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, Giuliani Kévin, Lobaccaro Jean Marc, Baron Silvère, Gilleron Jérôme, Fénichel Patrick, Descombes Xavier, Bost Frédéric, Clavel Stéphan & Chevalier Nicolas.
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
Registration, Evaluation and Authorization of Chemicals

Promotes alternative methods for the hazard assessment of substances.

Adapted from EndocrineScience.org
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
Introduction ~ Aim

Mitochondria, a cell sensor

Fragmented

Tubular

Hyperfused

Apoptosis

Healthy

Stress

Mitochondria, a cell sensor

Introduction ~ Aim

Mitochondria, a cell sensor

Mitochondria, a cell sensor

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
Quantitative image based analysis of mitochondrial functions

Multiparametric cell-based assay

Automated image acquisition
(Nikon A1R-20X)

Image processing

1) Dapi masking:
   cell counting

2) Dye masking:
   fluorescence intensity
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:

![Graph showing ROS production on DU145 with different EDCs concentrations.](image)

* 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.
Forms classification of mitochondrial network

- Collaboration with

Fragmented, Tubular, Hyperfused
Forms classification of mitochondrial network

- Collaboration with

Fragmented, Tubular, Hyperfused

Image | Basic thresholding method | Developed method
--- | --- | ---
![Fragmented](image) | ![Basic thresholding method](image) | ![Developed method](image)
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
  - Proliferation
  - Cytotoxicity
  - Apoptosis
  - Maximal glycolitic and respiratory capacity
  - Migration/invasion

  EDCs effect on prostate cancer cells

  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