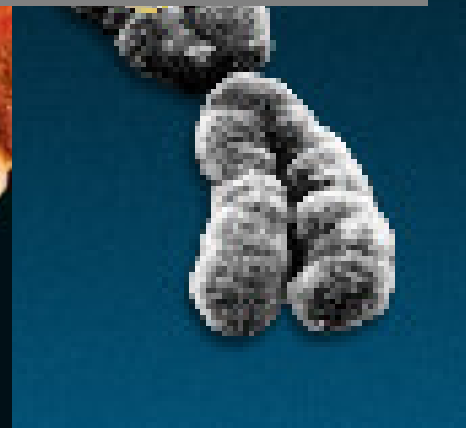
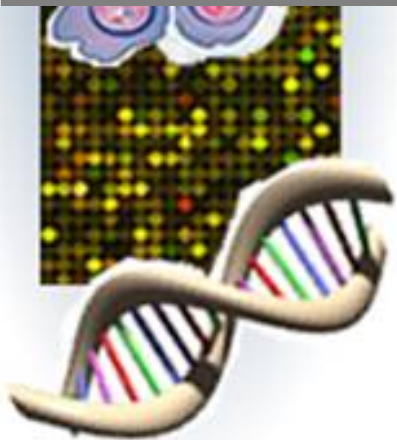


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AUSTRALIA

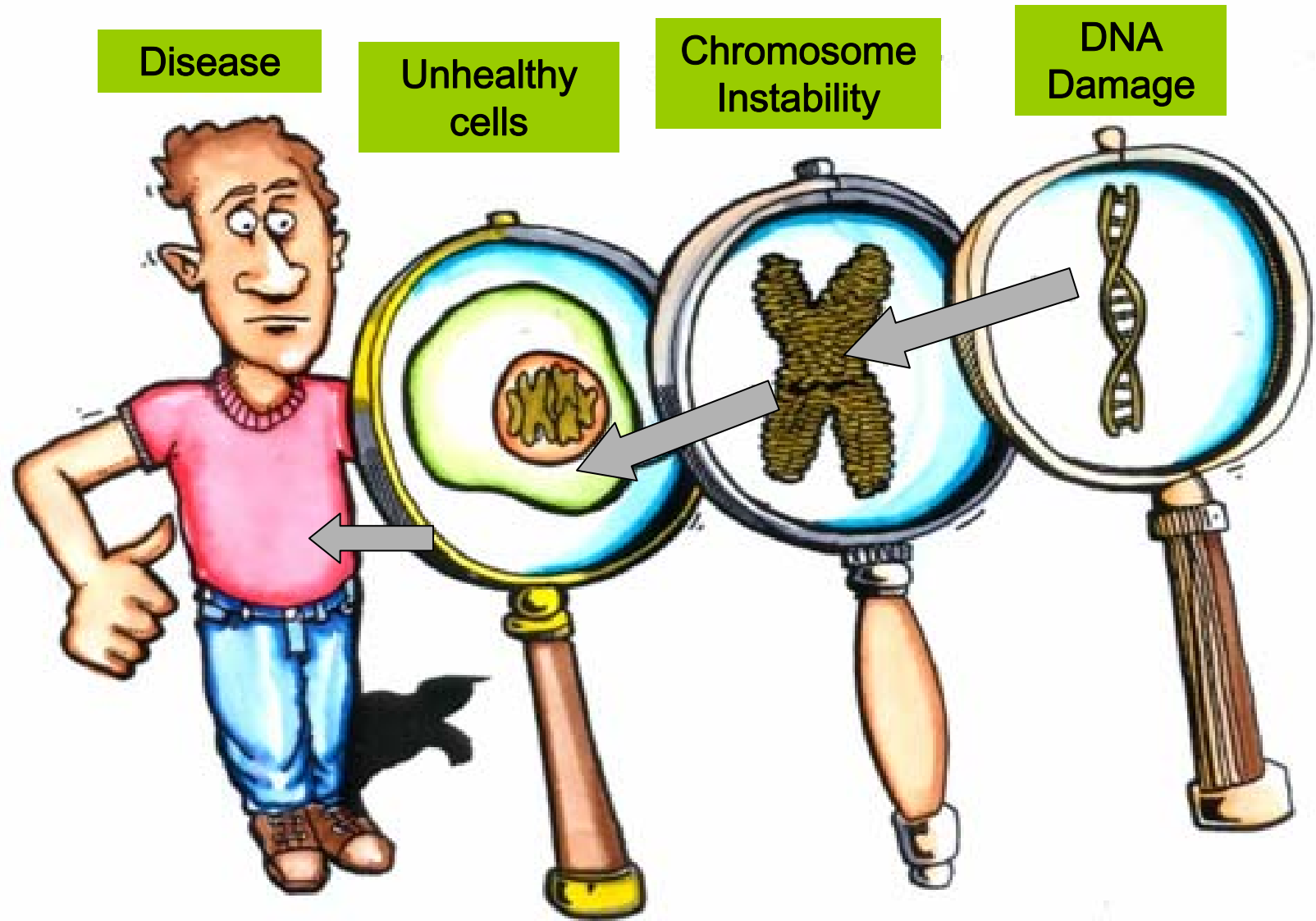




NUTRIGENOMICS

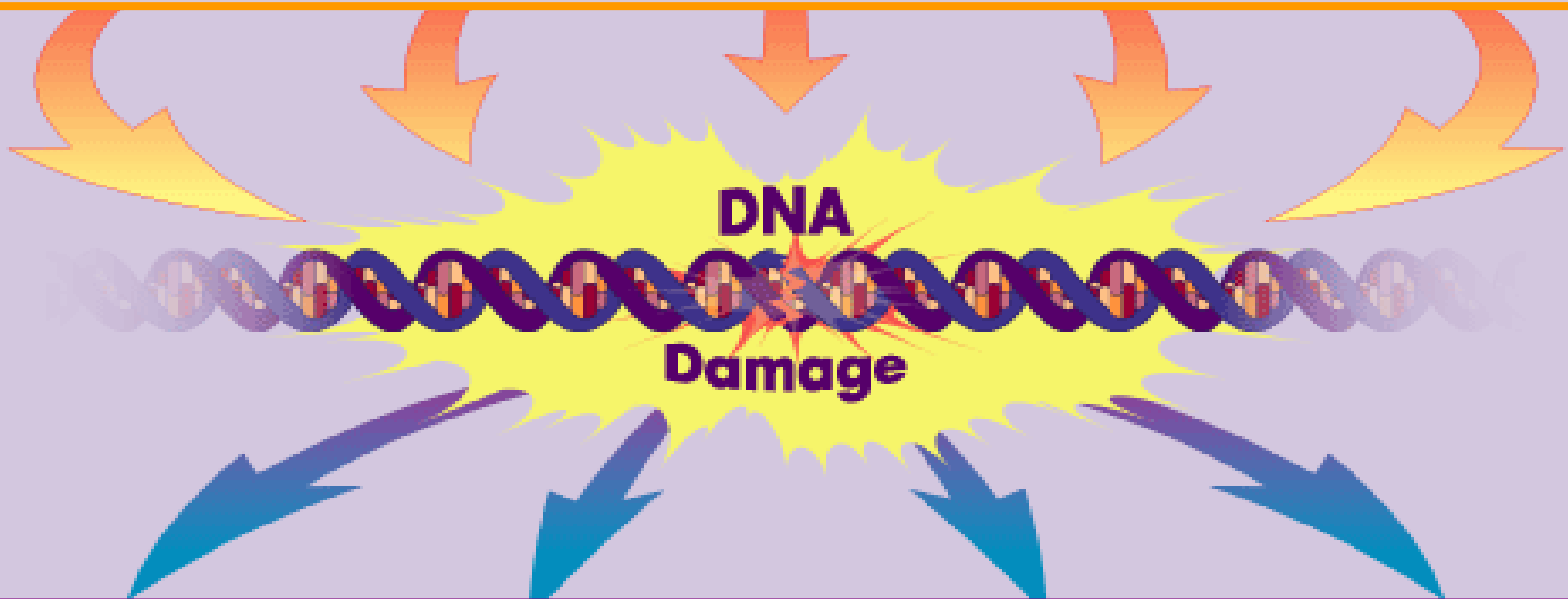


DNA and Disease



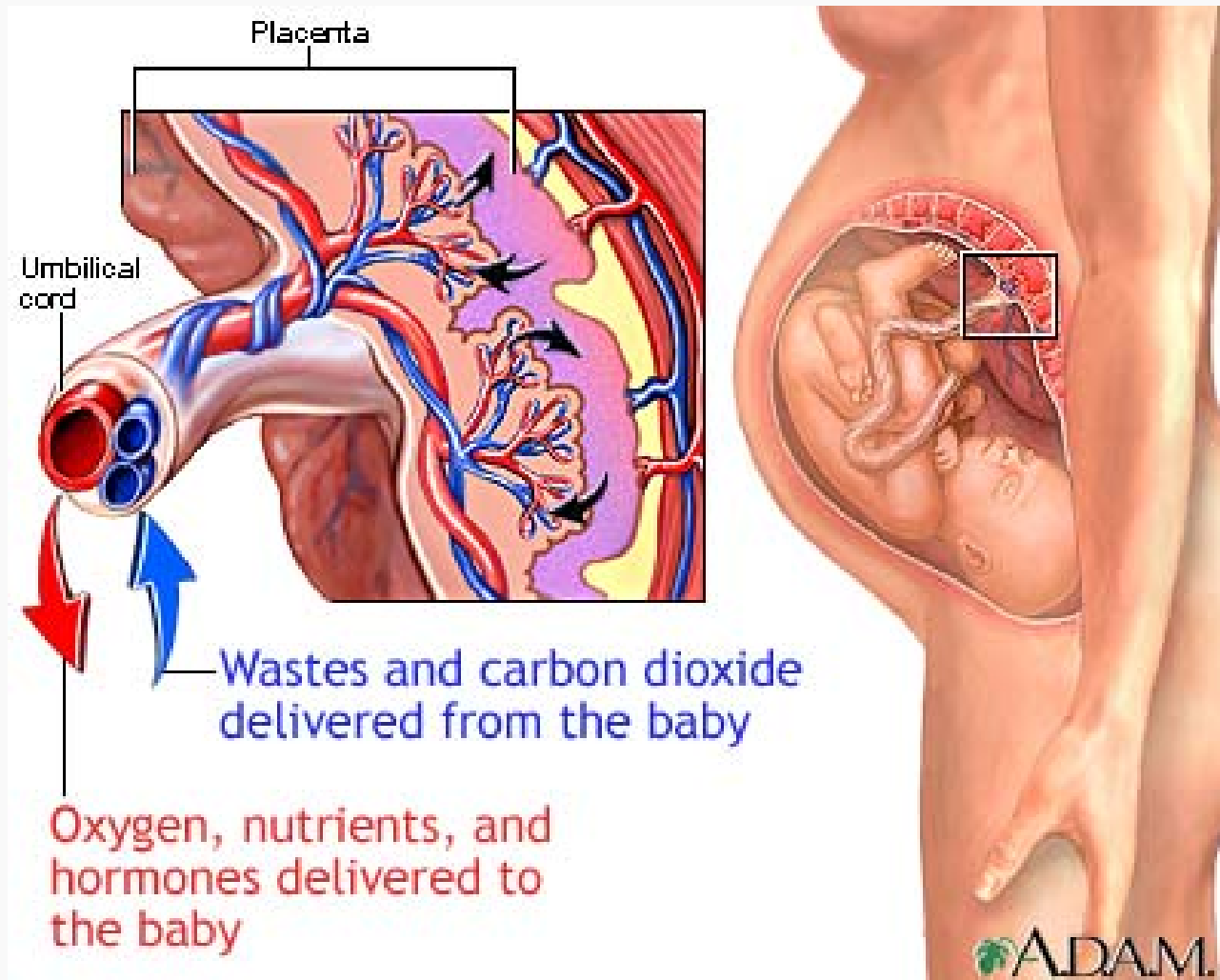
DNA Damage

ENVIRONMENTAL AND GENETIC FACTORS

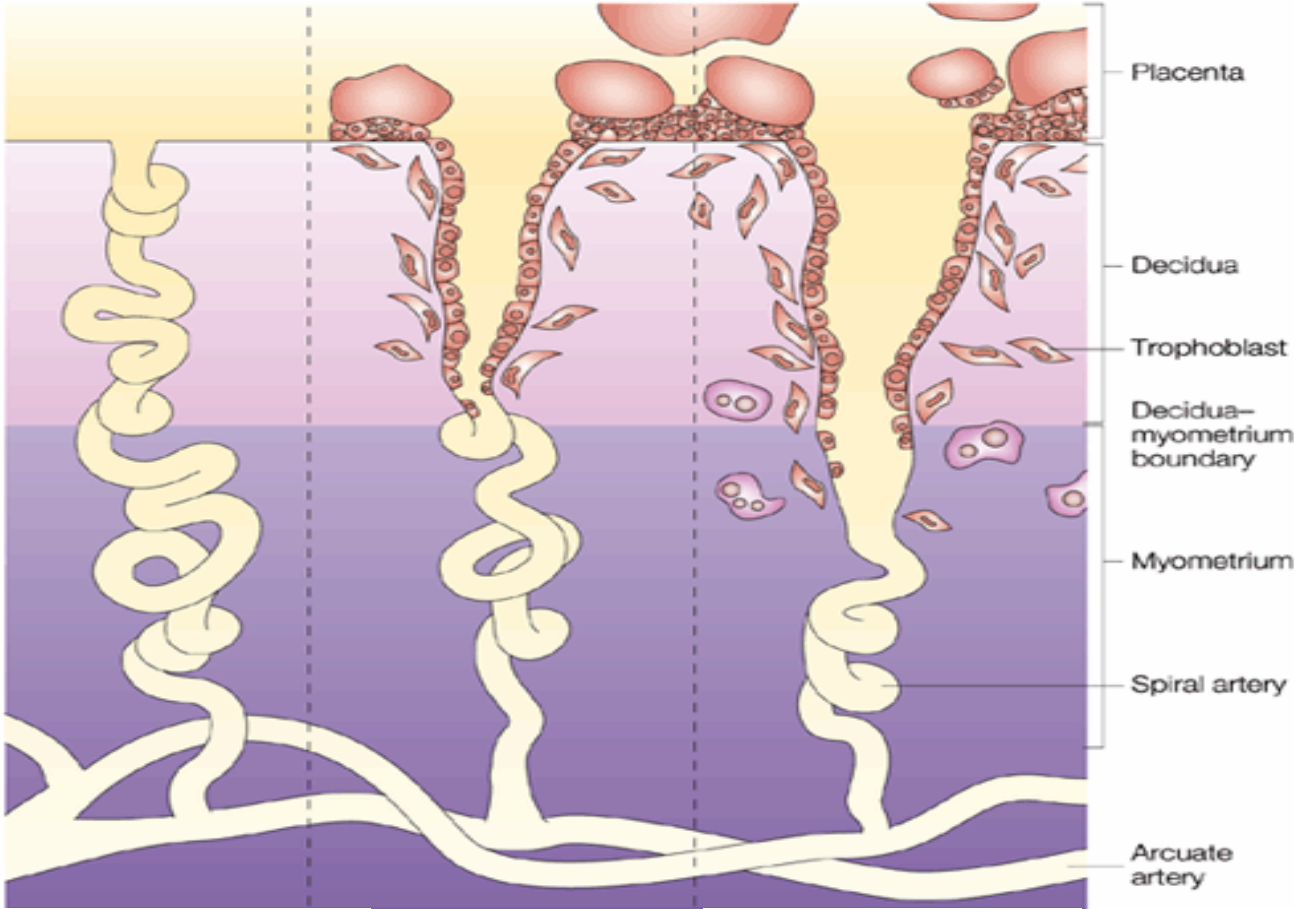


ALTERED CELL GROWTH AND FUNCTION

Placenta



Spiral Artery Remodelling



Non Pregnant

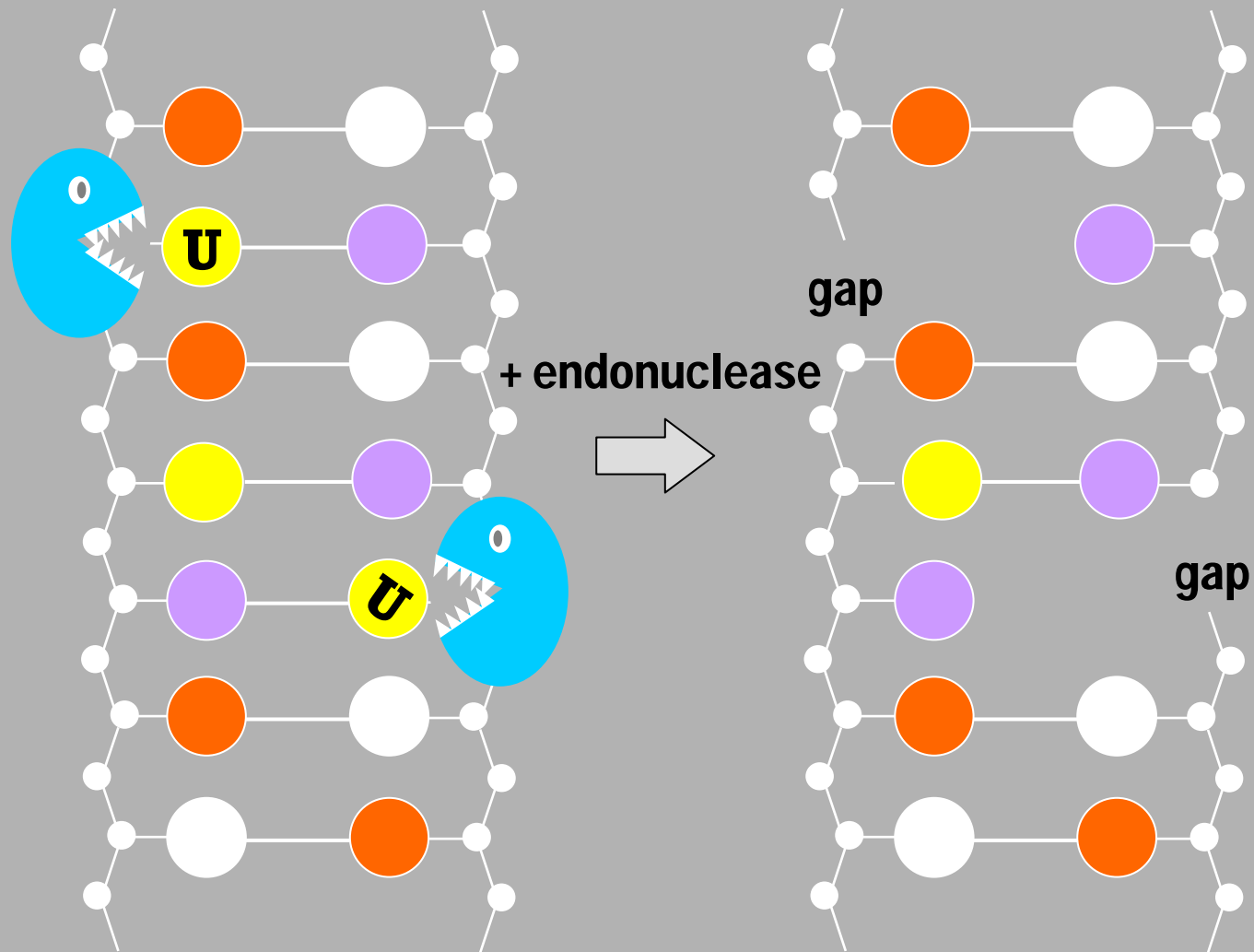
Preeclampsia/
IUGR

Normal

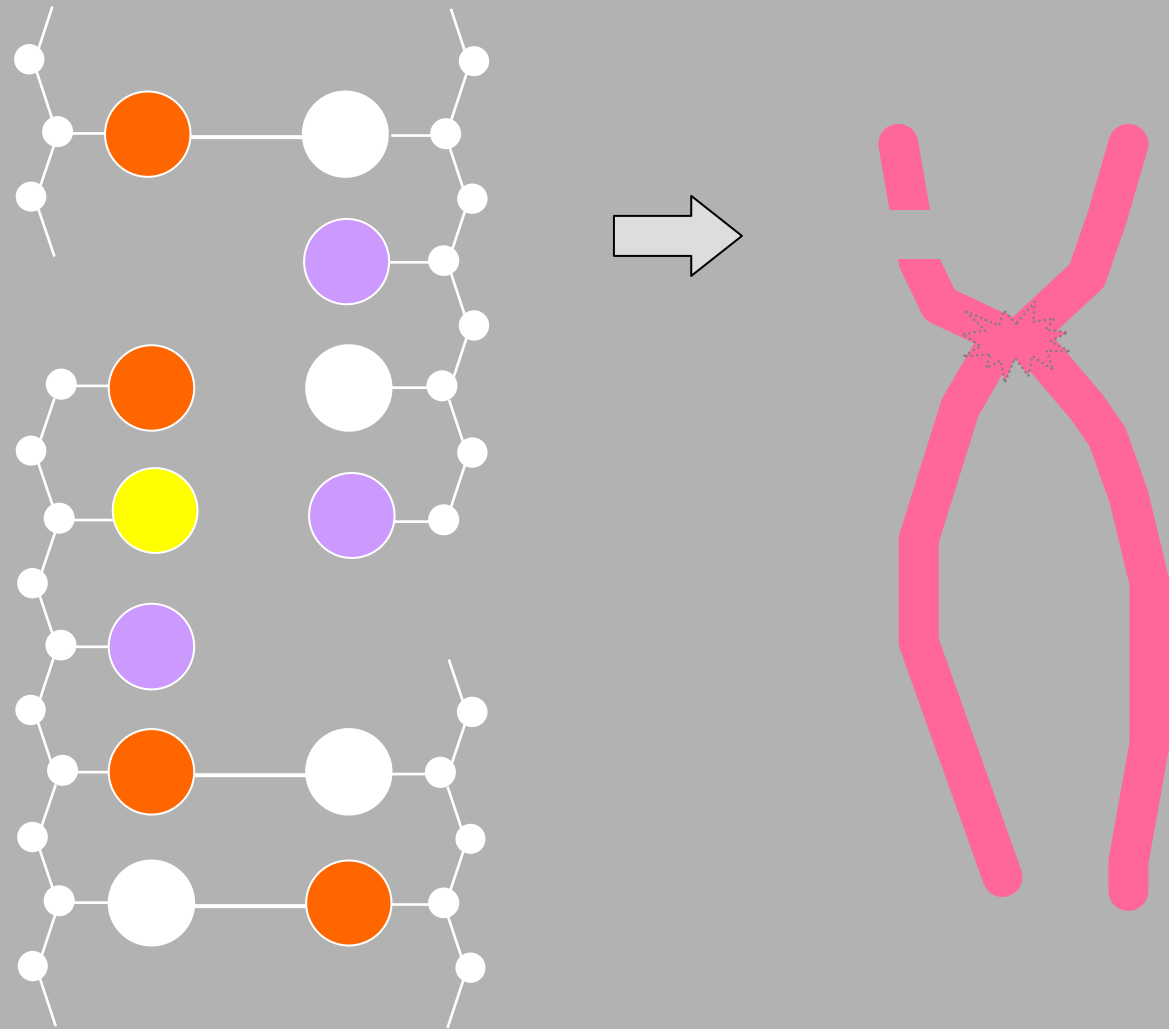
Uteroplacental Insufficiency (UPI)

- **Defects in placental transfer function**
 - Preeclampsia
 - Gestational hypertension
 - Intrauterine growth restriction (IUGR)
 - Placental abruption

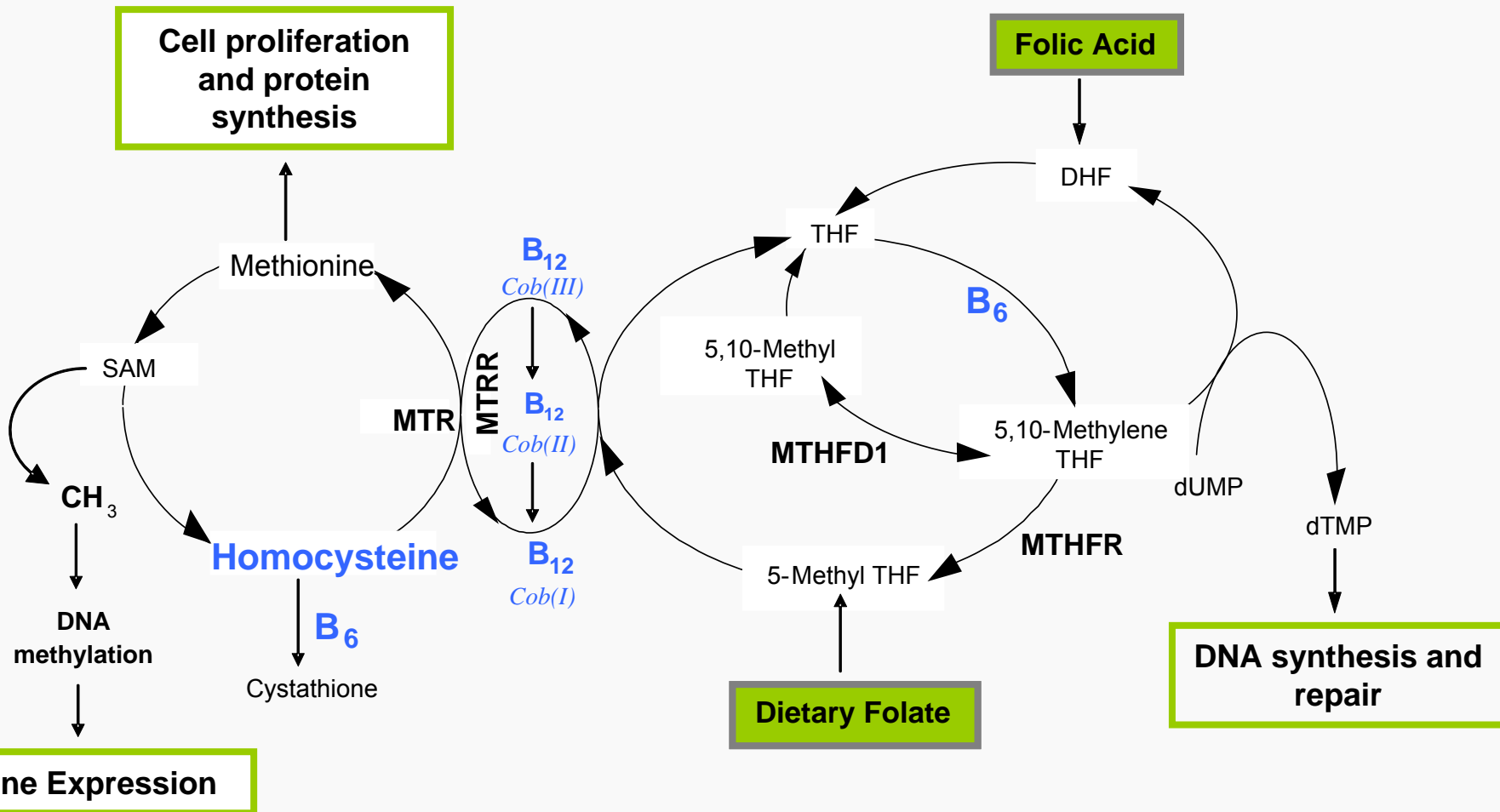
Uracil repair and DNA Breakage



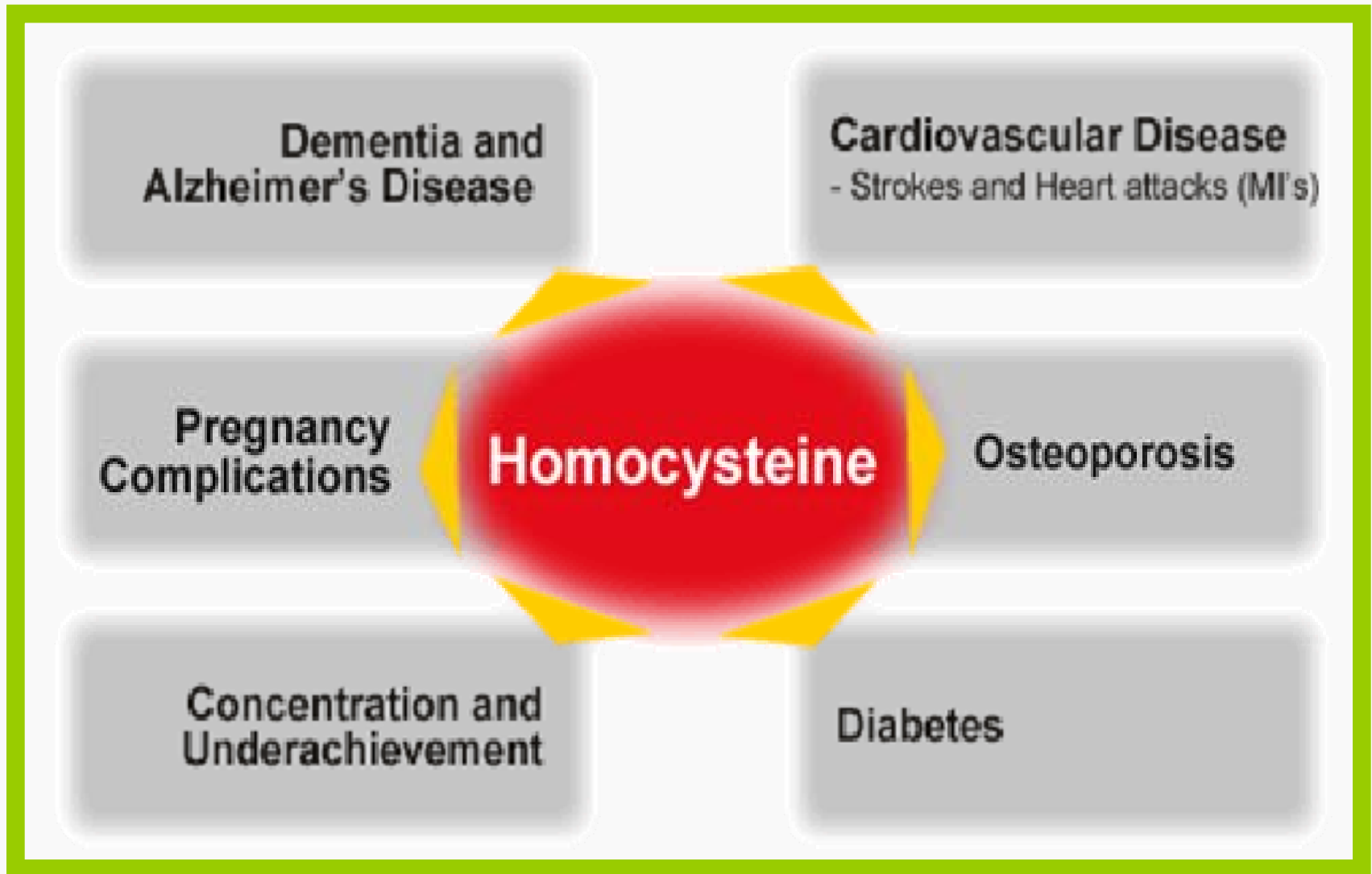
Uracil repair and DNA Breakage



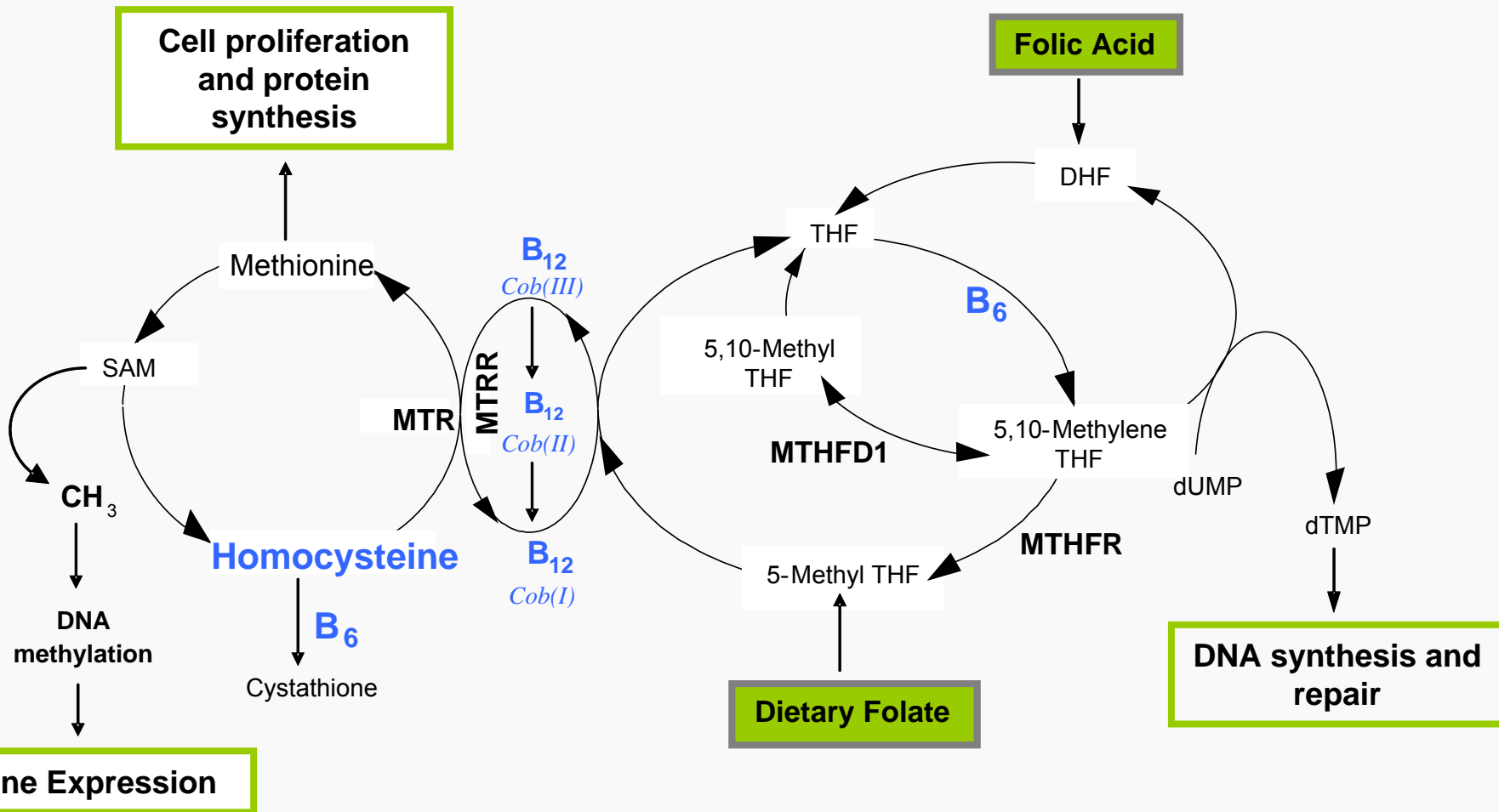
Folate Metabolism



Homocysteine



Folate Metabolism



Defects in Folate, Vitamin-B₁₂, Vitamin-B₆, metabolism

Altered DNA
methylation

Altered gene
expression

Genome Damage

Uracil in
DNA

Chromosome
breaks

Genome Damage

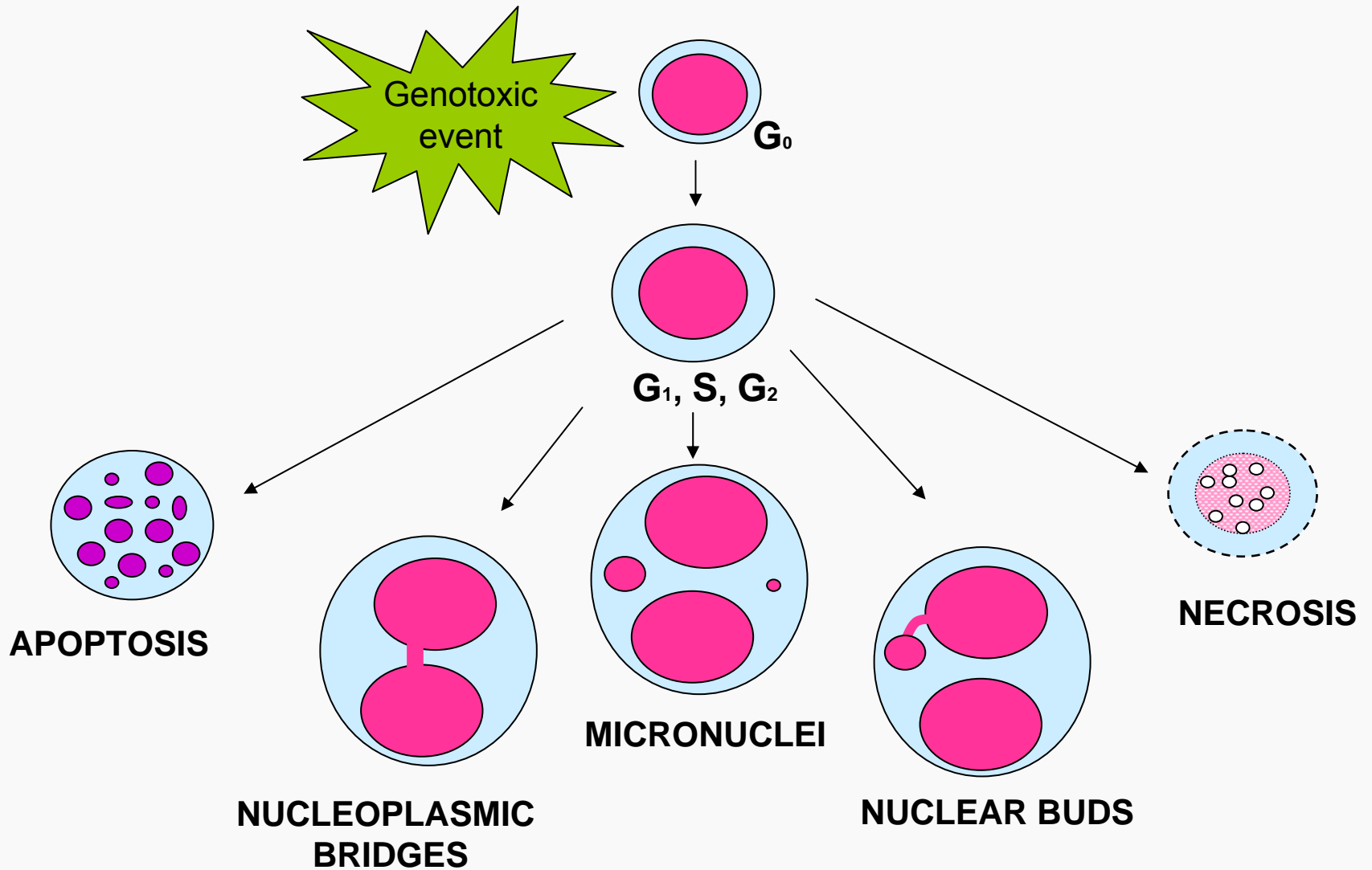
Increased
homocysteine

Endothelial
cell damage

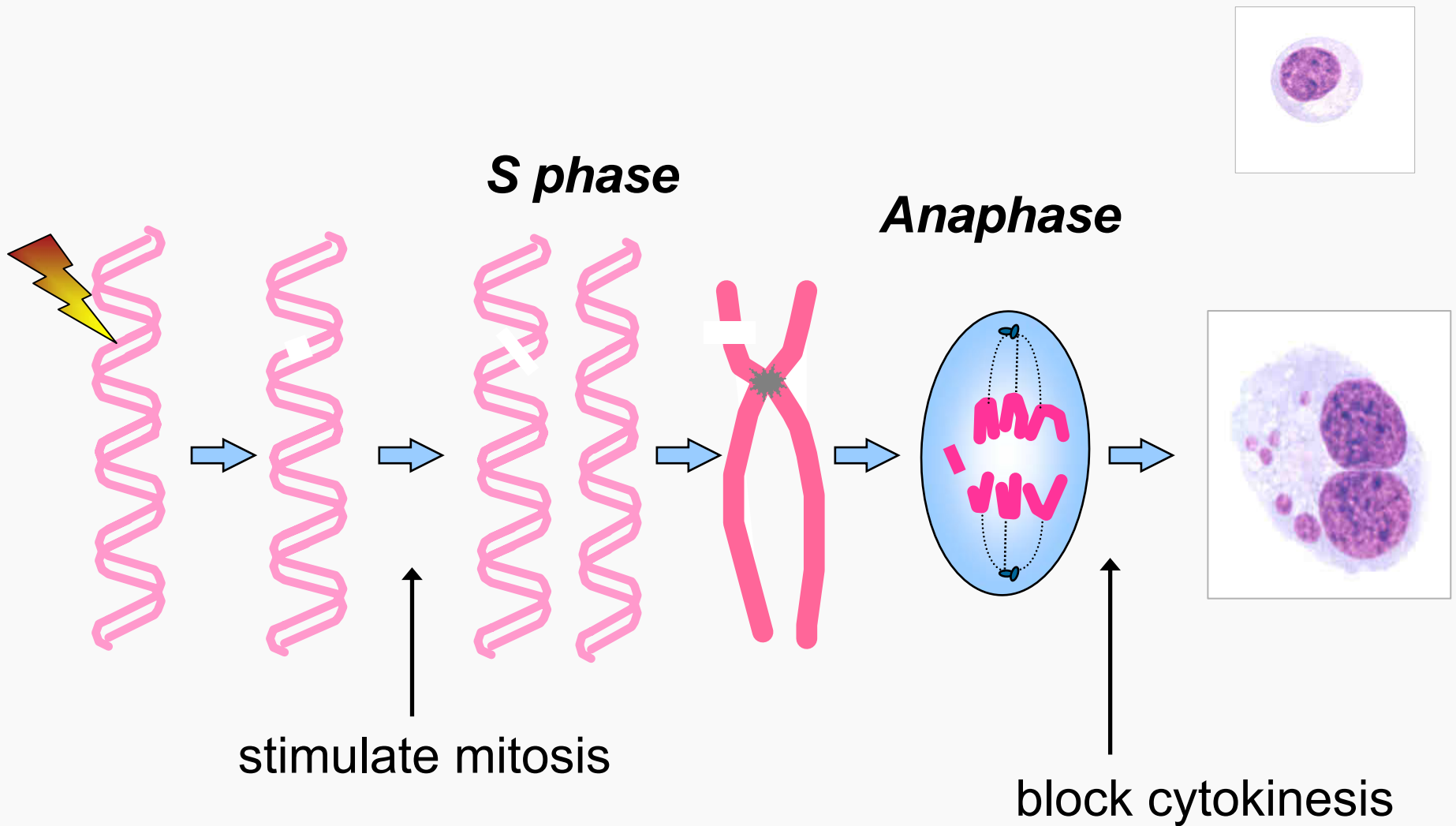
Abnormal
Placentation

Uteroplacental Insufficiency

CBMN Cytome Assay



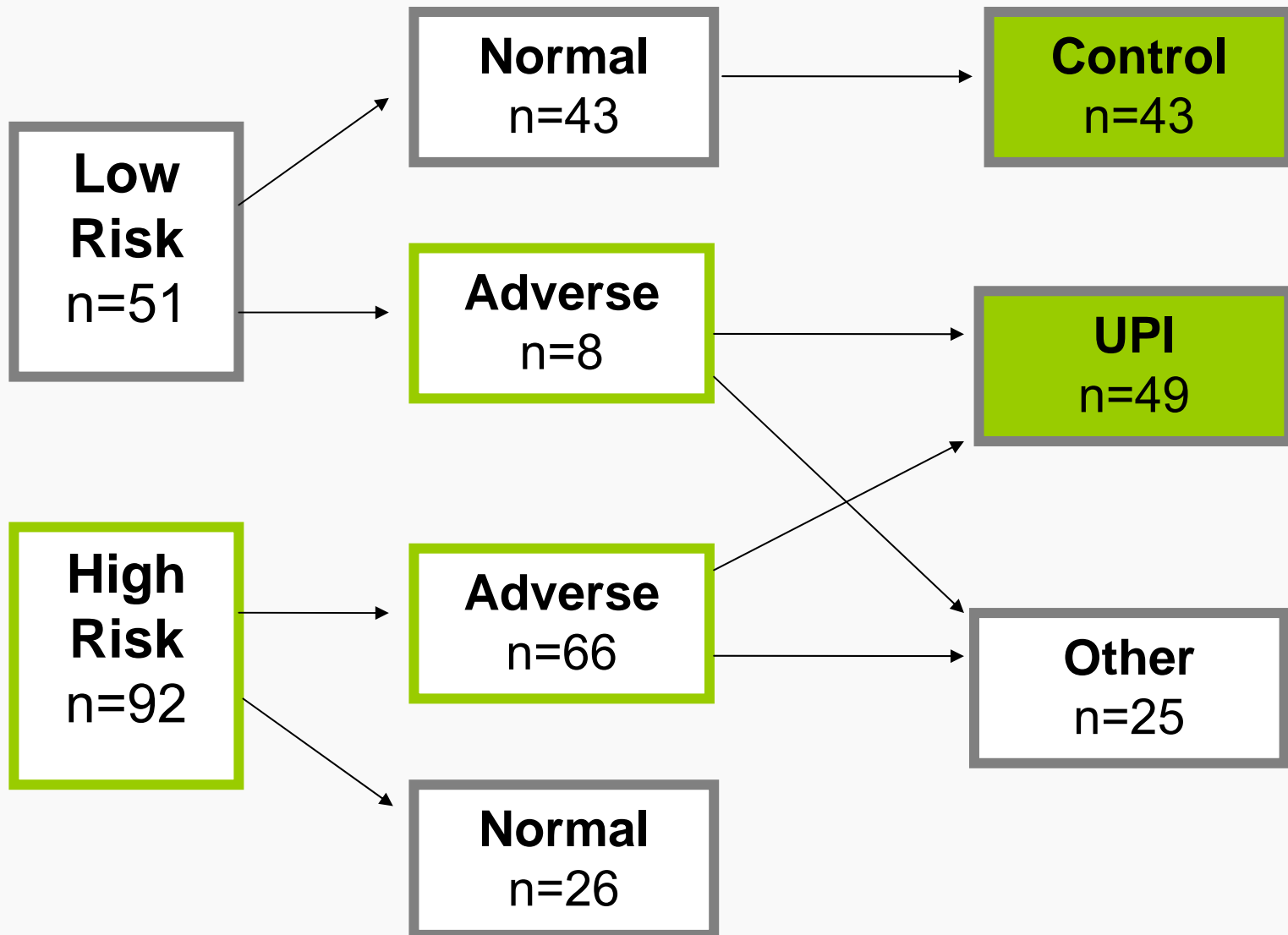
Micronuclei Formation



Study Design

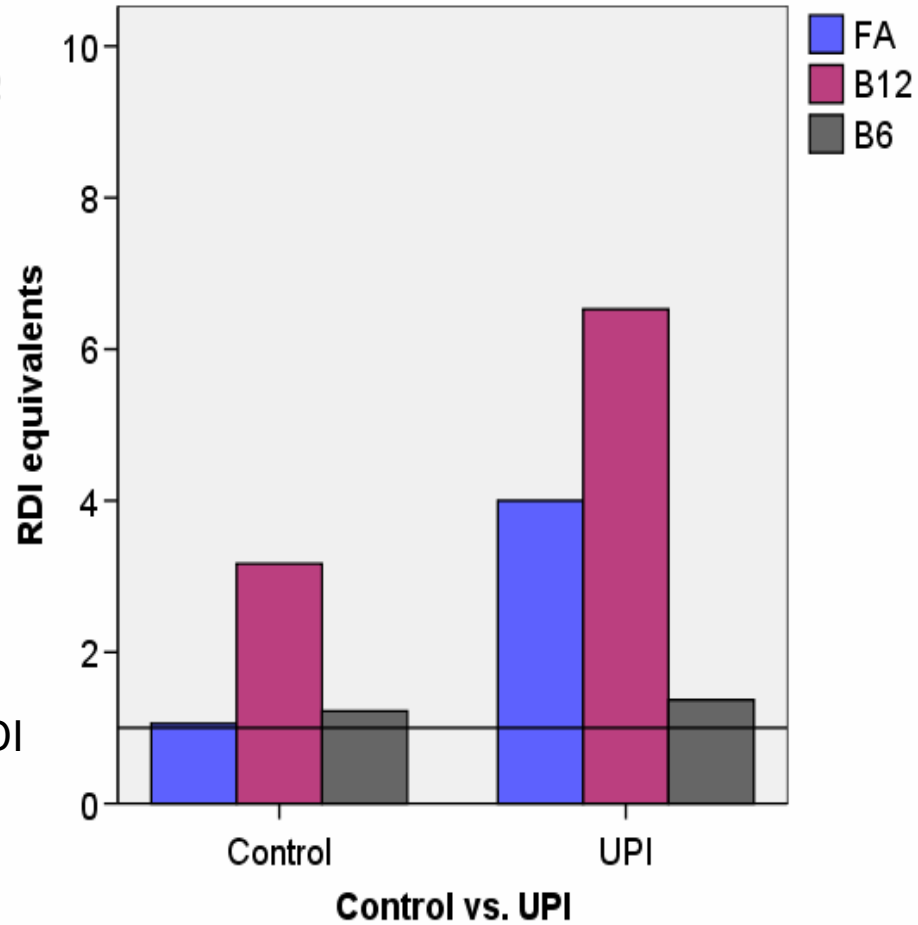
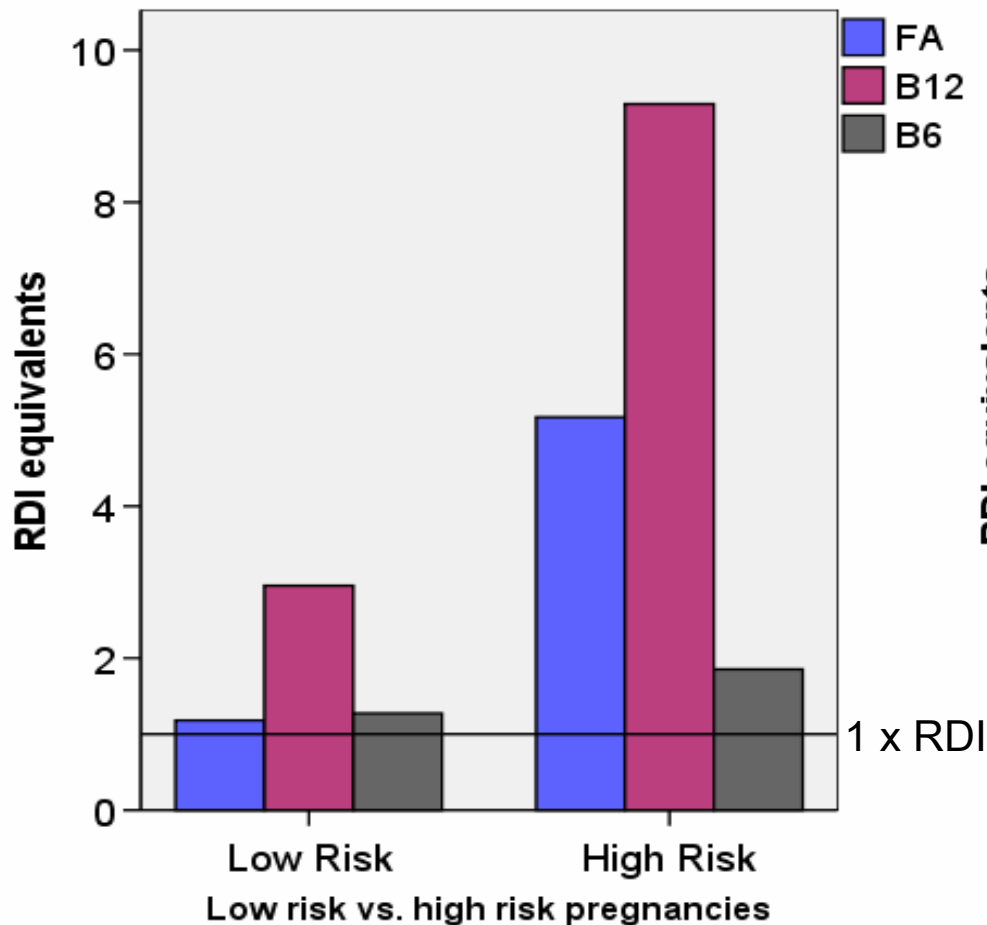
- **20 weeks gestation**
 - Dietary analysis
 - Collect maternal blood
 - Micronutrients – Folate, B12, B6 and homocysteine
 - CBMN – all genome damage markers
 - Delivery
 - Pregnancy outcome and details

Pregnancy Groups



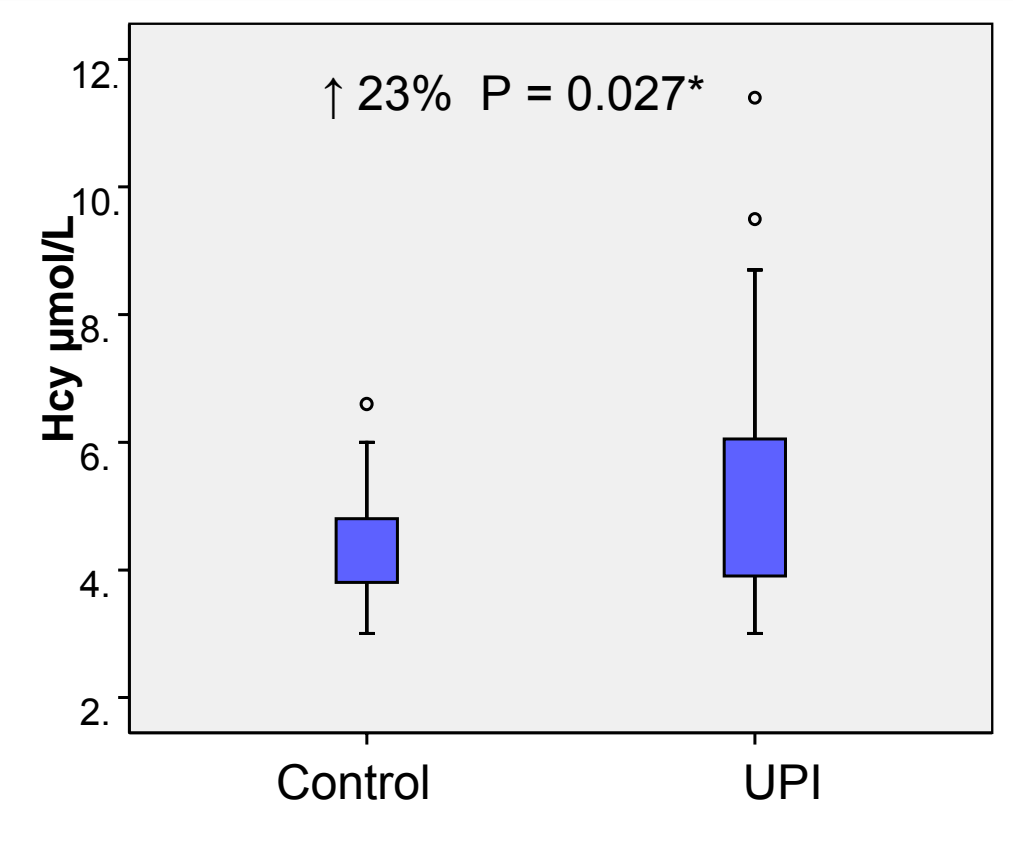
Supplement Intake

Folic Acid, Vitamin-B₁₂, Vitamin-B₆



Micronutrient Data - UPI

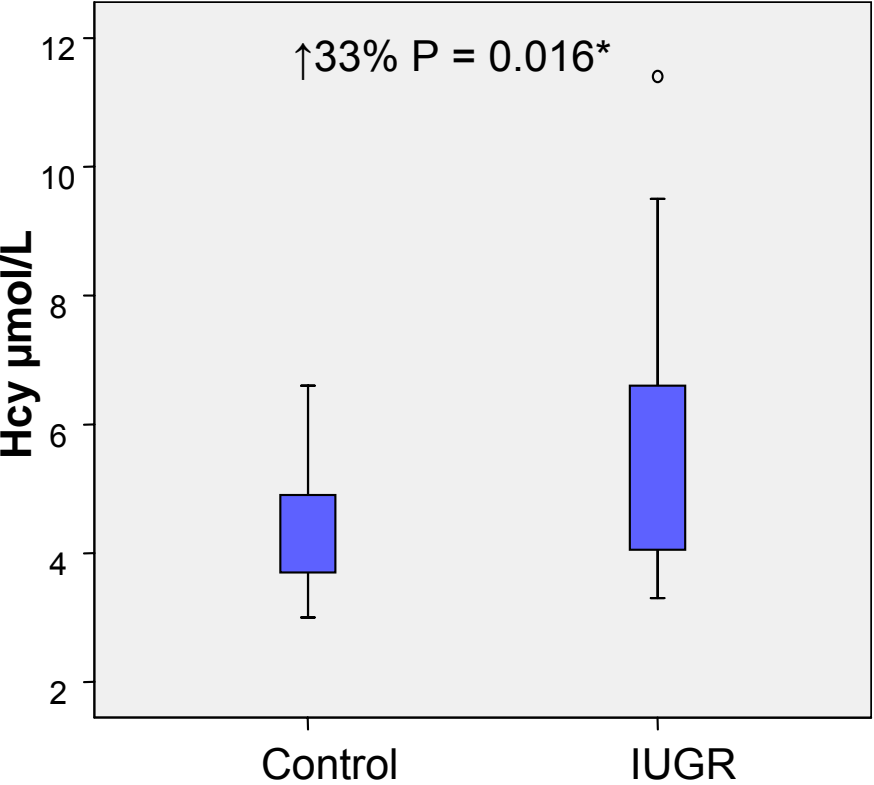
Homocysteine



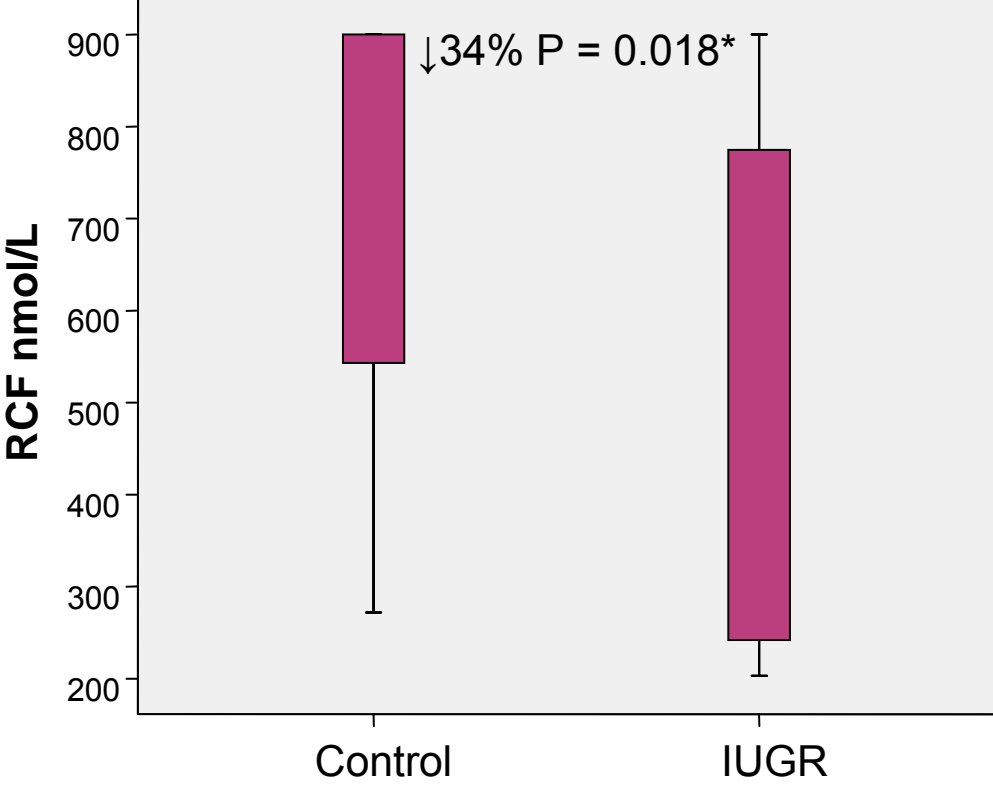
*Adjusted for age, BMI and smoking

Micronutrient Data - IUGR

Homocysteine

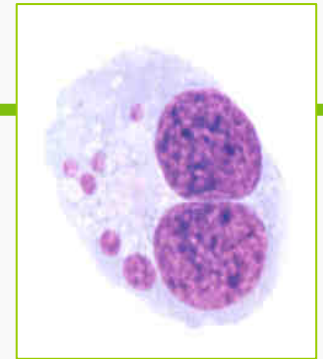


Red cell folate

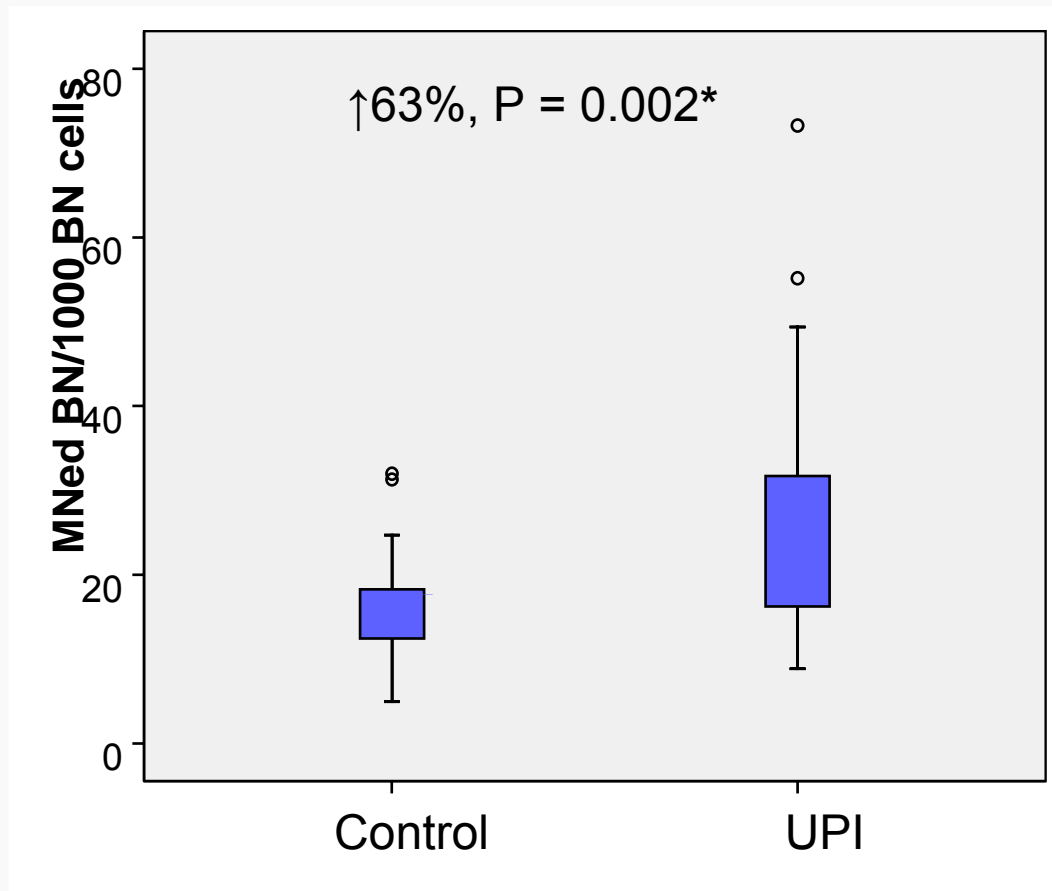


*Adjusted for age, BMI and smoking

Genome Damage Data - UPI



Micronucleated cells

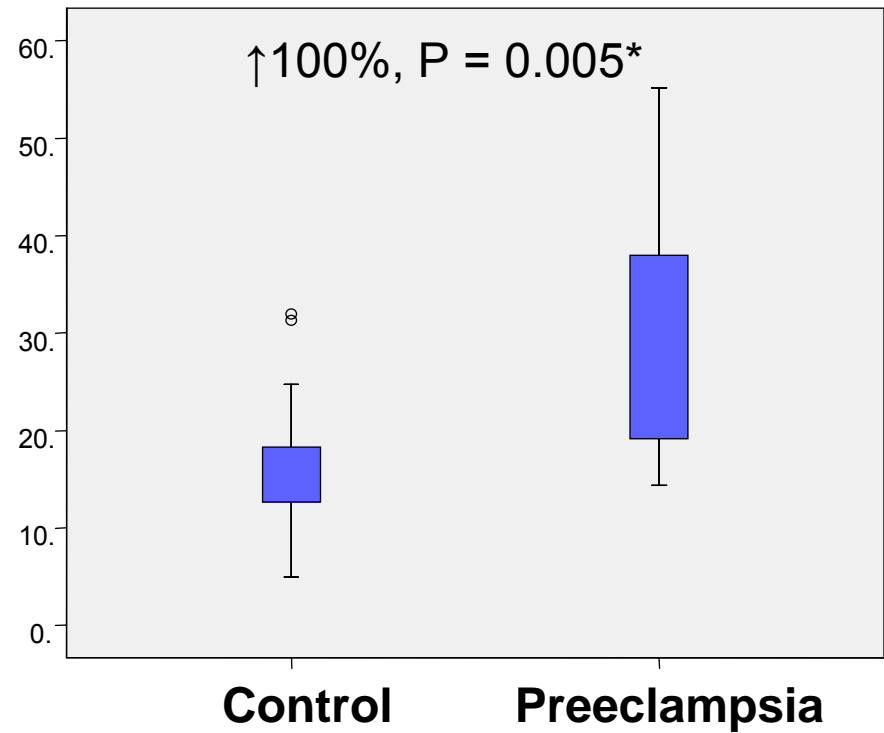
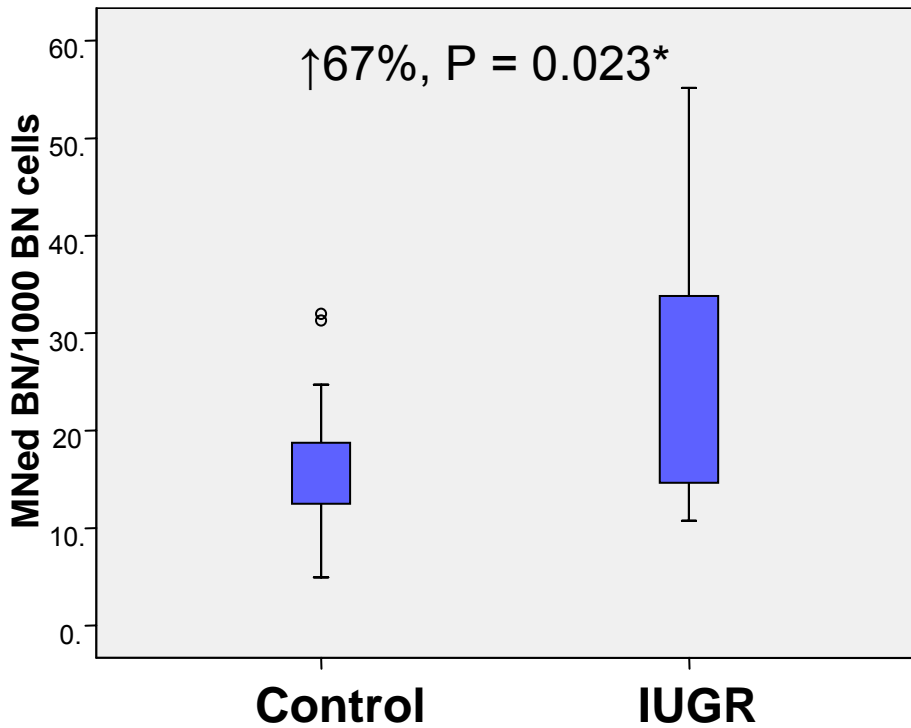


*Adjusted for age, BMI and smoking

Genome Damage Data



Micronucleated cells



*Adjusted for age, BMI and smoking

Conclusions

- The data suggest that genome damage is associated with uteroplacental insufficiency (UPI)
- The CBMN assay may be useful in predicting risk for UPI in mid pregnancy
- High homocysteine (Hcy) may be associated with UPI
- Folate deficiency and high Hcy may be associated with IUGR
- Supplementation is beneficial - other genetic or environmental factors are contributing to high Hcy and UPI

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