

# II International Health Congress Gaia-Porto

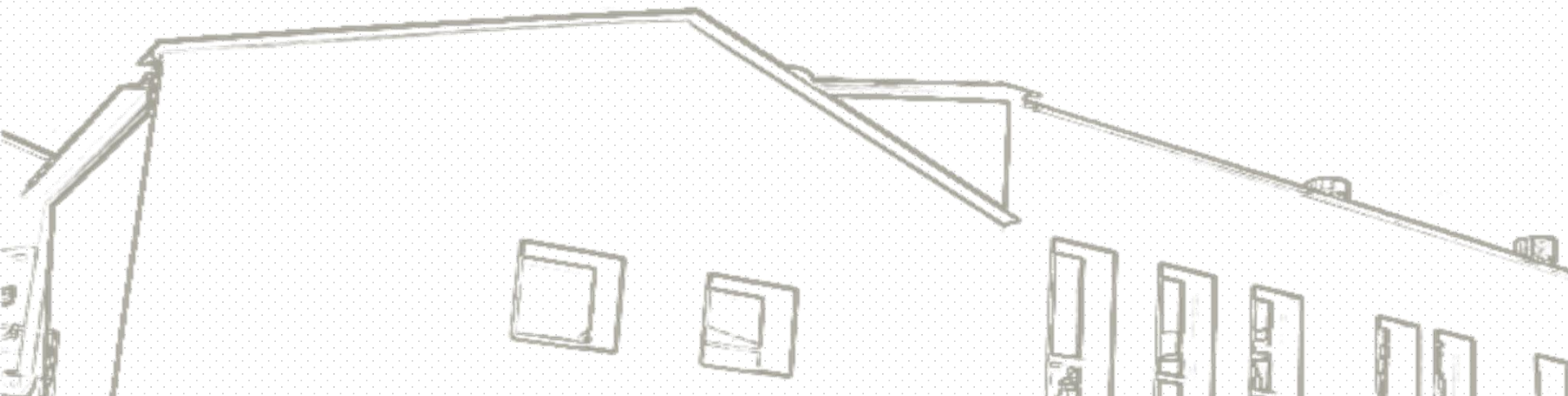
19<sup>th</sup>-21<sup>st</sup> November 2015

## Bisphenol A alters transcript levels of biomarker genes for Major Depressive Disorder

**Edna Ribeiro-Varandas**<sup>\*1,2</sup>, H. Sofia Pereira<sup>2</sup>, Wanda Viegas<sup>2</sup> and Margarida Delgado<sup>2</sup>

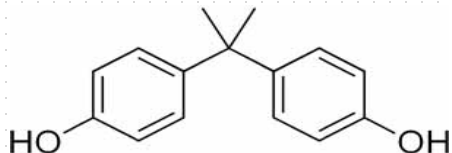
<sup>1</sup> Lisbon School of Health Technology, Instituto Politécnico de Lisboa, Av. D. João II, Lote 4.69.01, 1990-096 Lisboa, Portugal

<sup>2</sup> Landscape, Environment, Agriculture and Food (LEAF), Instituto Superior de Agronomia, Universidade de Lisboa, Tapada da Ajuda 1349-017 Lisboa, Portugal



# INTRODUCTION: Bisphenol A

Bisphenol A synthesised in 1891

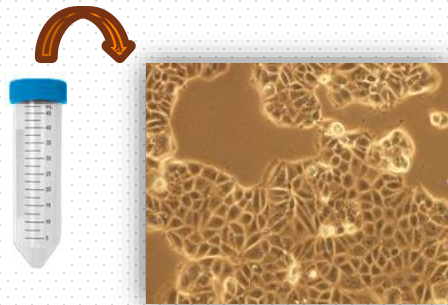


Widespread production since 1940

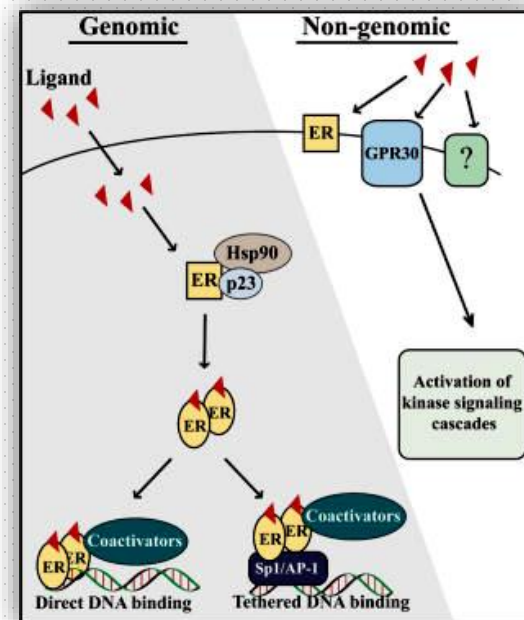


<http://news.softpedia.com/news/Bisphenol-A-Affects-Heart-Valve-Development-in-Fetuses-420407.shtml>

1993 - Increased proliferation rate of MCF7 cells



<http://www.tgrbio.com/cancer-cell-lines-primary-cell-cultures/cell-models-mcf7-cells.html>

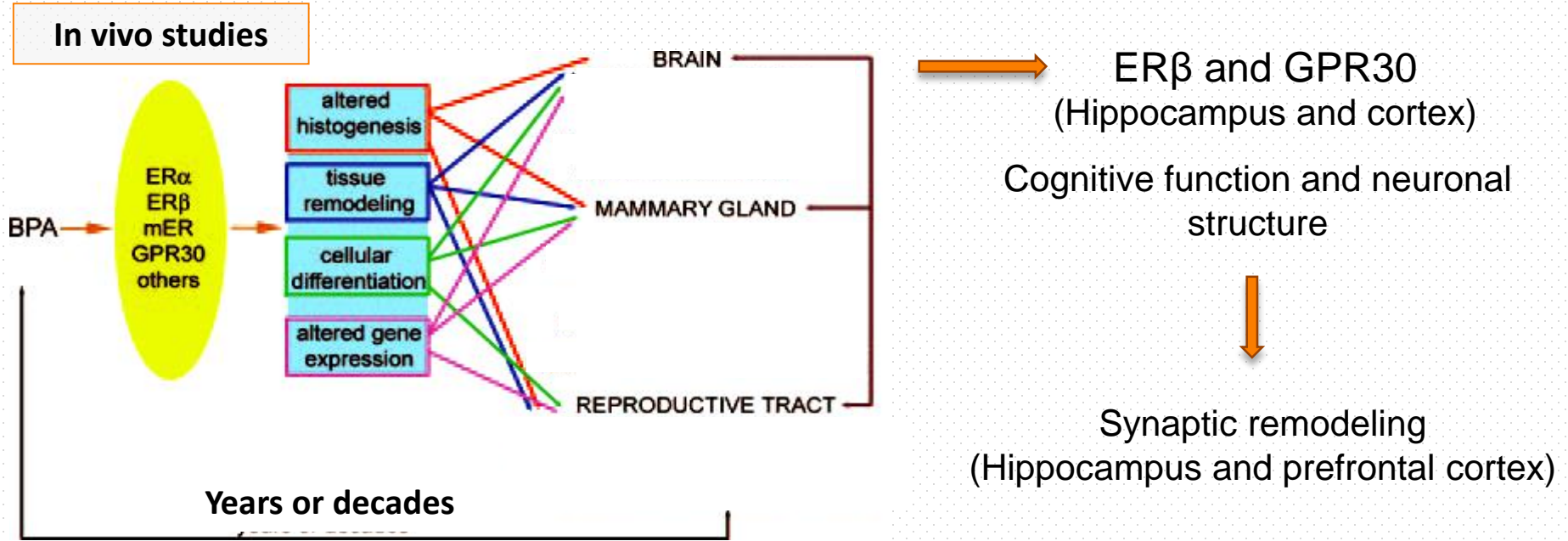


Erin K. Shanle and Wei Xu 2010

BPA as an endocrine disruptor chemical

# INTRODUCTION: Bisphenol A

2000-2014 -Worldwide risk assessment of BPA

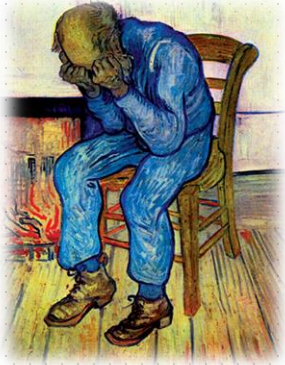


Adapted from Vandenberg L. et al 2009

## Human epidemiological studies

Childhood learning development and behavior problems  
Neuropsychiatric disorders (anxiety/depression)

# INTRODUCTION: Major Depressive Disorder (MDD)



MDD is a moderately heritable disorder characterized by one or more Major Depressive Episodes

Laboratory tests to support MDD diagnosis are not available



Diagnosis and treatment are based on various signs and symptoms not always fitting into strict diagnostic categories

Research for biological markers of neuropsychiatric disorders has been a challenge

## **Biomarker genes for MDD diagnostics :**

***PLSCR1*** (phospholipid scramblase 1): Multiple cellular processes - DNA binding, calcium ion binding, epidermal growth factor receptor binding, protein binding...

***CAPRN1*** (cell cycle associated protein 1): RNA binding

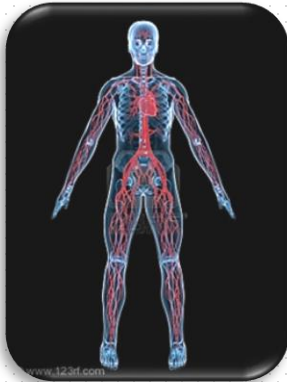
***PROK2*** (Prokineticin 2): Component of the circadian clock

***ZBTB16*** (zinc finger and BTB domain containing 16 ): Involved in cell cycle progression, and interacts with a histone deacetylase

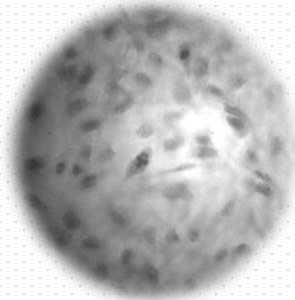
# METHODS: Cellular Models

## Vascular system

Human Umbilical Vein Endothelial Cells



HUVEC

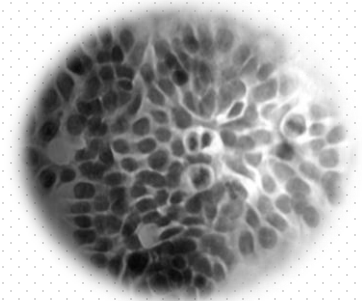


## Digestive tract system

Human Colon Adenocarcinoma Cells



HT29



BPA “low-dose” effects - Biological changes occurring in the concentration range of typical human exposures

### BPA exposure:

**10ng/ml (44nM)** (found in human biological samples in environmental exposure)

**1µg/ml (4µM)**(found in human biological samples in occupational exposure)

# METHODS

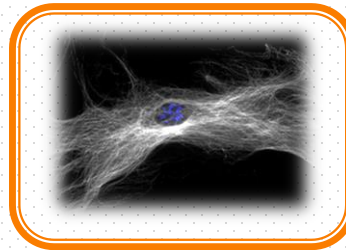
## Cell cultures



HT29 (RPMI) HUVEC (EGM-2)



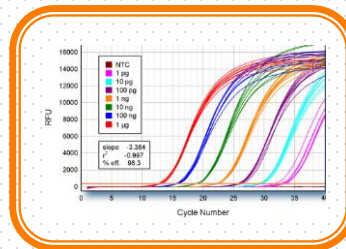
## Cytological analysis



Immunofluorescence  
DNA DAPI stain



## Transcriptional analysis



RNA Extraction

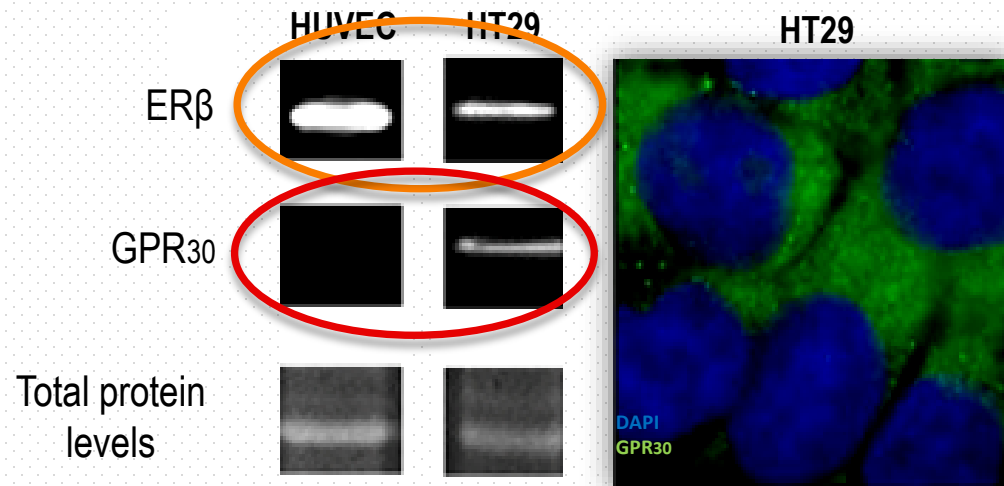


qRT-PCR

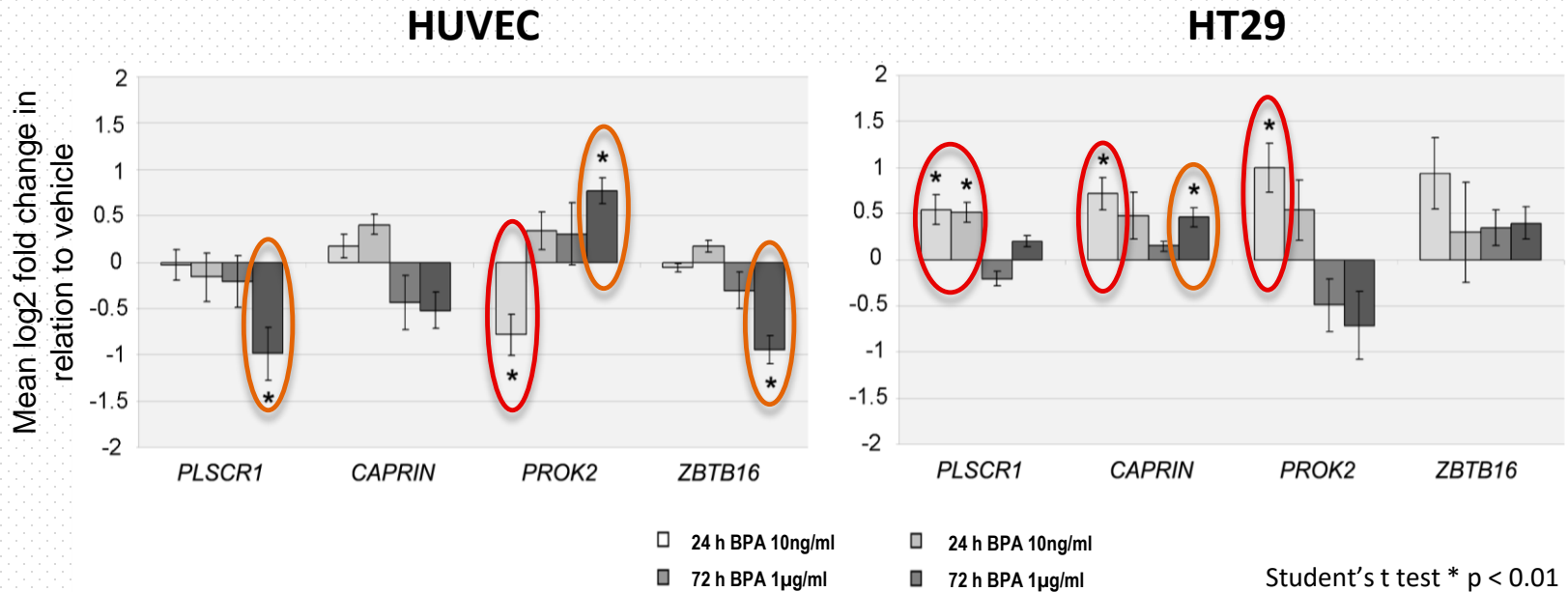
# RESULTS: Characterization of Estrogen Receptors

HUVEC and HT29 cell line - Negative for ER $\alpha$   
- Positive for ER $\beta$

HUVEC - Negative for GPR30 in culture conditions



# RESULTS: BPA transcriptional effects on MDD biomarkers



**HUVEC:** BPA induces more marked effects after prolonged exposures (72 h) to the higher BPA dose

**HT29:** Stronger effects are detected after short exposure (24 h) to the lower assayed concentration

Edna Ribeiro-Varandas, H Sofia Pereira, Wanda Viegas, Margarida Delgado. Bisphenol A alters transcript levels of biomarker genes for Major Depressive Disorder in Vascular Endothelial Cells and Colon Cancer Cells.

Accepted in Chemosphere ID:CHEM36227.

# CONCLUSION

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- MDD biomarkers are differentially altered by BPA
- Importance of a better understanding of BPA cellular effects
- Substantiate increasing concerns that this xenoestrogen may have hazardous effects on human health

## Importance of BPA risk assessment



# ACKNOWLEDGMENTS



# FCT

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MINISTÉRIO DA CIÊNCIA, TECNOLOGIA E ENSINO SUPERIOR

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