Synergistic health effects of chemical pollutants and electromagnetic fields.

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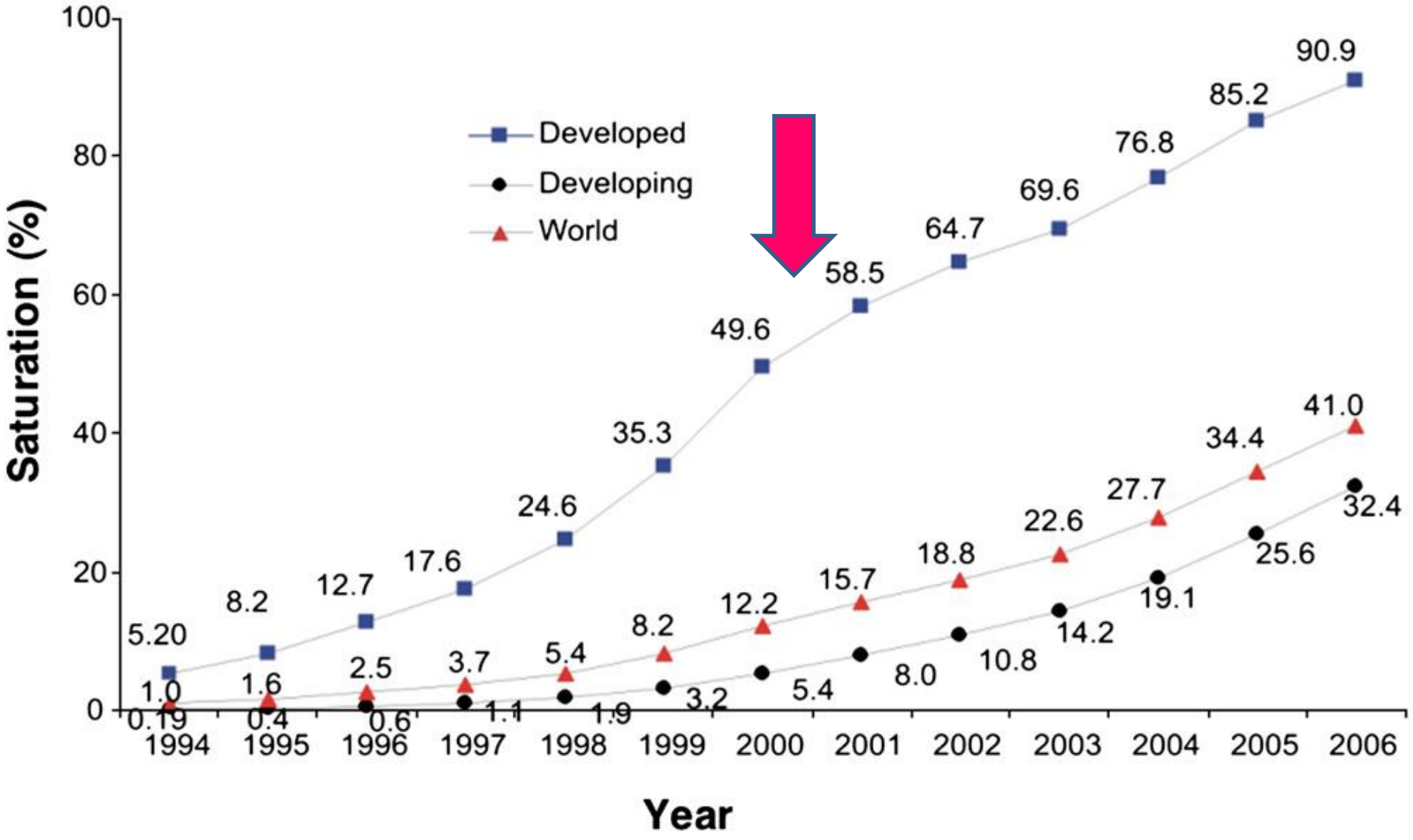
Pollutants

- **Agriculture**
  - ◊ **Pesticides, fertilizers, …** (*France is the 3rd pesticide user in the world, behind USA and India.)*
- **Urban and industrial activities**
  - ◊ **Heavy metals and related, radionuclides**
  - ◊ **Electromagnetic Fields**
  - ◊ **Organics (petrol derivatives…)**



Worldwide saturation: Cell phone subscribers per 100 inhabitants, 1994 to 2006 (data source: International Telecommunication Union, 2007).

Vini G. Khurana, Charles Teo, Michael Kundi, Lennart Hardell, Michael Carlberg,. Cell phones and brain tumors: a review including the long-term epidemiologic data. Surgical Neurology (2009)

Thèse de Doctorat

Présentée à l'Université Blaise Pascal

En vue de l'obtention du titre de

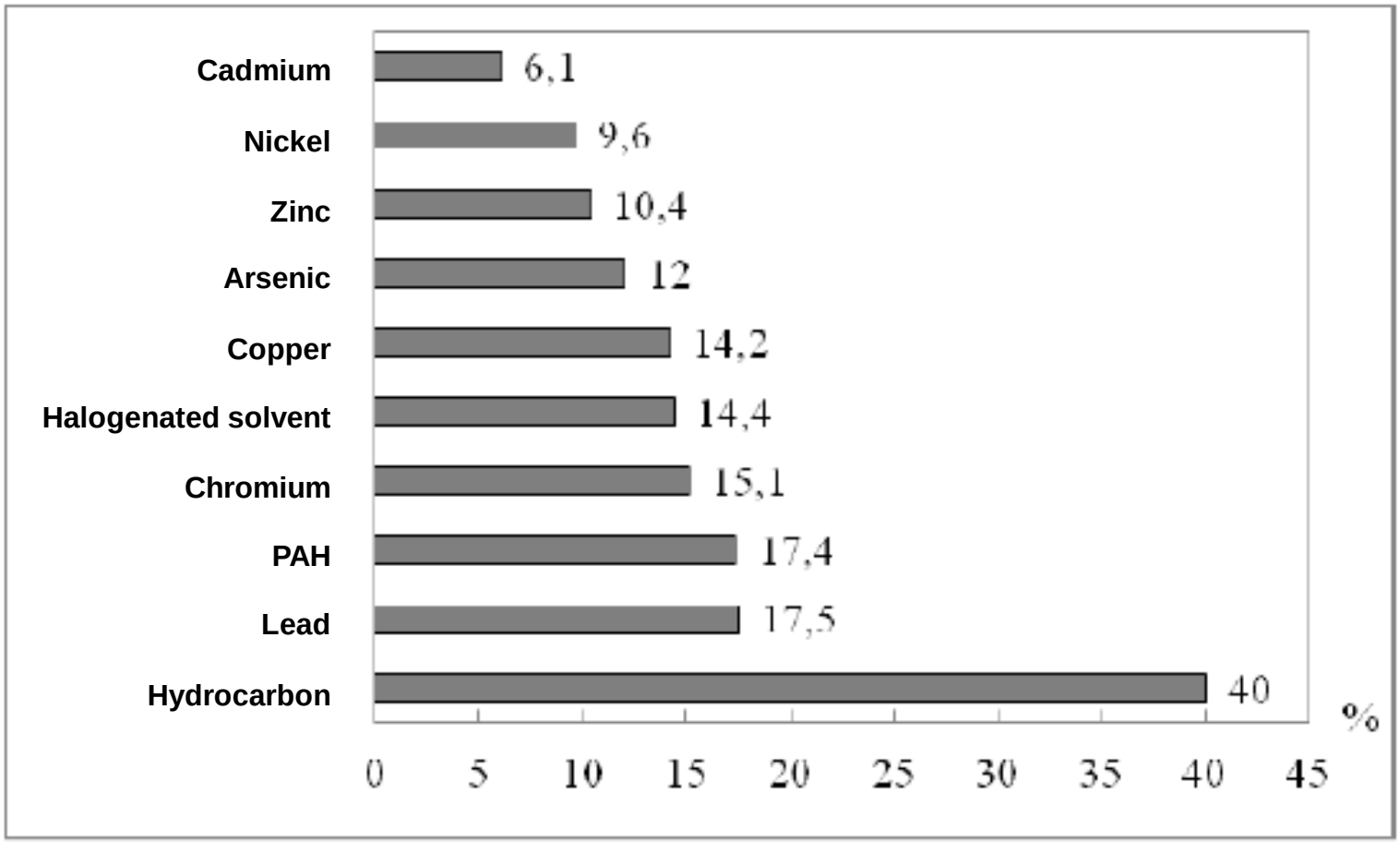
Docteur en Physiologie et Génétique Moléculaire

Présentée par

AUSTRUY Annabelle

Soutenue le 14 juin 2012

Aspects physiologiques et biochimiques de la tolérance à l'arsenic chez les plantes supérieures dans un contexte de phytostabilisation d'une friche industrielle

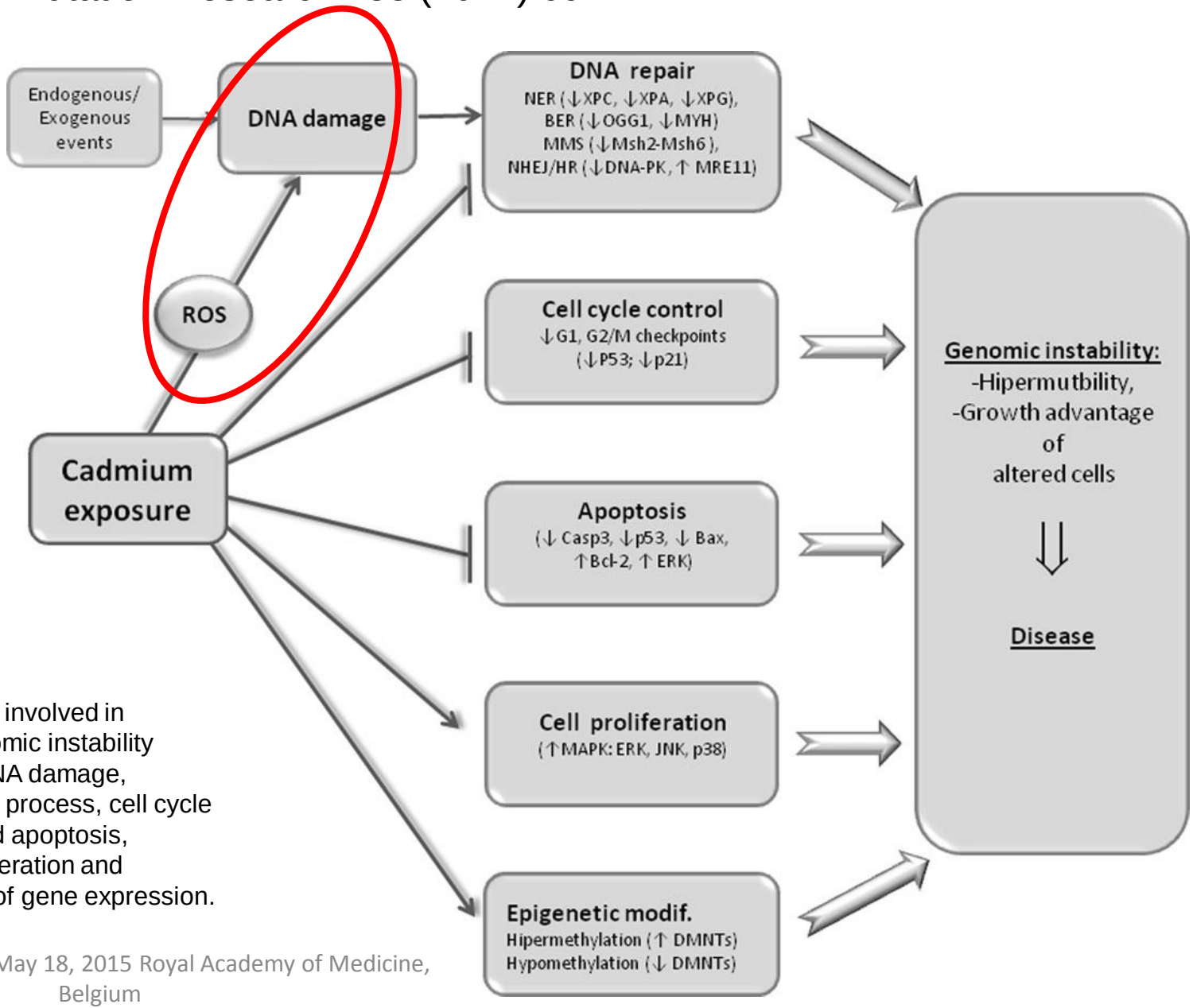


Main pollutants described in contaminated sites in France (BASOL, 2006).

Review

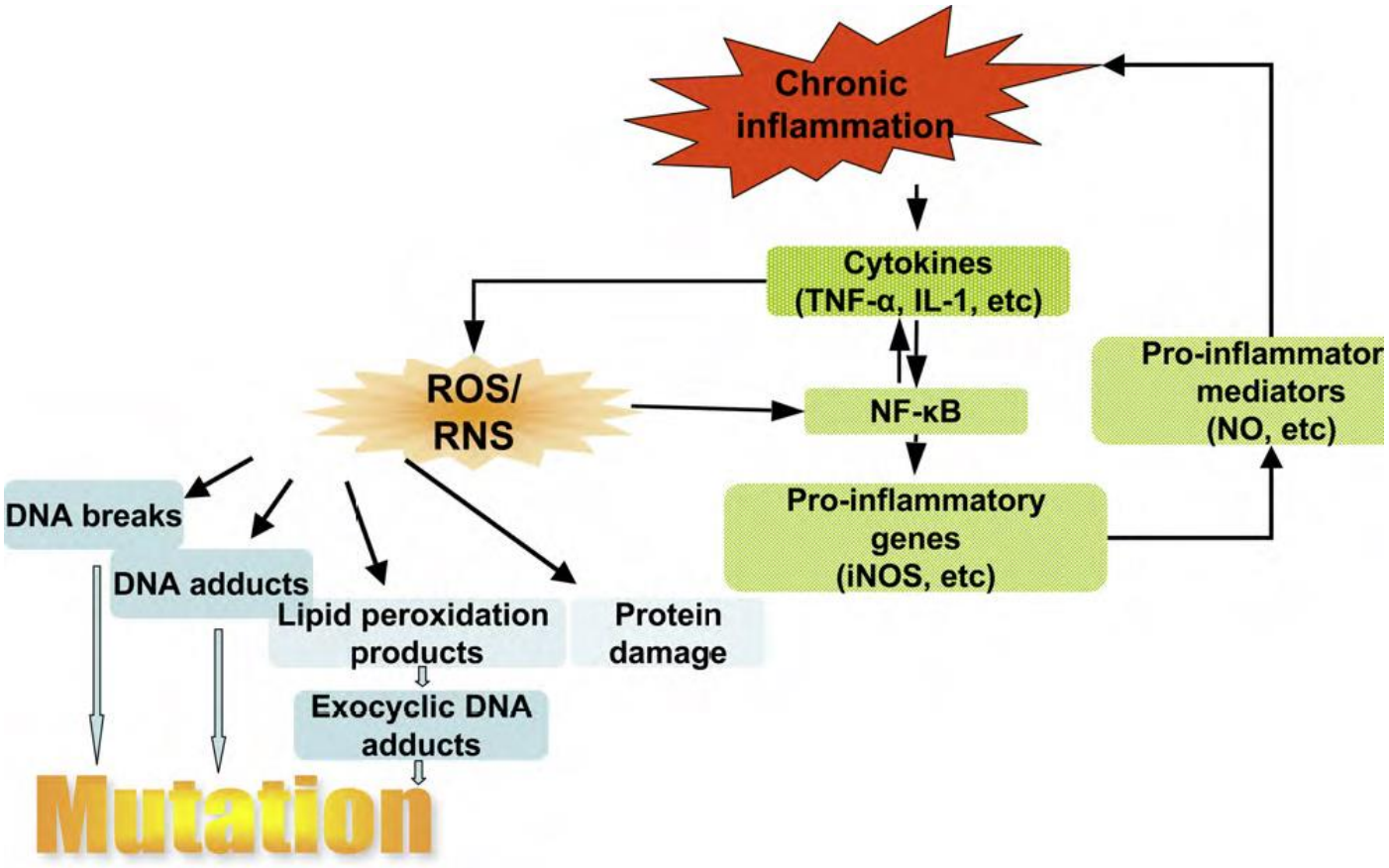
Mechanisms of cadmium induced genomic instability

Metka Filipic. Mutation Research 733 (2012) 69– 77



Proposed mechanisms involved in cadmium induced genomic instability through induction of DNA damage, inhibition of DNA repair process, cell cycle progression control and apoptosis, stimulation of cell proliferation and epigenetic modulation of gene expression.

Review
Chronic inflammation and mutagenesis
Lynnette R. Ferguson. Mutation Research 690 (2010) 3–11



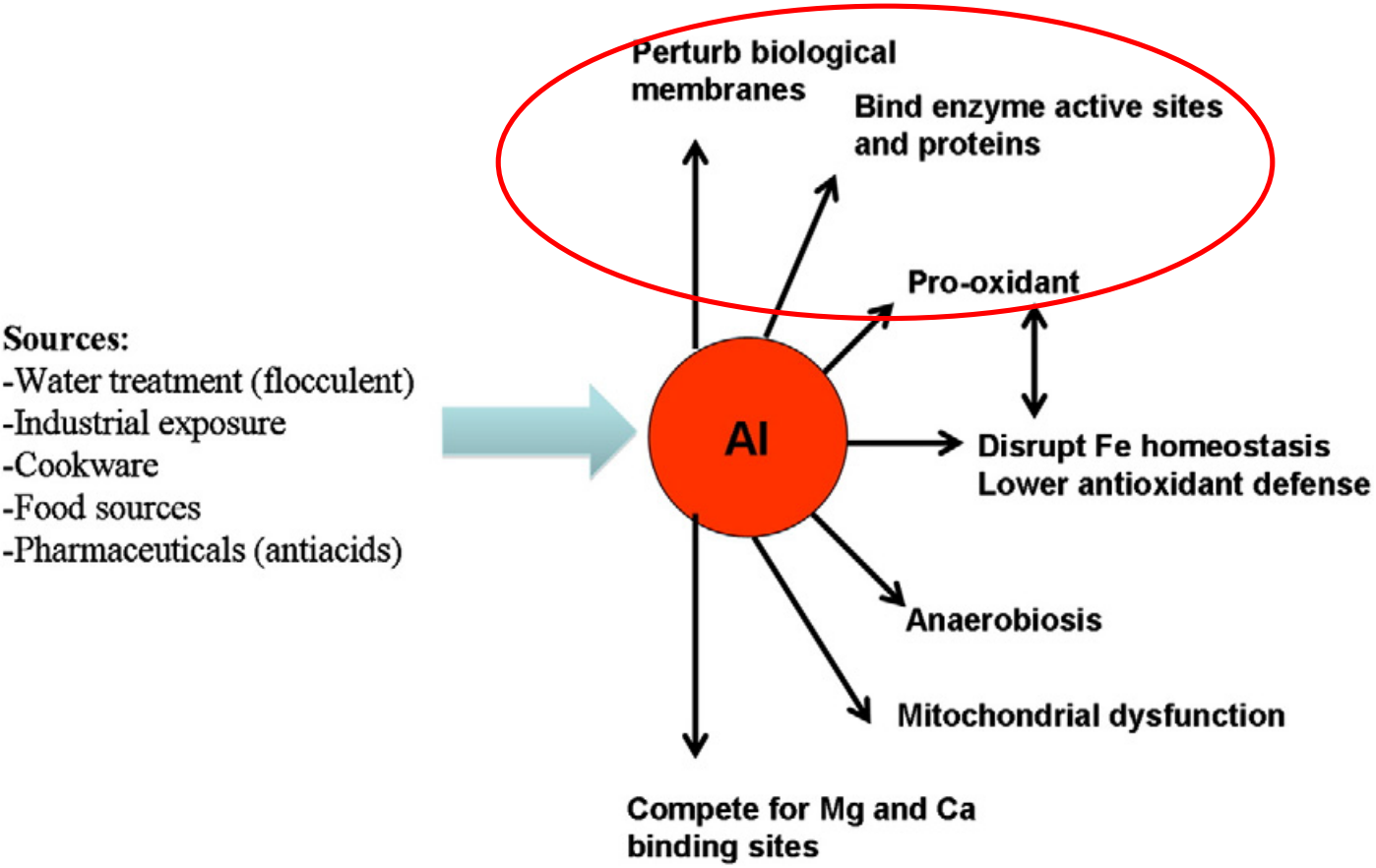
Ways in which chronic inflammation can lead to mutagenesis

Review Article

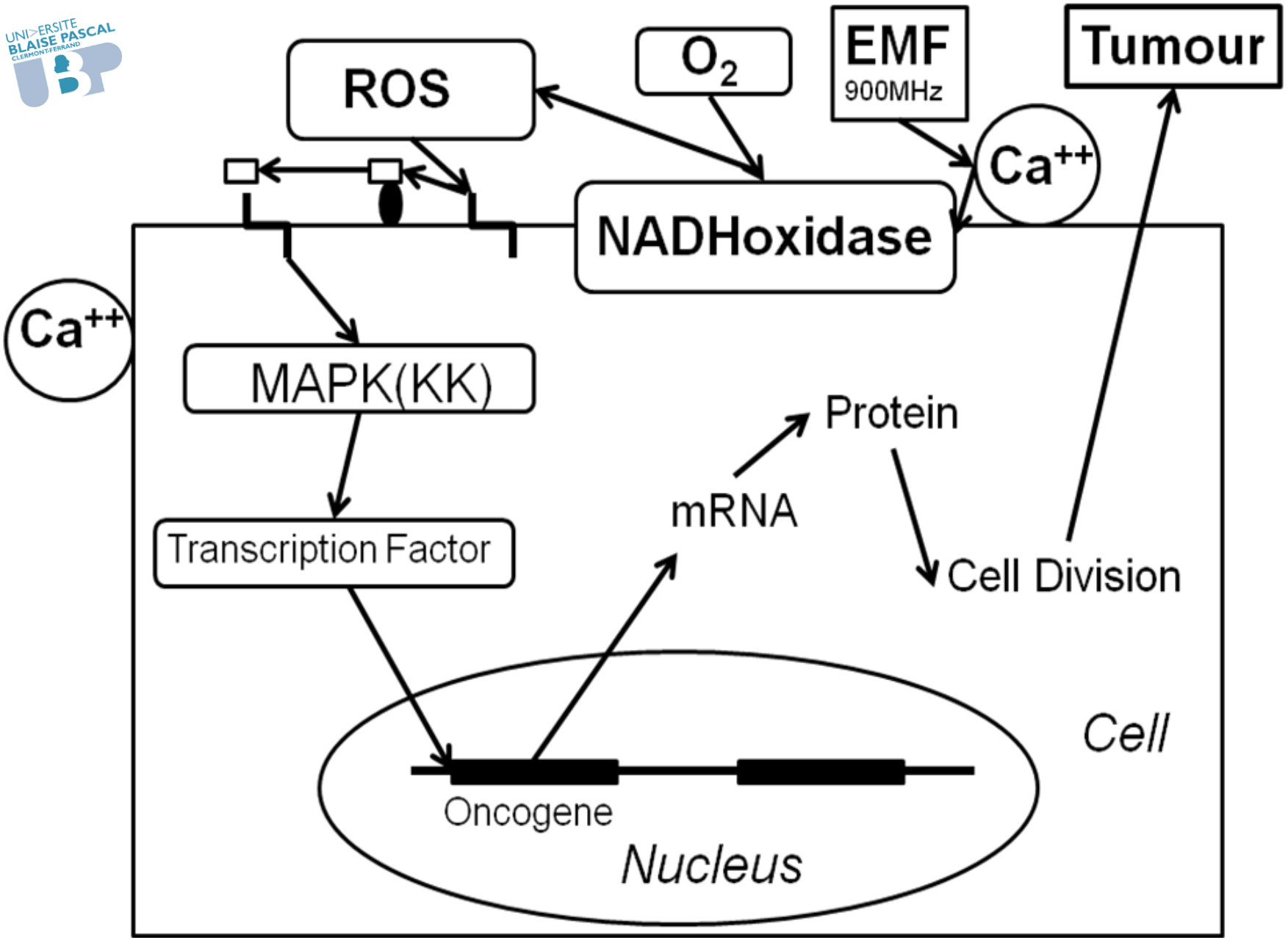
Hepatic response to aluminum toxicity: Dyslipidemia and liver diseases

Ryan J. Mailloux, Joseph Lemire, Vasu D. Appanna.

E X P E R I M E N T A L C E L L R E S E A R C H 3 1 7 (2 0 1 1) 2 2 3 1 – 2 2 3 8

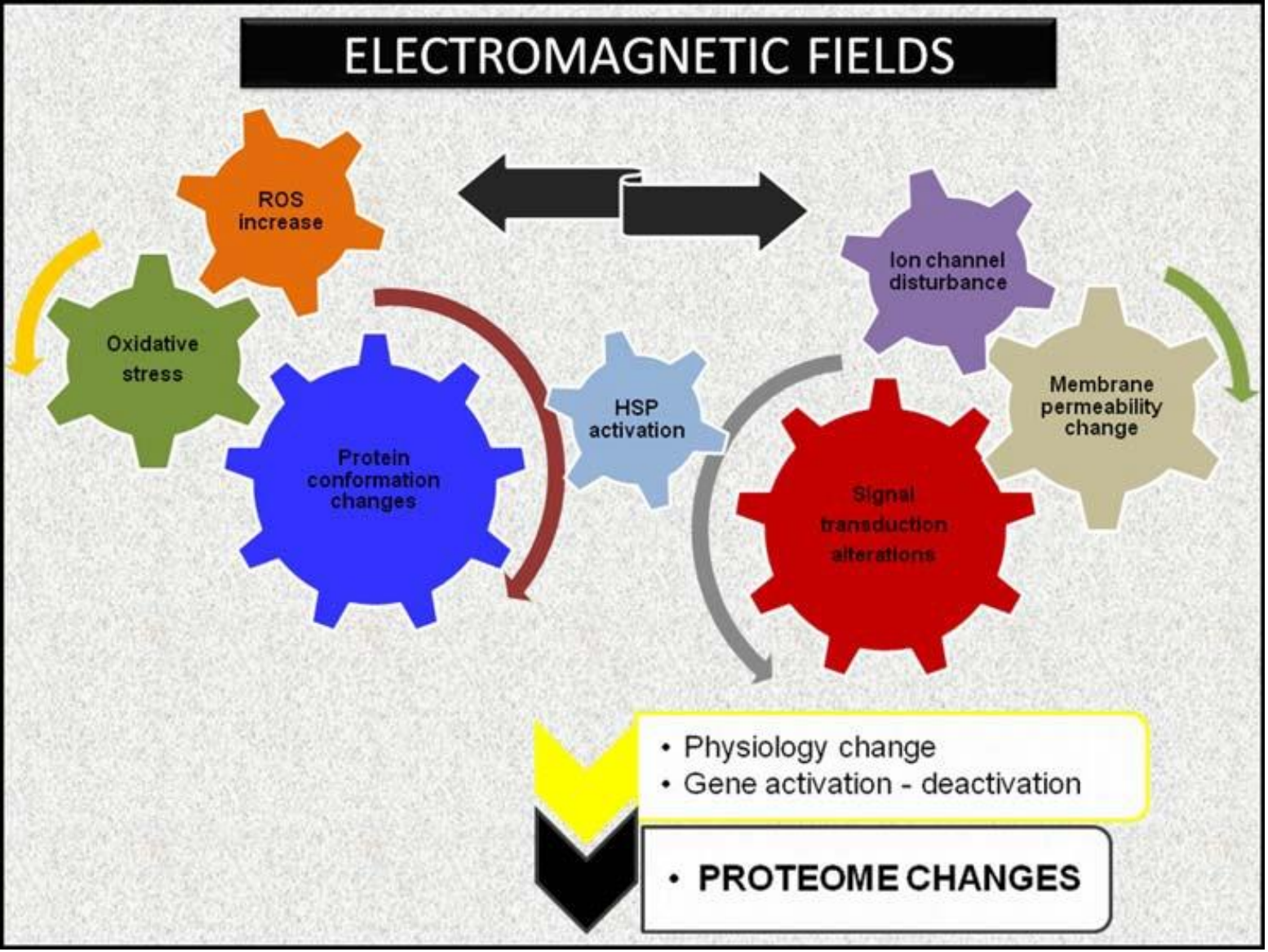


Exposure to Al and its toxicological impacts. Dietary uptake represents the major route of Al uptake. Due to the chemical properties of Al, this trivalent metal disrupts multiple cellular processes. The ability of Al to exert these negative effects on cells has been linked to a number of pathologies.



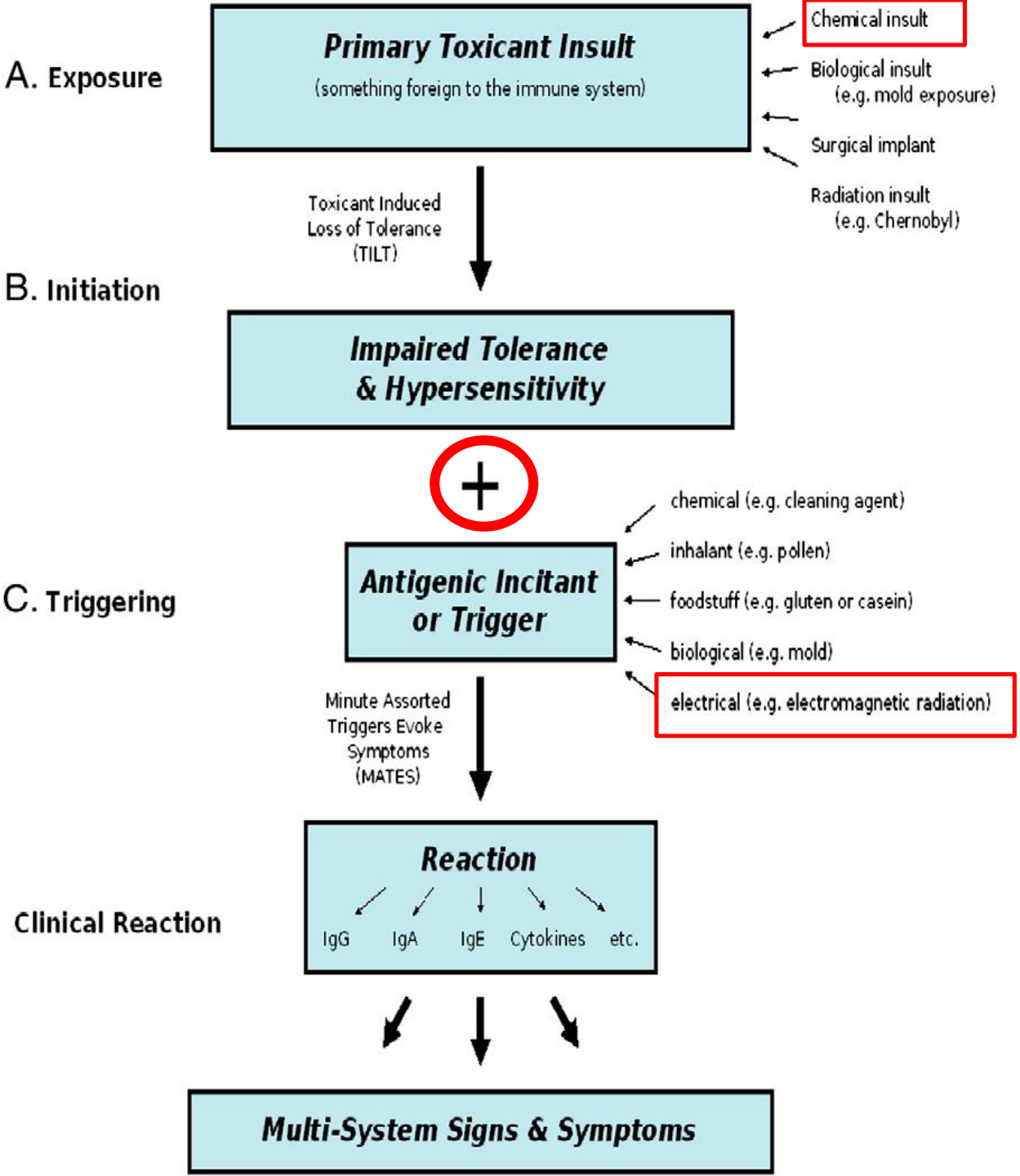
Cell survival after EMF stimuli.

Cancer induction pathways and HF-EMF irradiation. G. LEDOIGT, D. BELPOMME. Advances in Biological Chemistry. May 2013.



Brain proteome response following whole body exposure of mice to mobile phone or wireless DECT base radiation. Adamantia F. Fragopoulou et al Electromagnetic Biology and Medicine, Early Online: 1–25, 2012

Schematic drawing depicting a suggested mechanism of EMF interaction with living matter. It is considered, on the basis of the available data and the present work, that the end result of protein expression changes may have derived through a cascade of events starting from ROS increase and ion channel disturbance, followed by oxidative stress and signal transduction changers. Key role in the events may be played by the heat shock proteins activation.



Electromagnetic hypersensitivity: Fact or fiction? Stephen J. Genuis , Christopher T. Lipp. Science of the Total Environment 414 (2012) 103–112

Sensitivity-related illness: The escalating pandemic of allergy, food intolerance and chemical sensitivity, **Stephen J. Genuis.** Science of the Total Environment 408 (2010) 6047–6061

Cross-contaminations

Effects on Health

EMF and « Heavy metals »

Heavy metal exposure in patients suffering from electromagnetic hypersensitivity	Ghezel-Ahmadi et al (2010) *Science of the Total Environment*	Heavy metal load is of no concern in most cases of EHS but might play a role in exceptional cases.
In EHS individuals, nonspecific adverse health effects associated with heavy metals may not be dose related.	Costa et al (2010) *Science of the Total Environment*	Alternative Explanation: lead, mercury, and cadmium may induce immunotoxic effects (i.e., release of proinflammatory cytokines)
Influence of static magnetic field on cadmium toxicity: Study of oxidative stress and DNA damage in rat tissues	Amara et al (2006) *Journal of Trace Elements in Medicine and Biology*	SMF associated to Cd disrupt the antioxidant response in liver compared to Cd-treated rats
Effects of static magnetic field and cadmium on oxidative stress and DNA damage in rat cortex brain and hippocampus.	Amara et al (2011) *Toxicol Ind Health.*	SMF + Cd increase oxidative stress in brain
Assessing of plasma protein denaturation induced by exposure to cadmium, electromagnetic fields and their combined actions on rat .	Hassan and Abdelkawi (2014) *Electromagn Biol Med*	EMF + Cd increase modifications of molecular structure of proteins.
The role of zinc supplementation in the inhibition of tissue damage caused by exposure to electromagnetic field in rat lung and liver tissues.	Baltaci et al (2012) *Bratisl Lek Listy.*	EMF + Zn ↗ glutathione rate ↘ cell damages
Zinc prevents hematological and biochemical alteration induced by static magnetic field in rats.	Amara et al (2005) *Pharmacol. Rep.*	preventive effect of zinc to metallothioneins induction and zinc accumulation in liver and kidney of SMF-exposed rats
Zinc supplementation ameliorates static magnetic field-induced oxidative stress in rat tissues	Amara et al (2007) *Environmental Toxicology and Pharmacology*	zinc supplementation minimizes the adverse effect of oxidative stress induced by SMF in rat tissues

EMF and « Heavy metals »

High-field MRI and mercury release from dental amalgam fillings.	Mortazavi et al (2014) *Int J Occup Environ Med*	Difference between urinary mercury in the exposed and control group, that support for the noxious effect of MRI (exposure to strong magnetic field)and release of mercury from dental amalgam fillings.
Selenium supplementation ameliorates static magnetic field-induced disorders in antioxidant status in rat tissues	Ghodbane et al (2011) *Environmental Toxicology and Pharmacology*	Exposure to SMF altered the antioxidant response by decreasing the level of total selenium in kidney, muscle and brain. Selenium supplementation ameliorates antioxidant capacity in rat tissues exposed to SMF.
Extremely low-frequency magnetic field decreased calcium, zinc and magnesium levels in costa of rat.	Ulku et al (2011) *Biol Trace Elem Res*	Exposure to long-term ELF-MF (500 microT) may affect the chemical structure and bone metabolism in rats by changing the levels of certain important elements such as Ca, Mg and Zn

Sulcotrione: 10^{-5}M
Mikado® : 11µL/L
Grape Marc: 10mg/L

	Oxidative molecules		Enzyme activity		Gene expression						Cell death
	MDA	H_2O_2	CAT	GPX	CAT	Cu/Zn-SOD Cy	Cu/Zn-SOD CH	APX	*Hsp70.1*	ubiquitin	
Grape Marc (GM) / Control	(+)	+	0	+	++	0	++	+	++	++	↗
Sulcotrione / Control	+	++	+	++	++	++	++	++	++	++	↗
Mikado® / Control	+	+	+	++	(+)	++	++	++	++	++	↗
Mikado® / Sulcotrione	0	0	(+)	0	(-)	(+)	(-)	0	(+)	(+)	↗
Sulcotrione +(GM) / Sulcotrione	+	+	+	+	++	++	++	++	++	++	↗
Mikado® +GM / Mikado®	++	+	+	+	++	++	- -	(-)	(+)	++	↗

↗ Increase of cell death

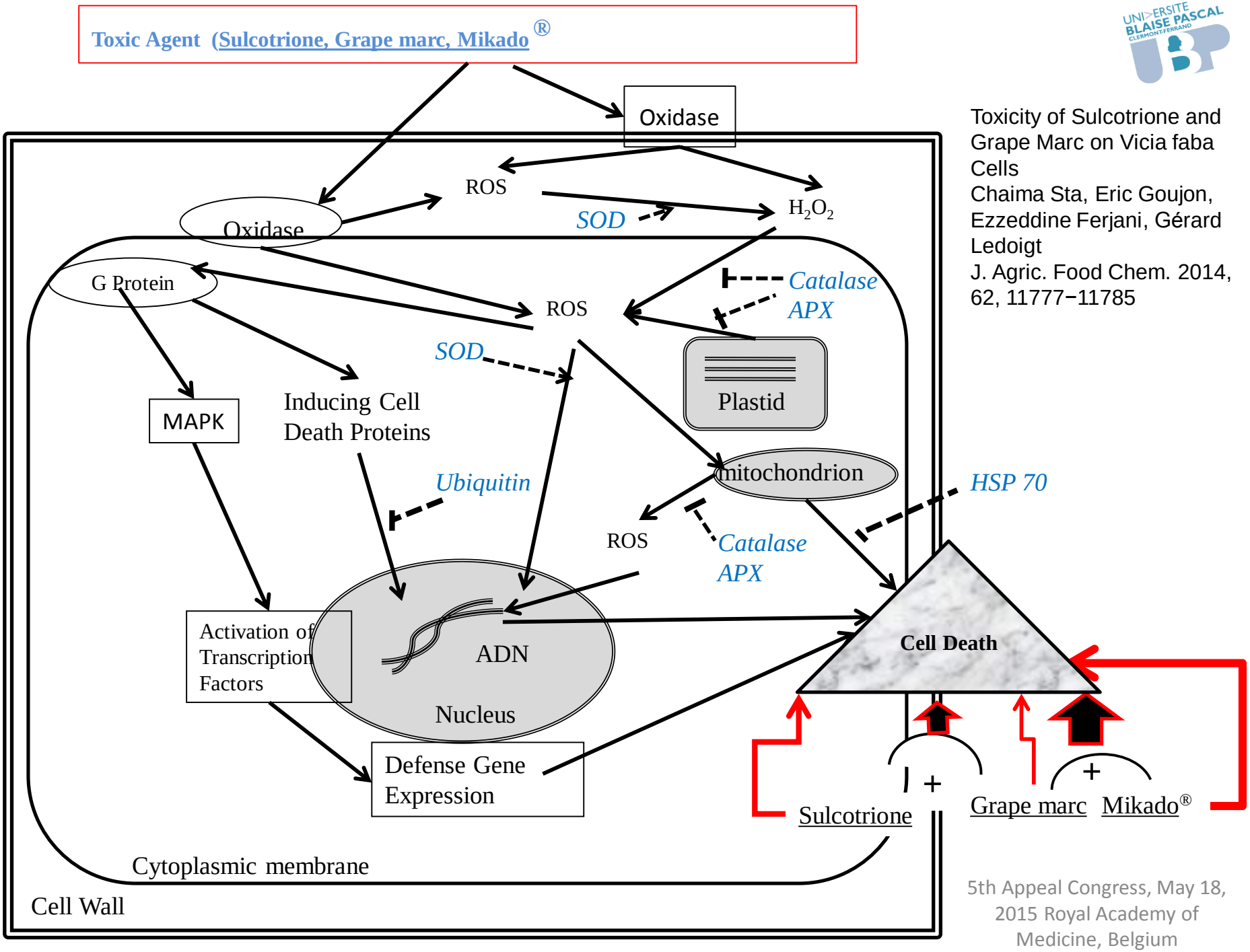
(+) (-) No significative increase and decrease of values

++ Highly significative increase

\+ Significative increase

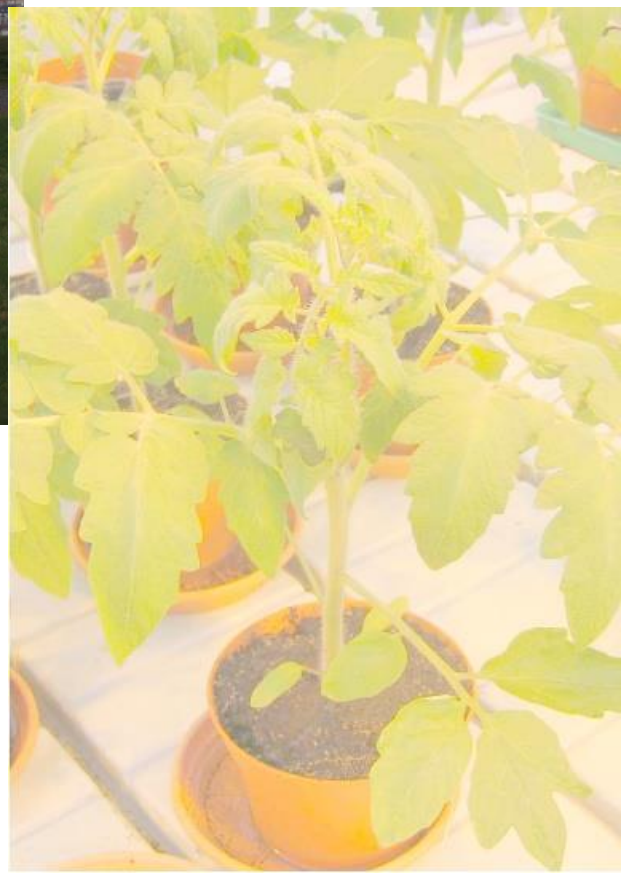
- - Highly significative depletion

0 No difference



Toxicity of Sulcotrione and Grape Marc on Vicia faba Cells
Chaima Sta, Eric Goujon, Ezzeddine Ferjani, Gérard Ledoigt
J. Agric. Food Chem. 2014, 62, 11777−11785

Gérard LEDOIGT



Thank you
for your attention

Conclusions :

-La sulcotrione présente une génotoxicité et une cytoxicité indépendantes de son action herbicide.

-L'addition de différentes molécules (adjuvants, extrait de raisin ou photoproduits) à la sulcotrione modifie sa cytotoxicité.

-Le Mikado® présente une plus grande toxicité cellulaire que la sulcotrione seule.

- Quelle que soit la nature biochimique de cette interaction, il est montré que la combinaison de la sulcotrione et de l'extrait de marc de raisin améliorent l'efficacité toxique de l'herbicide.

-Les différents aspects de la génotoxicité , micronoyaux et anomalies chromosomiques, ne sont pas nécessairement corrélées ni entre elles ni à l'indice mitotique, indiquant plusieurs mécanismes d'action cytotoxique des produits utilisés.

Mixtures of grape marc and herbicides enhanced transcript accumulation for ubiquitin, hsp 70, and cytosolic superoxide dismutase, but did not change ascorbate peroxidase transcript accumulation. The results thus provide evidence that sulcotrione, Mikado, and mixtures with grape marc can trigger cell death and specific gene expressions. Cocktails of products with sulcotrione, such as commercial additives and grape marc, can modify biological features of pesticide. Moreover, grape marc differently enhanced cell toxicity of sulcotrione and Mikado, suggesting a synergy between pesticide products and grape marc.
Adjuvant can modify the biological features of sulcotrione.