Quantitative image based analysis of endocrine disruptor effects on mitochondria morphology-function in prostate cancer cells
Aurélie Charazac, Célia Decondé Le Butor, Kévin Giulietti, Jean-Marc A. Lobaccaro, Silvère Baron, Jérôme Gilleron, Patrick Fenichel, Xavier Descombes, Frédéric Bost, Clavel Stéphan, et al.

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Quantitative image based analysis of endocrine disruptor effects on mitochondria morphology-function in prostate cancer cells.

Charazac Aurélie, Decondé le Butor Célia, Giulietti Kévin, Lobaccaro Jean Marc, Baron Silvère, Gilleron Jérôme, Fénichel Patrick, Descombes Xavier, Bost Frédéric, Clavel Stéphan & Chevalier Nicolas.
Endocrine Disruptor Compounds

"An endocrine disruptor is an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub) populations."

World Health Organization

Pesticides
- Aldrine...

Perfluorinated Compounds
- PFOA...

Flame Retardants
- BDE 28...

Polychlorinated Biphenyls
- PCB 153...

Dioxins
- TCDD...

Pineal gland
- Hypothalamus
- Pituitary gland
- Thyroid gland
- Parathyroid gland
- Thymus
- Adrenal gland
- Pancreas
- Testis

Centre Méditerranéen de Médecine Moléculaire Inserm U1065
Urgent need for multiparametric, robust and high throughput cell-based assay:

- To investigate the mechanisms underlying the adverse effects of known EDCs
- To identify new compounds with endocrine-disrupting potential
Mitochondria, a cell sensor

Introduction - Aim

Apoptosis

Healthy

Stress

Mitochondria, a cell sensor

Introduction ~ Aim

Apoptosis
Calcium signalling
Cell growth and differentiation

Healthy

Stress
Cell cycle control
Cell death

Mitochondria, a cell sensor

Introduction - Aim

Alteration of **mitochondrial forms and functions** by EDCs?

1) Quantitative image based analysis of mitochondrial functions
   → High throughput screening

2) Computational image based analysis of mitochondrial morphology
   → Image analysis and classification
Multiparametric cell-based assay

Automated image acquisition (Nikon A1R-20X)

1) Dapi masking: cell counting

2) Dye masking: fluorescence intensity

Image processing
Multiparametric cell-based assay

Automated image acquisition
(Nikon A1R-20X)

Image processing

1) Dapi masking:
cell counting

2) Dye masking:
fluorescence intensity

- Multiparameter:
  - mitochondrial membrane potential (MitoTracker Red™)
  - superoxide anion production (MitoSox™)
  - mitophagy (Keima probe)
EDCs affect the mitochondrial function

- ROS production on DU145:

Superoxide anion production (FI/cell)

EDCs concentration (mol/L)

10^{-12} 10^{-11} 10^{-10} 10^{-9} 10^{-8}

* significantly different from the control, p≤0.005.
EDCs affect the mitochondrial function

Mitochondrial membrane potential on DU145:

- Significantly different from the control, p≤0.005.

Mitochondrial membrane potential (FI/cell) vs. EDCs concentration (mol/L)

* significantly different from the control, p≤0.005.
Forms classification of mitochondrial network

- Collaboration with
Forms classification of mitochondrial network

• Collaboration with

Fragmented, Tubular, Hyperfused
Exemple of developed method

Tubular

Aggregates Tubular Hyperfilamentous
Exemple of developed method

**Fragmented**
(Rotenone, 100nM)

**Tubular**

**Fused**
(Compound C, 20µM)

Aggregates Tubular Hyperfilamentous
Final Goal

- Development of a multiparametric high throughput cell based screening:
  
  **Mitochondrial functional parameters**
  - Mitochondrial morphological parameters
  - EDCs effect on prostate cancer cells
  
  - Proliferation
  - Cytotoxicity
  - Apoptosis
  - Migration/invasion
  - Maximal glycolitic and respiratory capacity
Final Goal

- Development of a multiparametric high throughput cell based screening:
  - Mitochondrial functional parameters
  - Mitochondrial morphological parameters
  - EDCs effect on prostate cancer cells
    - Proliferation
    - Cytotoxicity
    - Apoptosis
    - Migration/invasion
    - Maximal glycolitic and respiratory capacity

→ Signature of EDCs based on their effects on cell metabolism
→ New perspective in identification and characterization of EDCs
Thanks…

Team 7
Frédéric Bost
Jean-François Tanti
Mireille Cormont
Stephan Clavel
Célia Deconde Le Butor
Lisa Kaminski
Kathiane Laurent
Nicolas Chevallier
Jérôme Gilleron
Jade Evrard
Bastien Vergoni
Gwenaëlle Bouget
Karine Dumas
Marine Bourcier
Mounia Tannour-Louet
Calypso Vacher-Chicane
Sophie Giorgetti-Péraldi
Sophia Fazio
Jean-François Louet
Stéphanie Torrino
Faustine Pastor