

**BPA exposure during
pregnancy: risk for
gestational diabetes and
diabetes following
pregnancy**

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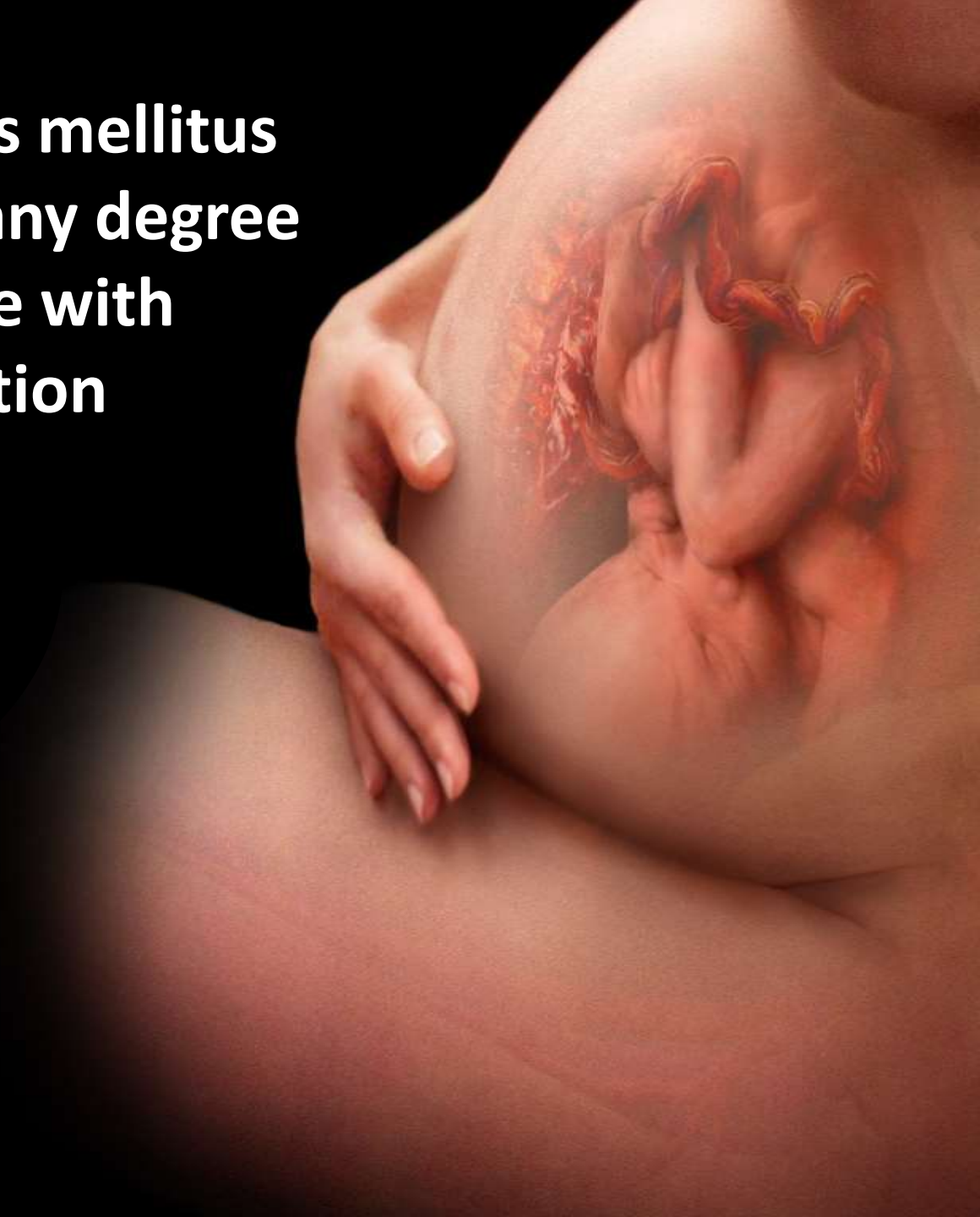
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***Pregnancy transiently
drives women into a
metabolic stress
scenario that can
determinate their health
status in later life***




- Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy

- Approximately 7% of all pregnancies are complicated by GDM resulting in more than 200,000 cases annually.



RISKS FACTORS FOR GDM

- 
- ✓ **Age**
 - ✓ **History of gestational diabetes**
 - ✓ **Obesity**
 - ✓ **Ethnicity**
 - ✓ **Sedentary lifestyle**
 - ✓ **History of smoking**

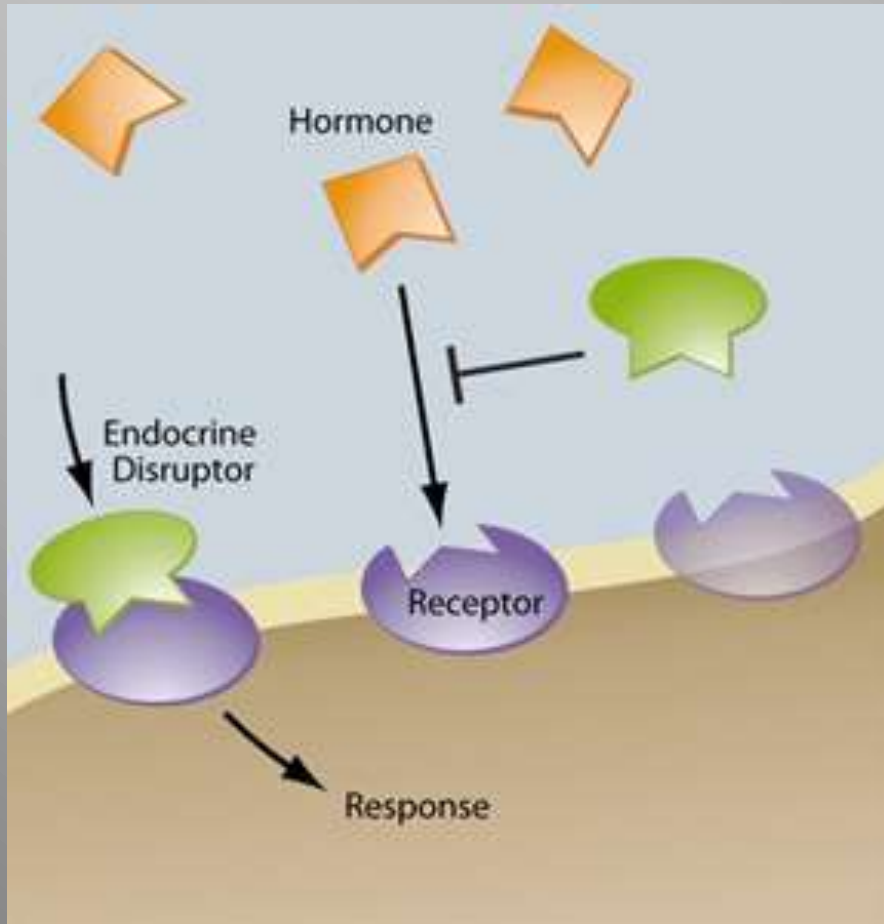
**CONSEQUENCES OF GESTATIONAL
DIABETES IN THE LONG TERM.....**

THROUGH THE LOOKING GLASS



- During post-partum most of the women return to euglycemic state, however carbohydrate intolerance can return with age.
- Women with GDM are at increased risk for the development of diabetes, usually type 2, after pregnancy.

Glucose intolerance during pregnancy as a predictor of maternal long-term health



“ENDOCRINE DISRUPTORS have been defined as exogenous substances that alter function(s) of the endocrine system and consequently cause adverse health effects in an intact organism, its progeny, or subpopulations”

**The International Program for
Chemical Safety**

- **WHAT HAPPEN IF MOTHERS ARE EXPOSED TO THESE COMPOUNDS DURING PREGNANCY?**

RISKS FACTORS FOR GDM AND LONG-TERM COMPLICATIONS

- ✓ **Age**
- ✓ **History of gestational diabetes**

ENDOCRINE DISRUPTOR CHEMICALS

- ✓ **Sedentary lifestyle**
- ✓ **History of smoking**
- ✓ **PCOs**

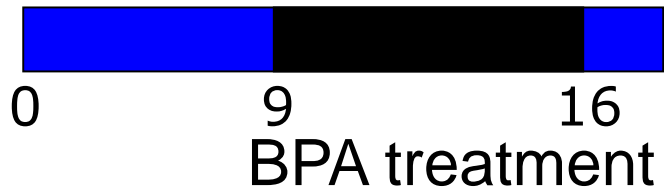
BISPHENOL-A CONCENTRATION IN HUMAN SAMPLES:

BPA has been detected in 93% of the urine samples in USA (Calafat et al, 2008)

0.3-4.4 ng/ml (1.3-19.4 nM) unconjugated BPA in human blood from adult men and women (Vandenberg et al, EHP 2010)

BPA levels detected in amniotic fluid, neonatal blood, placenta, cord blood and human breast milk.

Bisphenol-A action on pregnant mice



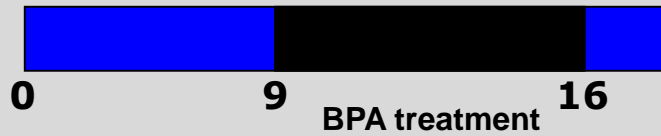
End points measured at pregnancy days 17 and 18

BPA 10 $\mu\text{g}/\text{kg}/\text{day}$

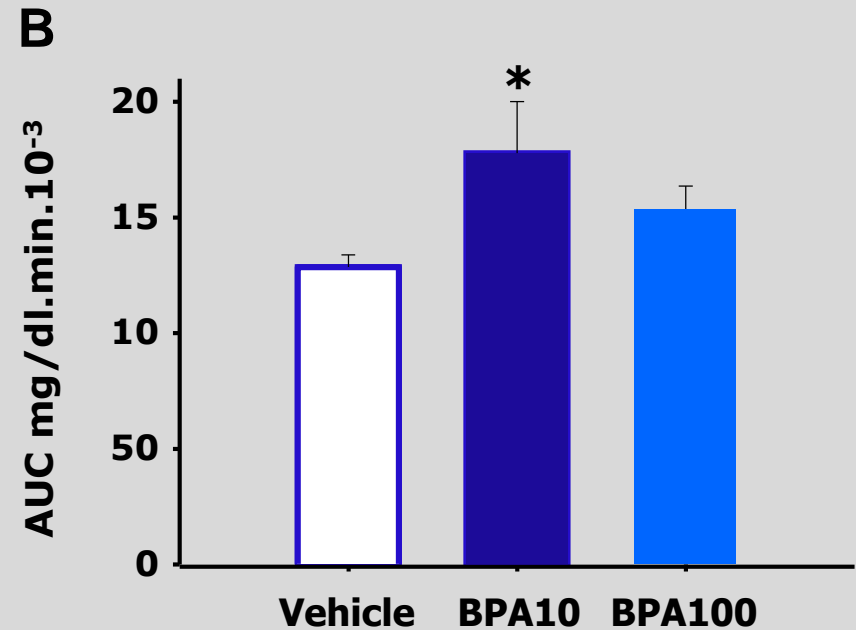
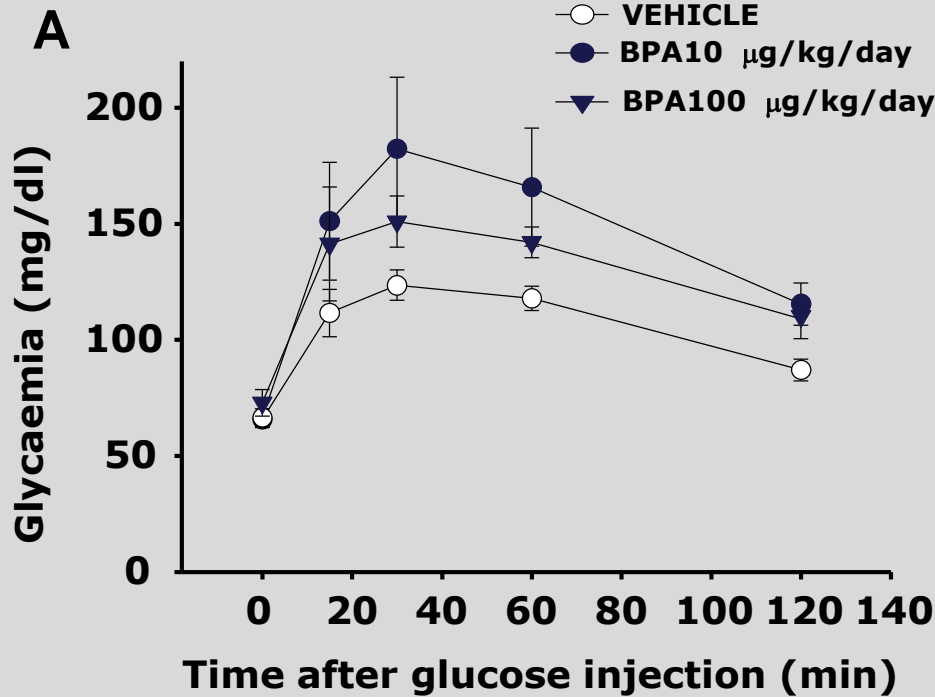
BPA 100 $\mu\text{g}/\text{kg}/\text{day}$



Pregnancy



End points measured at pregnancy days 17 and 18



GLUCOSE TOLERANCE TEST

Insulin signaling in BPA-10 pregnant treated mice

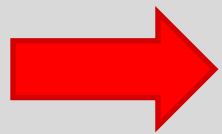
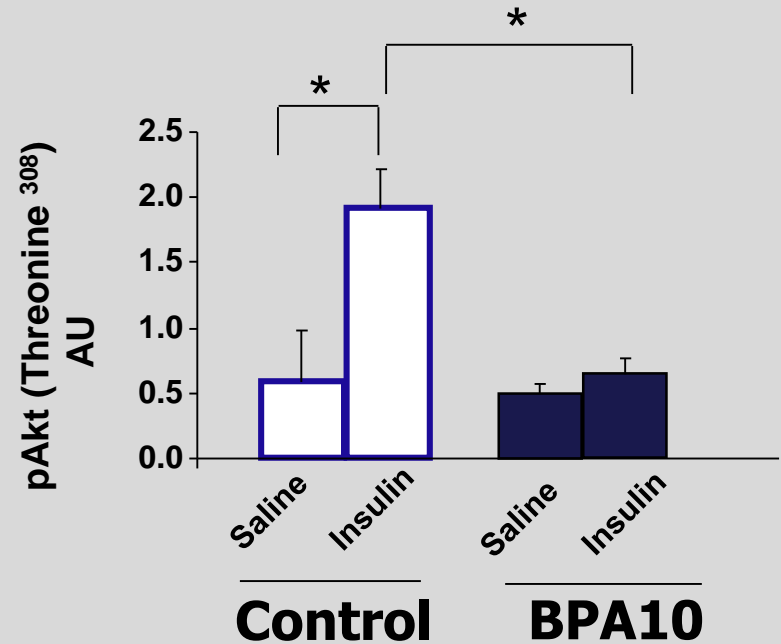
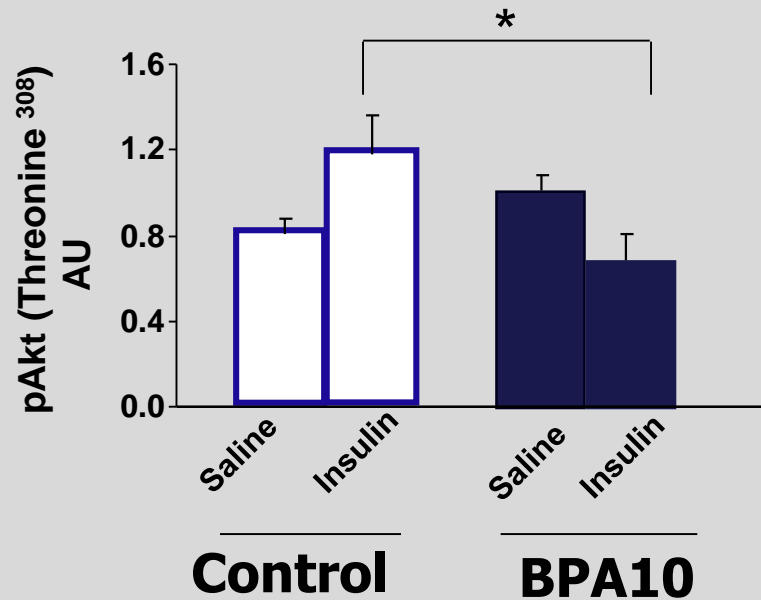
Liver

Skeletal muscle

A



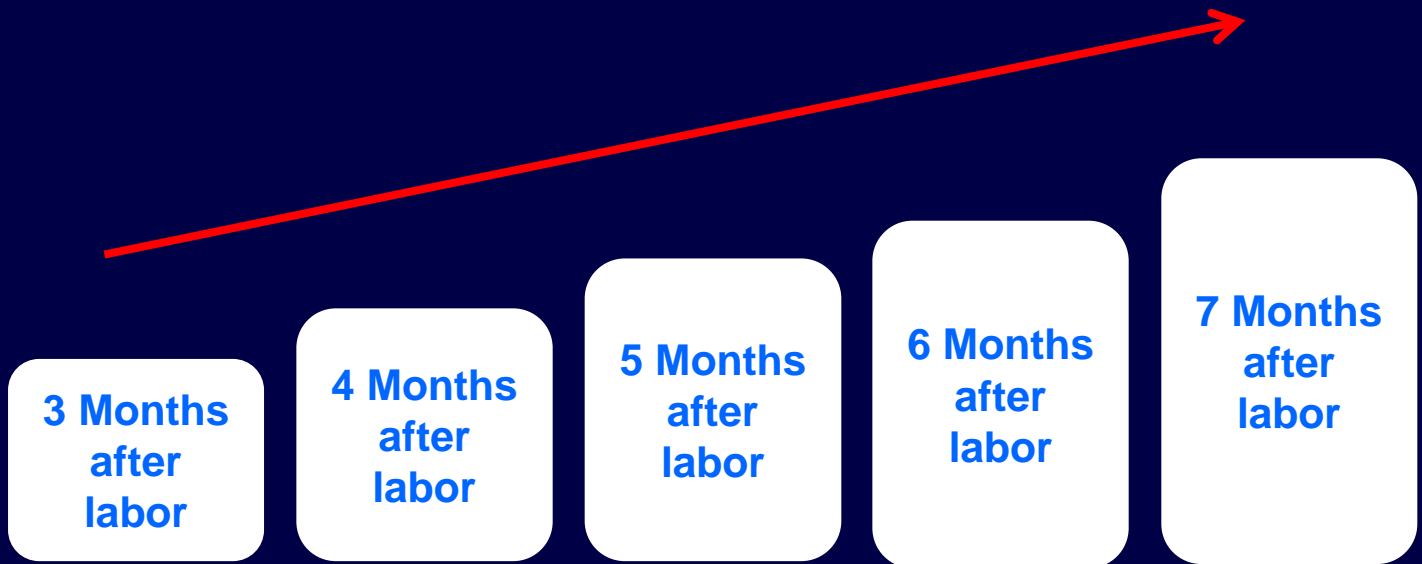
B



Bisphenol-A alters glucose and lipid

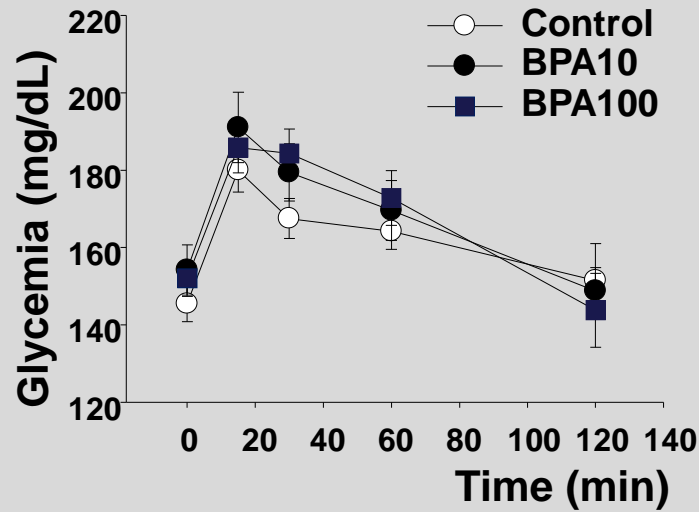
metabolism during pregnancy

EVOLUTION OF THE MOTHER AFTER DELIVERY

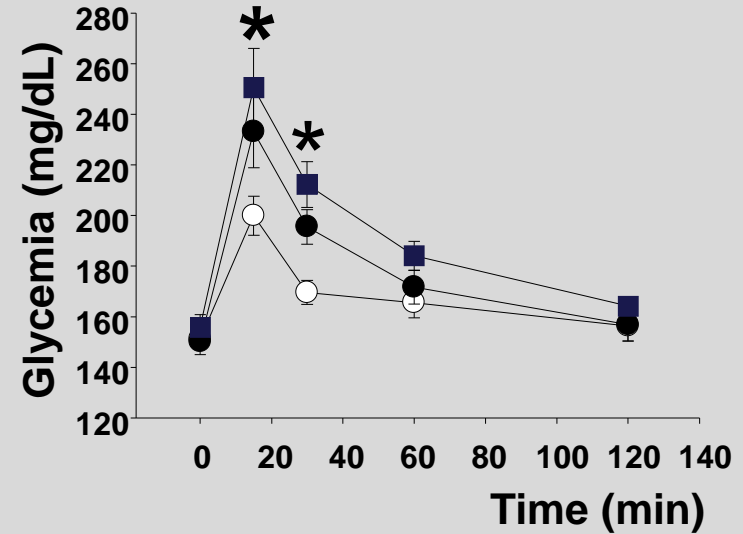


GLUCOSE TOLERANCE TEST in the mother after labor

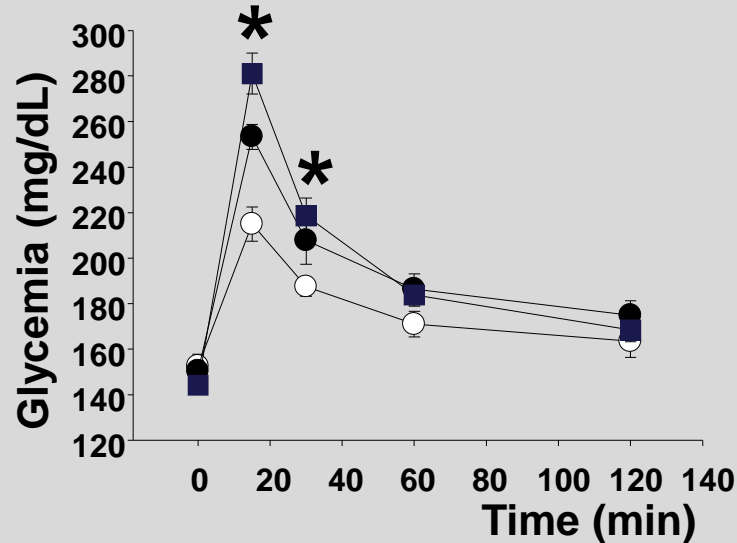
A 3 MONTHS POSTPARTUM



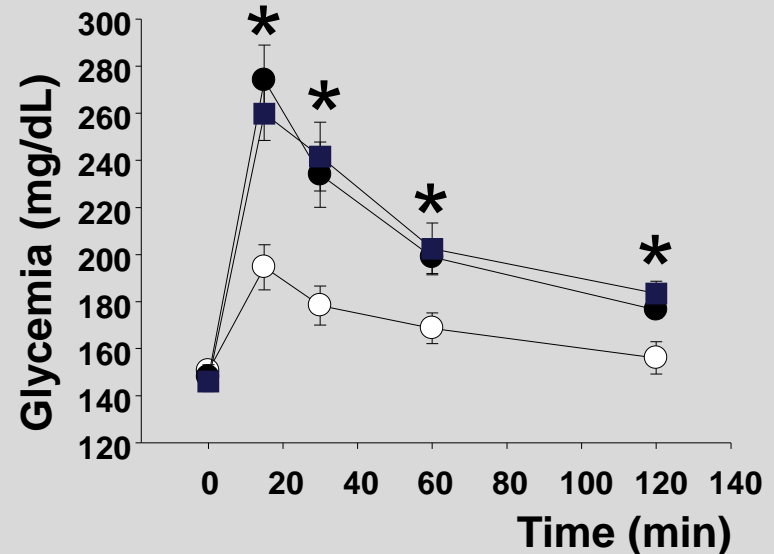
B 4 MONTHS POSTPARTUM



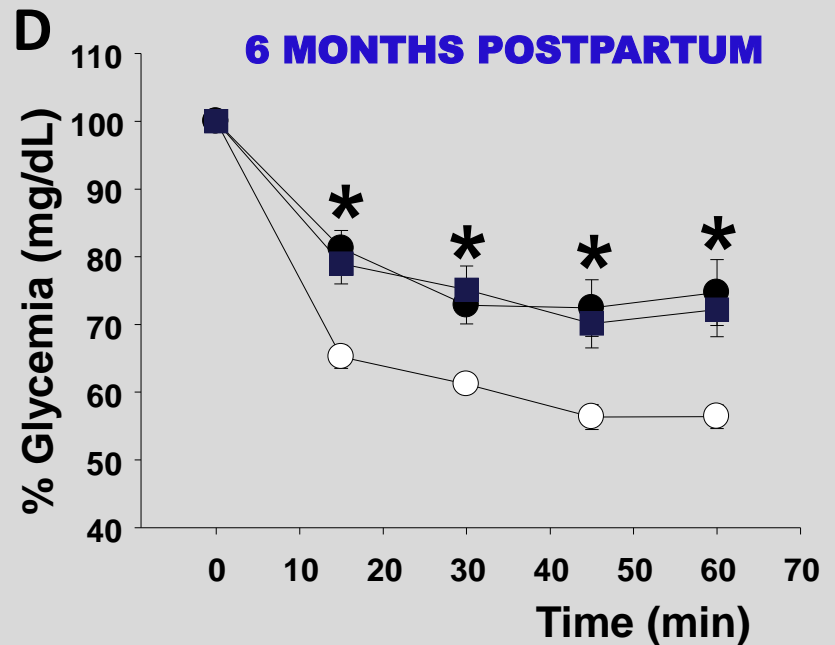
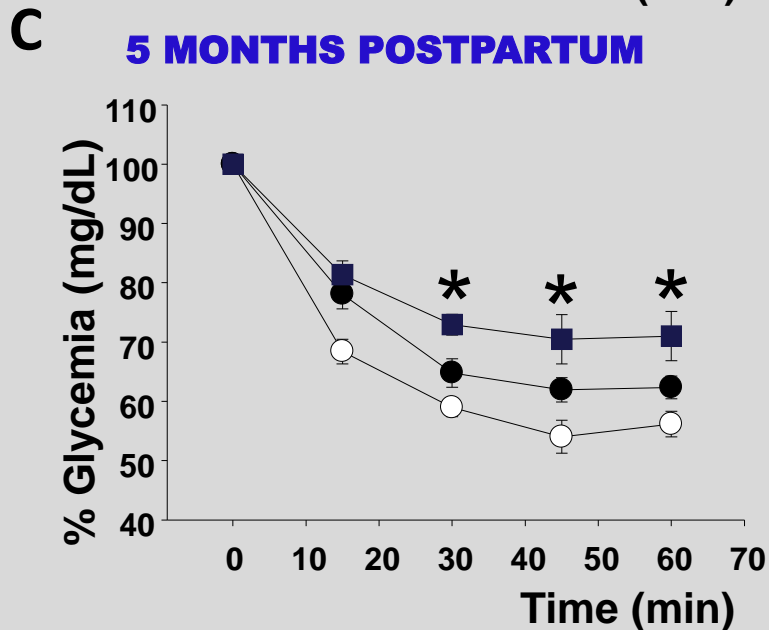
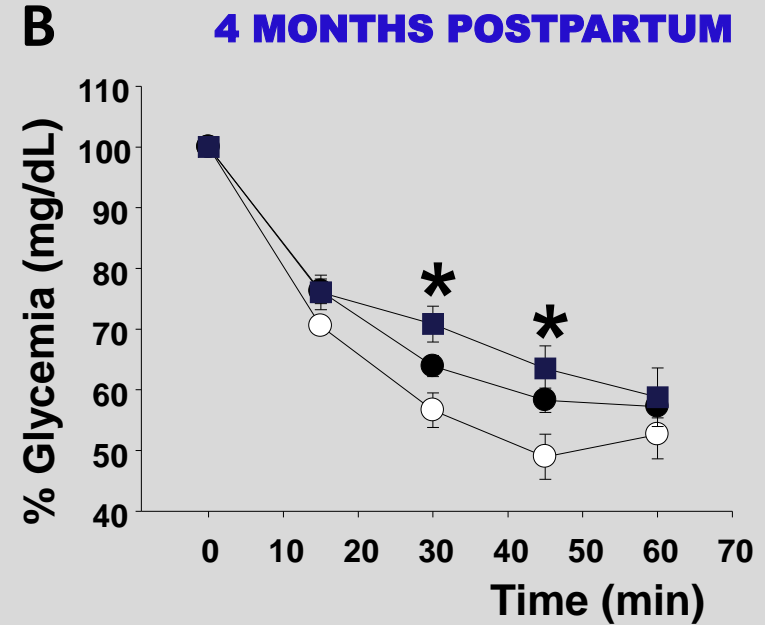
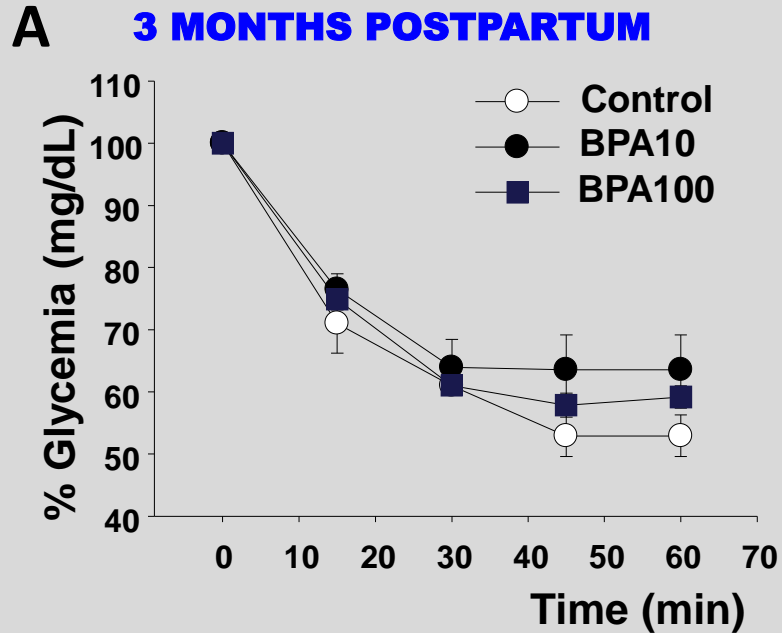
C 5 MONTHS POSTPARTUM



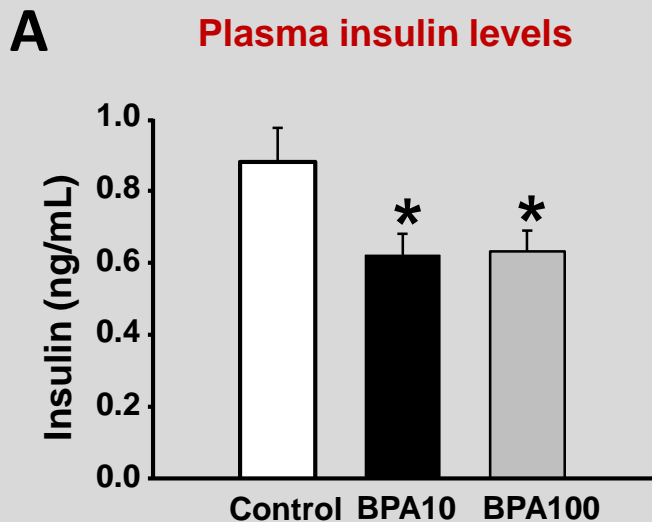
D 6 MONTHS POSTPARTUM



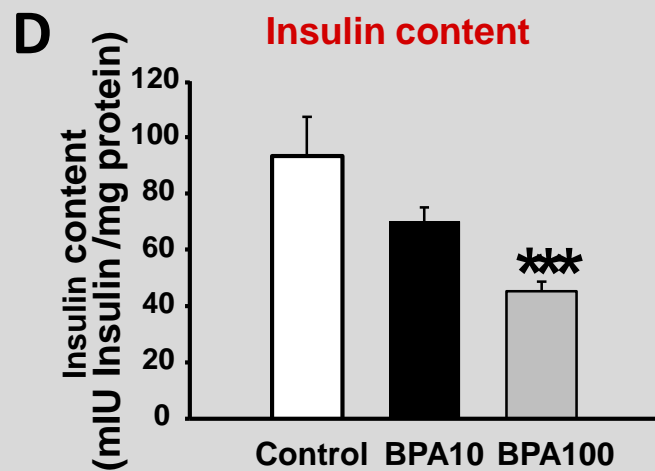
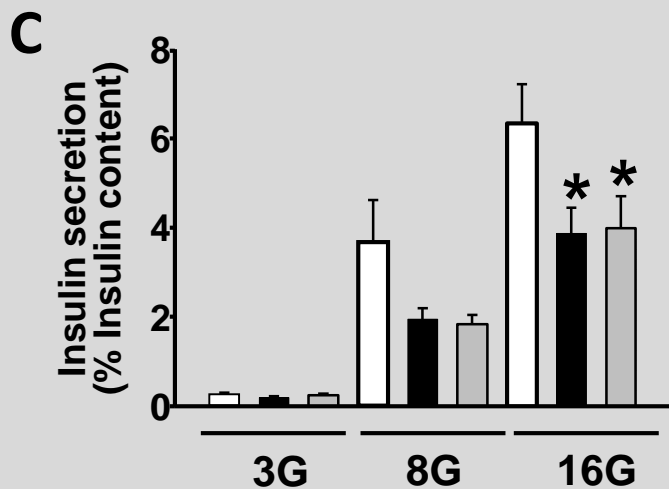
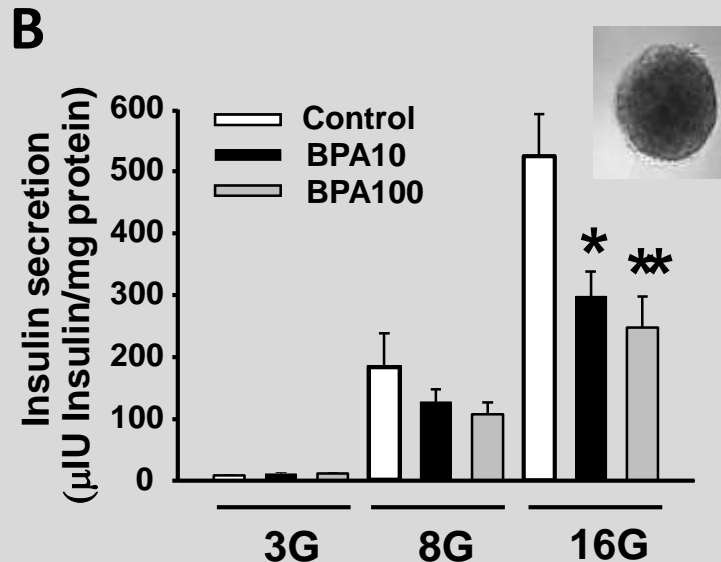
INSULIN TOLERANCE TEST in the mother after labor



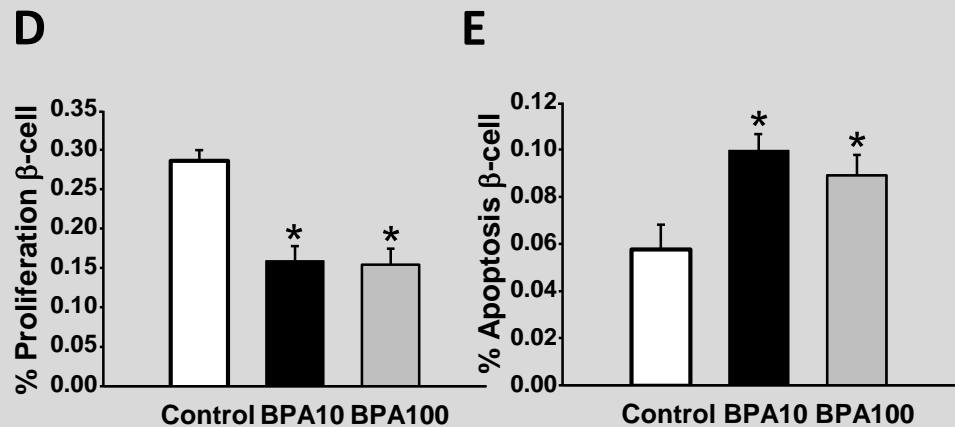
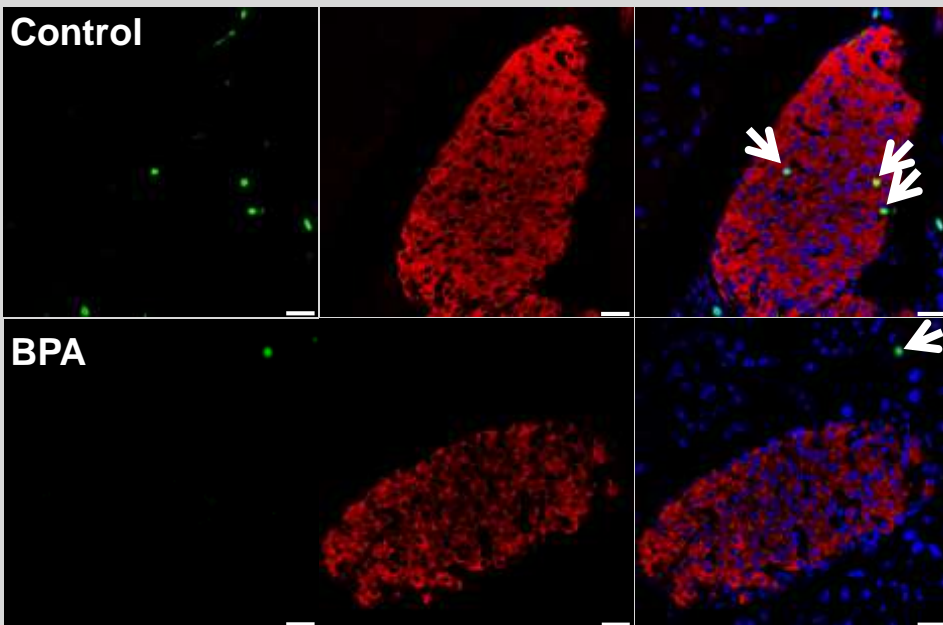
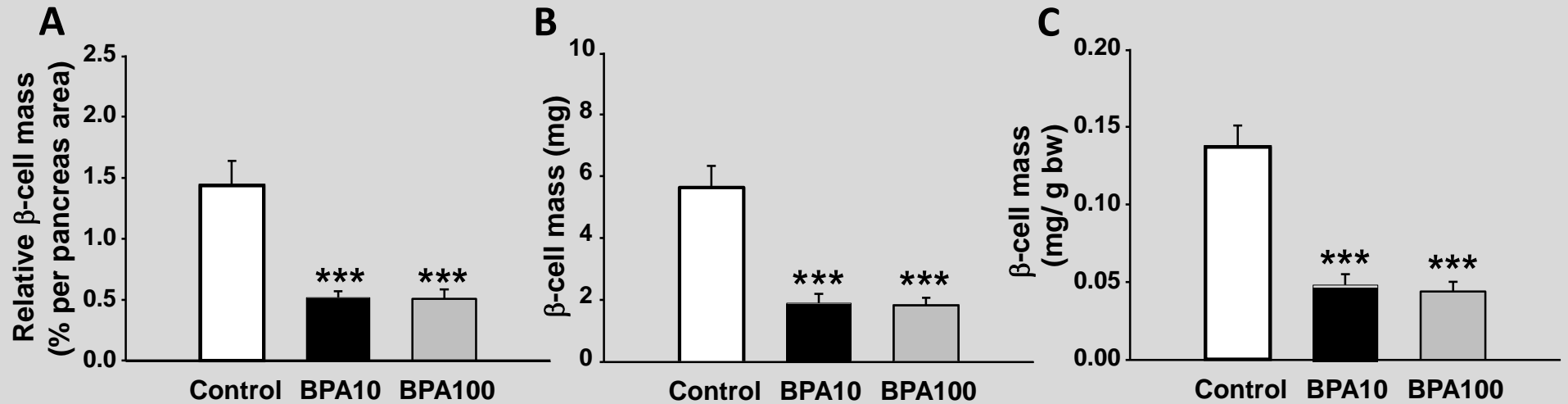
Seven months after labor mothers that have been treated with BPA show a decline of pancreatic β -cell function

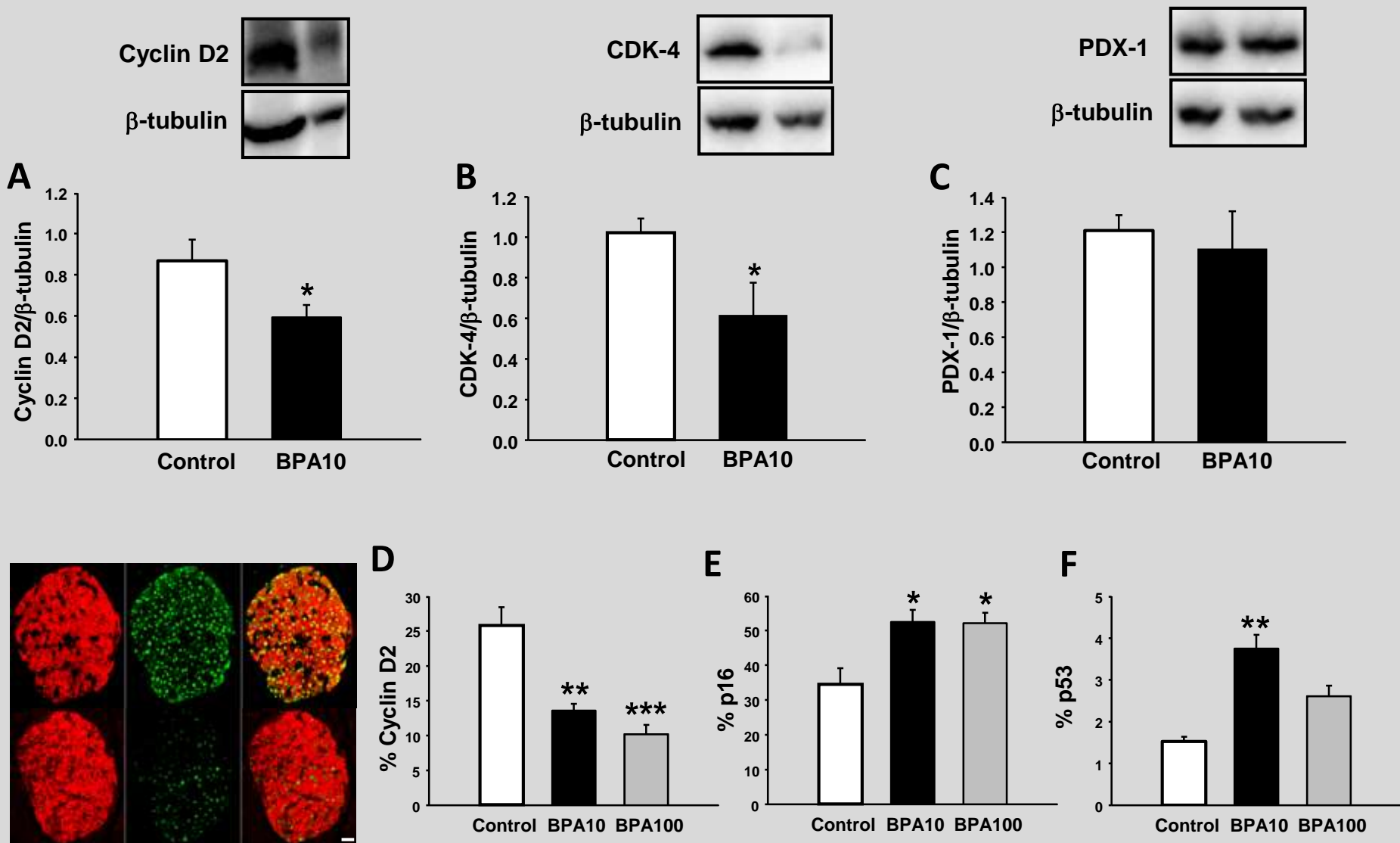


Glucose-stimulated insulin secretion



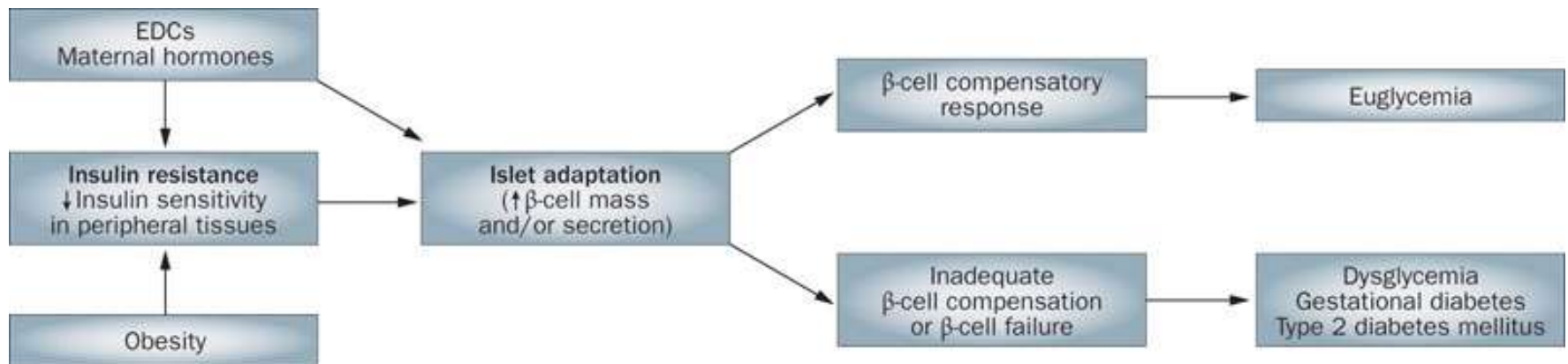
Seven months after labor mothers that have been treated with BPA show reduced β -cell mass, reduced β -cell proliferation and increase rate of apoptosis





- **BPA exposure in mice during pregnancy resulted in an impairment of glucose tolerance and decreased insulin sensitivity in mothers.**
- **Alterations on glucose metabolism were resolved after parturition but were triggered again some months later**
- **Six months after delivery those moms that have been treated with BPA during pregnancy exhibited marked glucose intolerance and insulin resistance**
- **Seven months after delivery they showed decrease β -cell function, β -cell mass and increased apoptosis.**
- **They also showed an altered expression of several cell cycle regulators.**
- **BPA exposure during pregnancy could be considered a new risk factor for the deterioration of maternal glucose metabolism and the increased occurrence of diabetes**

Figure 1 Pregnancy-like actions of endocrine disrupting chemicals on islet function and glucose homeostasis



Alonso-Magdalena, P. *et al.* (2011) Endocrine disruptors in the etiology of type 2 diabetes mellitus
Nat. Rev. Endocrinol. doi:10.1038/nrendo.2011.56



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