SALIVARY ADVANCED GLYCATION END PRODUCTS (AGES) AS NOVEL BIOMARKERS IN EVALUATION OF RISK FACTORS FOR DIET-RELATED DISEASES: RESULTS FROM THE EUROPEAN NETWORK SALIVAGES

Debora Collotta[1], Fausto Chiazza[1], Raffaella Mastrocola[1], Manuela Aragno[2], Chiara Cordero[1], Erica Liberto[1], Rosa M. Sáinz[3], Vanesa Cepas[3], Aranka Ileaa[4], Bianca A. Boscab[4], Jared Q. Gerlach[5], Marie Le Berre[5], Lokesh Joshi[5], Thomas Henle[6], Friederike Manig[6], Michael Hellwig[6], Massimo Collino[1]

[1]Dept. of Drug Science and Technology, University of Turin, Turin - Italy, [2]Dept. of Clinical and Biological Sciences, University of Turin, Turin - Italy, [3]Department of Morphology and Cell Biology, University of Oviedo, Oviedo - Spain, [4]Department of Oral Rehabilitation, Oral Health and Dental Office Management, Faculty of Dentistry, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romenia, Cluj-Napoca - Romenia, [5]Glycoscience Group, National Centre for Biomedical Engineering Science, National University of Ireland Galway, Galway - Ireland, [6]Technische Universität Dresden, Dresden - Germany

Introduction: Advanced Glycation End Products (AGEs) are reactive compounds deriving from glycoxidation reactions between the amino groups of proteins and reducing carbohydrates. Recent findings convincingly demonstrate that Advanced Glycation End Products (AGEs) are modifiable by diet and reflect changes in healthy state. The multidisciplinary project SALIVAGES, granted by the European ERA-NET Cofund ERA-HDHL programme, focuses on the identification and validation of non-invasive strategies for monitoring AGEs in the saliva as early and easily accessible biomarkers that are modulated by diet and that potentially indicate a change in health status and/or the risk of developing diet-related diseases.

Methods: The scientific network, coordinated by Prof. Collino (University of Turin) involves five different European countries: ITALY (University of Turin), SPAIN (University of Oviedo), IRLAND (National University of Ireland Galway), ROMANIA (University of Cluj-Napoca), GERMANY (Technische Universität Dresden). Preliminary data based on the integration of preclinical biological and molecular studies, analytical and food chemistry, information technologies, and glycomic analyses will be illustrated and discussed.

Results: Both in vitro and *in vivo* studies showed that exposure to different dietary AGEs evokes oxidative stress, free radical production and impairment in local inflammatory response, being 3-deoxygalactosone (3-DGal), 3,4-dideoxyglucosone-3-ene (3,4-DGE) and Pyrraline (Pyr) the most cytotoxic AGEs. Pharmacological modulation of AGEs by the antiglycating compound pyridoxamine resulted in significant improvement in diet-related metabolic injury. The impact of dietary AGEs on salivary AGE level was tested during a crossover-study in healthy subjects exposed to diets poor or enriched in AGEs. The AGE-levels of Pyr, FruLys, MG-H1were significantly higher than those levels during the raw food period. Changes in saliva metabolic signatures in obese individuals were investigated by comprehensive two-dimensional gas chromatography combined with time of flight mass spectrometry (GC×GC-TOFMS), showing meaningful variations of several saliva metabolites (mainly maltose, glyceric acid, urea and N-acetyl glucosamine) among subjects. Preliminary glycoprofiling of biological fluid glycoproteins confirm tendency towards reliable association with diet-related groups.

Discussion and conclusions: Overall, these results demonstrate that AGEs can be detected within the saliva and they may act both as biomarker and trigger of metabolic derangements. A salivary biosensor prototype is under development for a non-invasive monitoring of salivary AGEs with the aim of monitoring health in patients and for self-management at home.