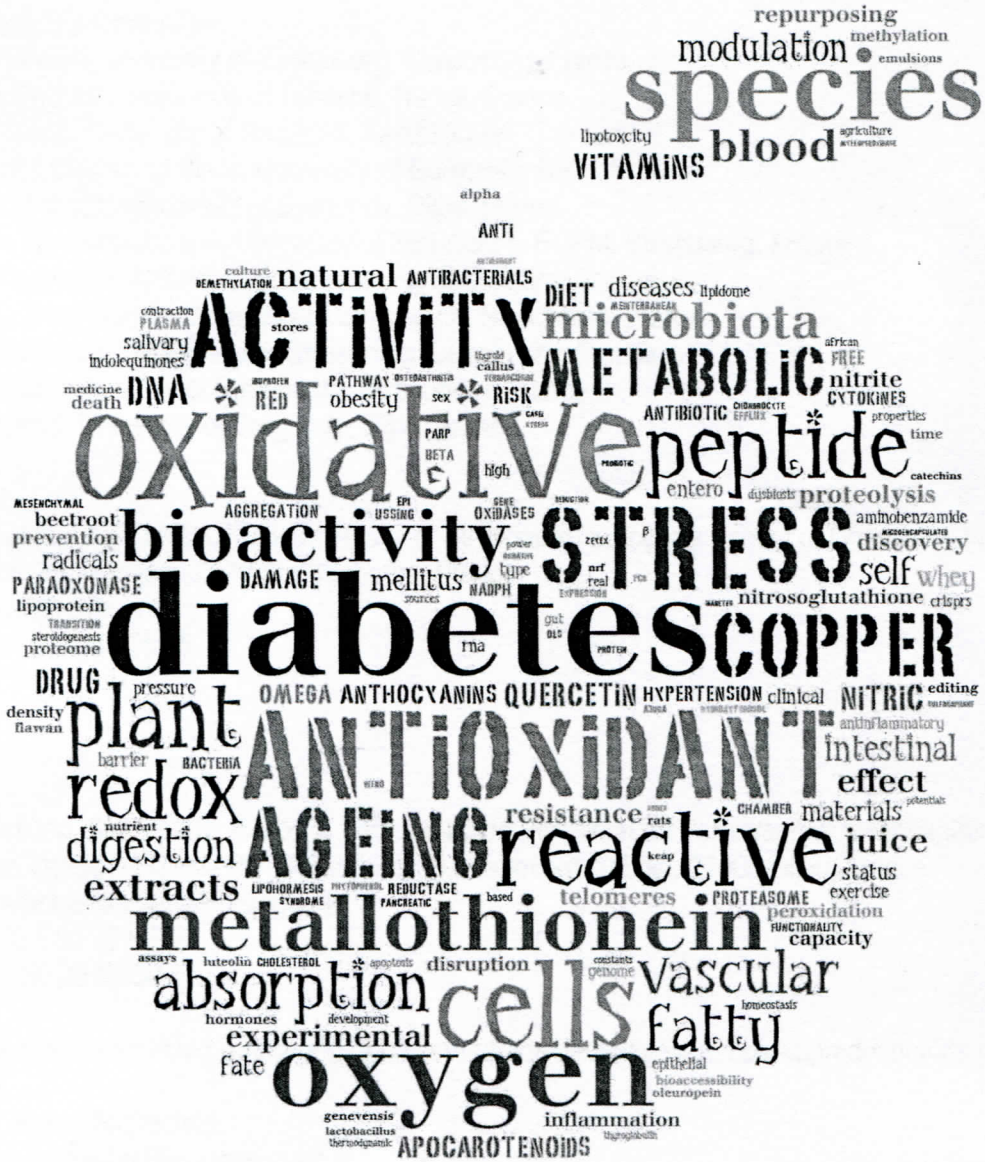
The NutRedOx COST Action CA16112 & the 6th NutriOx Atelier 2017

Preventing Age-Related Diseases with Redox-Active Compounds: a taste of controversy?

Strasbourg, ECPM, University of Strasbourg
27 – 29 September 2017



Produced using all your keywords

Scientific Committee

Prof Mustapha Cherkaoui Malki, University of Burgundy, Dijon, France
Prof Agnieszka Bartoszek, Gdansk University of Technology, Gdansk, Poland
Prof Claus Jacob, University of Saarland, Saarbrücken, Germany
Prof Patrick Chaimbault, University of Lorraine, Metz, France
Dr Mohammad Tadayyon, Pharmidex, London, United Kingdom
Prof Josep A. Tur, University of the Balearic Islands, Palma de Mallorca, Spain
Prof Elke Richling, TU Kaiserslautern, Kaiserslautern, Germany
Prof Nina Hermans, University of Antwerp, Antwerp, Belgium
Dr Claudia Santos, Instituto Biologia Experimental e Tecnologica, Oeiras, Portugal
Prof Marc Diederich, LBMCC Hopital Kirchberg, Luxembourg, Luxembourg
Dr Linda Giblin, Teagasc Food Research Centre, Fermoy, Co.Cork, Ireland

Local Organizing Committee

Dr Mourad Elhabiri, University of Strasbourg, Strasbourg, France
Dr Caroline Gaucher, University of Lorraine, Nancy, France
Prof Claus Jacob, University of Saarland, Saarbrücken, Germany
Prof Mustapha Cherkaoui Malki, University of Burgundy, Dijon, France
Dr Pierre Andreoletti, University of Burgundy, Dijon, France
Dr Elisabeth Davioud-Charvet, University of Strasbourg, ECPM, Strasbourg, France
Angéline Cherbonnel, University of Strasbourg, Strasbourg, France
Dr Léandro Cotos-Munoz, University of Strasbourg, Strasbourg, France
Vrushali Khobragade, University of Strasbourg, Strasbourg, France
Didier Boettger, University of Strasbourg, Strasbourg, France
Nathalie Bancod, University of Burgundy, Dijon, France

Secretariat

Mourad Elhabiri, UMR 7509 CNRS-University of Strasbourg, European School of Chemistry, Polymers and Materials, 25, rue Becquerel 67200 Strasbourg, France
Email: elhabiri@unistra.fr
Phone: (+33) 3 68 85 26 85
Fax: (+ 33) 3 68 85 27 42

and

Nathalie, Bancod, BioPeroxIL, EA7270, Laboratoire de Biochimie du Peroxysome, Inflammation & Métabolisme Lipidique, University of Burgundy, 6, Boulevard Gabriel, 21000 Dijon, France
Email: nathalie.bancod@u-bourgogne.fr
Phone: (+33) 3 80 39 62 37
Fax: (+33) 3 80 39 62 50

Congress website: http://blog.u-bourgogne.fr/cost-nutredox/events/event/cost-nutredoxnutriox-joint-meeting-strasbourg/
Contact: Dr Pierre Andreoletti
Email: pierre.andreoletti@u-bourgogne.fr

NutRedOx COST Action CA16112 & Postgraduate Training Network "NutriOx" 2017
Strasbourg, 27 – 29 September 2017

Cellular Reprogramming *via* Epi-CRISPRs-Induced Targeted DNA Methylation

Melita Vidaković[1], Marija Sinadinović[1], Jovana Rajić[1], Jelena Arambašić Jovanović[1], Nevena Grdović[1], Anja Tolić[1], Miloš Đorđević[1], Mirjana Mihailović[1], Aleksandra Uskoković[1], Goran Poznanović[1], Svetlana Dinić[1], Tomasz P Jurkowski[2]

[1]Institute for Biological Research "Siniša Stanković", University of Belgrade, Belgrade, Serbia; [2]Institute for Biochemistry, University of Stuttgart, Stuttgart, Germany

Diabetes is the perfect candidate for cell replacement therapy, since it is caused by either an absolute (type 1 diabetes) or relative (type 2 diabetes) defect of insulin-producing pancreatic beta cells. Our research is focused on applying a novel synthetic epigenetic tool (Epi-CRISPRs) for straightforward, one-step mouse pancreatic alpha (a-cells) to beta cell transdifferentiation by targeted DNA methylation and suppression of genes essential for maintaining pancreatic cell identity (homeobox Arx gene (Arx)). Up to now, we succeeded to transiently transfect a-cells with Epi-CRISPR constructs and 275 gRNA or mix gRNA. The suppression of Arx in a-cells was confirmed on day 5 and 8 post-transfection. The reduction of glucagon synthesis and beginning of insulin production in transfected a-cell was confirmed and visualised by immunostaining. DNA methylation-mediated suppression of Arx in a-cells leads to their transdifferentiation to insulin-producing beta cells will be confirmed by bisulfite sequencing (undergoing experiments).

Furthermore, we are also investigating an epithelial-mesenchymal transition (ETM), the mechanism which underlies the progressive decline in organ functioning in diabetes, such as the development of kidney and liver fibrosis. ETM is a process of reprogramming epithelial cells from a fully differentiated epithelial state to a more mesenchymal state. Our aim is to analyse the DNA methylation profile and gene expression of either epithelial (E-cadherin) or mesenchymal markers (α-smooth muscle actin and fibronectin) whose differential methylation and gene suppression could lead to more epithelial-like or mesenchyme-like phenotype. This will be accomplished using an *in vitro* model system based on epithelial cells treated with TGF-β1 and 2. The obtained data should enable ETM reversal and stop fibrosis in diabetes and other pathologies using different compounds that act as DNA methylating/demethylating agents or using Epi-CRISPRs-based targeted DNA methylation/demethylation in future.

We are on the way to develop a clear-cut technology able to provide a perfect delivery system for increase of insulin-producing cells *in vitro*. This system will allow for targeted gene silencing via increased DNA methylation of gene of interest. In addition, we are able to test if any compound used for treatment in different pathological conditions affects the DNA methylation profile of the examined cells. On the other hand, there is a great need for chemical compounds able to act as DNA hypo or hypermethylated agents.

***Keywords**: DNA methylation and demethylation, diabetes, Epi-CRISPRs, epithelial-mesenchymal transition, genome editing, pancreatic alpha cells.*