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EUROPEAN COOPERATION
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NutRedOX
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The NutRedOx COST Action CA16112 meeting

Gdańsk 19-21.09.2018

GDAŃSK UNIVERSITY
OF TECHNOLOGY

GDAŃSKI UNIWERSYTET MEDYCZNY

Programme

Session 30 BIO 2018

„Redox control of major age-related diseases"

EUROPEAN COOPERATION IN SCIENCE & TECHNOLOGY

NutRedOx network

GDAŃSK UNIVERSITY OF TECHNOLOGY

Congress BIO2018
Gdańsk, September 18-21

Personalized Nutrition in aging society:

redox control of major age-related diseases

COST Action 16112

NutRedOx

19th – 21th September 2018

Gdańsk, Poland

ORGANIZING COMMITTEE

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WELCOME

Dear Colleagues,

We have the great pleasure to welcome you to the historical city of Gdańsk to attend the 3rd Management Committee of COST Action 16112 NutRedOx meeting and Working Groups meetings. The WG Meetings will take place at Gdańsk University of Technology campus listed among 10 most beautiful university campuses in Europe. The scientific part of our gathering will be incorporated into the annual congress of Polish Biochemical Society and related bio-societies - ***Congress BIO2018,*** *as one of the regular sessions –* ***Session 30 entitled "Redox control of major age-related diseases"*** *– including keynote lectures by invited speakers, oral and poster presentations. This scientific part of our COST Action NutRedOx meeting will be open to all interested participants of Congress BIO2018, which will give us opportunity to spread the information about our activities.*

We wish you a very inspiring and fruitful meetings and a pleasant stay in Gdańsk.

Agnieszka Bartoszek and Jędrzej Antosiewicz

COST Action 16112 NUTREDOX MC and WG meetings

FRAMEWORK PROGRAMME

Wednesday, 19 September 2018

WG meetings at GUT

9^{00} – 10^{00} ***Arrival to Gdańsk University of Technology, Faculty of Chemistry*** *(Bldg A)*

10^{00} – 10^{30} ***Welcome and opening of Cost Action NutRedOx meetings***

Prof. Sławomir Milewski *- Dean of Faculty of Chemistry, GUT*
Prof. Hanna Staroszczyk *- Head of Department of Food Chemistry, Technology and Biotechnology, GUT*

10^{30} – 13^{00} ***Meetings of Working Groups***

13^{00} – 13^{30} ***Coffee break and snacks***

13^{30} – 14^{00} ***Walk around GUT campus***

14^{00} ***Transfer to Congress BIO2018 venue at Gdańsk University***
(Faculty of Social Sciences and Institute of Geography)

COST Action NutRedOx/BIO2018 scientific session

15^{00} – 15^{15} ***Opening of the COST Action session: Congress BIO2018, Session 30 part I (Auditorium S211)***

15^{15} – 18^{00} ***Lectures and posters***

18^{00} ***Guided tour to Gdańsk***

Thursday, 20 September 2018

COST Action NutRedOx/BIO2018 scientific session

$9^{00} – 9^{30}$ ***Arrival to Congress BIO2018 venue at Gdańsk University***
(Faculty of Social Sciences and Institute of Geography)

$9^{30} – 9^{45}$ ***Opening of the COST Action session: Congress BIO2018, Session 30 part II***
(*Auditorium S211****)***

$9^{45} – 13^{30}$ ***Lectures and posters***

14^{00} ***Individual transfer to Eureka Hotel in Sopot***

Core Group meeting and Dissemination

$16^{00} – 17^{45}$ ***Core Group Meeting of COST Action 16112 NutRedOx***
(*Hotel Eureka conference room****)***

$18^{00} – 19^{30}$ ***COST Action 16112 NutRedOx Dissemination, M. Cherkaoui Malki***
(*Hotel Eureka conference room****)***

20^{00} ***Dinner***

Friday, 21 September 2018

MC meeting

$9^{00} – 11^{00}$ ***COST Action 16112 NutRedOx MC Meeting***
(*Hotel Eureka conference room****)***

Wednesday, 19 September 2018

COST Action 16112 NUTREDOX /BIO2018 scientific session

Session 30, part I: "Redox control of major age-related diseases"

$15^{00} – 15^{15}$ ***Opening of the COST Action session, part I***

Place: S211

Chairpersons: ***Caroline Gaucher*** *University of Lorraine, Nancy, France*
Jędrzej Antosiewicz *Medical University of Gdańsk, Poland*

$15^{15} – 15^{45}$ ***L.30.1.*** *Marc Diederich*. ***About canonical and less canonical cell death induction by natural compounds with pharmacological potential***. Seoul National University, South Korea

$15^{45} – 16^{15}$ ***L.30.2.*** *Marek Naruszewicz, A. Filipek.* ***Oleacein, translation from Mediterranean diet to preventive medicine***. Medical University of Warsaw, Poland

$16^{15} – 16^{35}$ ***L.30.3.*** *N. Sahakyan, M. Petrosyan, Armen Trchounian*. ***Antioxidant activity of alcohol extracts from some plants of Armenian flora: the highest level and its possible nature.*** Yerevan State University, Armenia

$16^{35} – 16^{50}$ ***POSTER FLASHES (30 sec presentation)***

$16^{50} – 17^{30}$ ***COFFEE BREAK AND POSTER SESSION***

$17^{30} – 17^{45}$ ***O.30.1.*** *Denisa Baci, A. Bruno, M. Gallazzi, C. Cascini, M. Tramacere, A. Albini, D. M. Noonan.* ***Acetyl-L-carnitine (ALCAR) inhibits angiogenesis, migration and macrophage recruitment in prostatic cancer cells***. IRCCS MultiMedica, Italy

$17^{45} – 18^{00}$ ***O.30.2.*** *Giorgia Del Favero, D. Marko.* ***Nrf2 and the intestine: chemical and physical regulators to highlight the difference between non-transformed intestinal epithelial cells and colorectal adenocarcinoma***. University of Vienna, Austria

Thursday, 20 September 2018

COST Action 16112 NUTREDOX /BIO2018 scientific session

Session 30, part II: "Redox control of major age-related diseases"

$9^{30} – 9^{45}$ ***Opening of the COST Action session, part II***

Place: S211

Chairpersons: ***Agnieszka Bartoszek,*** *Gdańsk University of Technology, Poland*

Mustafa C. Malki, *Université de Bourgogne, Dijon, France*

$9^{45} – 10^{15}$ ***L.30.4.*** *A. Corrochano, Linda Giblin.* ***Whey Protein: Can it boost cellular antioxidant processes?*** Teagasc Food Research Centre, Ireland

$10^{15} – 10^{45}$ ***L.30.5.*** *Jarosław Paluszczak, R. Kleszcz, A. Majchrzak-Celińska, E. Studzińska-Sroka, V. Krajka-Kuźniak, W. Baer-Dubowska.* ***Modulation of Wnt signaling by natural and synthetic compounds in cancer cells.*** Poznan University of Medical Sciences, Poland

$10^{45} – 11^{05}$ ***L.30.6.*** *Tomris Ozben, A. Cort.* ***Natural redox modulators in cancer therapy.*** Akdeniz University, Turkey

$11^{05} – 12^{15}$ ***COFFEE BREAK AND POSTER SESSION***

$12^{15} – 12^{30}$ ***O.30.3.*** *Vanja Todorovic, M. Baranowska, B. Kusznierewicz, B. Vidovic, S. Sobajic, A. Bartoszek.* ***Antioxidant and cytotoxic activity of cocoa powders.*** University of Belgrade, Serbia

$12^{30} – 12^{45}$ ***O.30.4.*** *Kari Espolin Fladmark, A.J. Edson, A.K. Froyset.* ***Role of the Parkinsons Disease-related protein DJ-1 in redox control and neuronal protection.*** University of Bergen, Norway

$12^{45} – 13^{00}$ ***O.30.5.*** *L. Sánchez-Alcoholado, C. Gutiérrez-Repiso, J. Alcaide, E. García-Fuentes, R.M. Bernal-López, F.J. Tinahones, Isabel Moreno-Indias.* ***Gut microbiota is differentially affected by distinct weight loss strategies.*** Universidad de Málaga, Spain

$13^{00} – 13^{30}$ ***L.30.7.*** *Carla Ferreri, C. Chatgilialoglu, A. Sansone, R. Scanferlato.* ***The interplay of desaturase enzymatic activities and the first observation of a de novo synthetic pathway to PUFA in human cancer cell line****.* Consiglio Nazionale delle Ricerche, Italy

$13^{15} – 13^{30}$ ***CLOSING REMARKS***

POSTER PRESENTATIONS

P.30.1. *D. Gjorgieva Ackova, K. Smilkov, A. Cvetkovski.* ***Biosynthesis of silver nanoparticles using plant extracts as reducing/capping agents****.* University Goce Delčev, Macedonia

P.30.2. *M. Baranowska, K. Suliborska, W. Chrzanowski, J. Namieśnik, A. Bartoszek.* ***The influence of catechins and phenolic acids on the redox balance of cells.*** Gdańsk University of Technology, Poland

P.30.3. *L. Bordoni, D. Fedeli, C. Nasuti, R. Gabbianelli.* ***Antioxidants protect overexpression of* Nurr1 *in stressed dopaminergic cells****.* University of Camerino, Italy

P.30.4. *A. Borkowska, J. Antosiewicz.* ***Homocysteine-induced changes in iron metabolism in HUVEC cells are mediated by Akt-FOXO3a signalling pathway.*** Gdańsk Medical University, Poland

P.30.5. *W. Brankiewicz, M. Bagiński.* ***Cancer inhibitory activity of dietary berries****.* Gdańsk University of Technology, Poland

P.30.6. *R. Celik, M.S. Kaymakci, D. Akalın, E. Karademir, B. Tuncer, A.M. Yilmaz, G. Bicim, A.S. Yalcin.* ***Effect of whey proteins on the immune system and its relation to examination stress****.* Marmara University, Turkey

P.30.7. *D. Dulko, A. Macierzanka.* ***Effect of the kinetic of protein digestion on sarcopenia inhibition****.* Gdańsk University of Technology, Poland

P.30.8. *J. Głazowska, A. Bartoszek.* ***Nucleic acids as food components and their impact on epigenome.*** Gdańsk University of Technology, Poland

P.30.9. *A. Hać, A. Herman-Antosiewicz****. The role of S6K1/2 kinases in the process of lysosomal membrane permeabilization and cell death induced by sulforaphane – a natural anticancer agent.*** Department of Medical Biology and Genetics, University of Gdansk, Gdansk, Poland

P.30.10. *M. Heldt, J. Lica, M. Misiak, A. Skladanowski, M. Bagiński.* ***ROS scavengers modulate anthrapyridazones activity****.* Gdansk University of Technology, Poland

P.30.11. *P. Jakubek, M. Baranowska, J. Rajić, M. Vidaković, A. Bartoszek, J. Namieśnik,* ***Catechins as epigenetic modulators****.* Gdańsk University of Technology, Poland

P.30.12. *J. Kamińska, P. Langa, A. Wardowska, M. Deptuła, J. Zieliński, M. Pikuła, P. Sachadyn.* ***Transcriptional acitivity of epigenetic remodelling genes in human skin and regenerative capacity****.* Gdańsk University of Technology, Poland

P.30.13. *M. Khvedelidze, T .Mdzinarashvili, E. Shekiladze****. Novel technology of preparation liposomes with antioxidant vitamins to treat age-related diseases****.* I. Javakhishvili Tbilisi State University, Georgia

P.30.14. *Z. Koziara, M. Baranowska, J. Namieśnik, A. Bartoszek.* ***The impact of redox active compounds belonging to different flavonoid groups on the antioxidant activity system of HT29 cells.*** Gdansk University of Technology, Poland

P.30.15. *T. Mdzinarashvili, M. Khvedelidze, N. Turkadze, I. Papukashvili, E. Lomadze.* ***On possible mechanisms of resistance of bacteria to antibiotics and phages - ways to overcome them***. I. Javakhishvili Tbilisi State University, Georgia

P.30.16. *N. Maciejewska, M. Bagiński.* ***Caffeine – new insight of known antioxidant.*** Department of Pharmaceutical Technology and Biochemistry Gdansk University of Technology, Gdansk

P.30.17. *K. Parchem, A. Bartoszek.* ***Dietary oxidized phospholipids: from digestion to biological effect.*** Gdansk University of Technology, Poland

P.30.18. *P. Riso, S. Bernardi, C. Del Bo, M. Porrini, G. Gargari, A. Cherubini, P. Kroon, C. Andres-Lacueva, S. Guglielmetti.* ***Rationale of MaPLE project focused on intestinal permeability in the older subjects***. Università degli Studi di Milano, Italy

P.30.19. *R. Sghaier, T. Nury, A. Vejux, M. Cherkaoui-Malki, T. Moreau, A. Masmoudi, A. Zarrouk, G. Lizard.* ***Prevention of 7β-hydroxycholesterol-induced mitochondrial dysfunction and cell death by dimethylfumarate and monomethylfumarate on 158N murine oligodendrocytes***. University Bourgogne Franche-Comté, France

P.30.20. *M. Tomczyk, J. Kortas, D. Flis, B. Kaczorowska, A. Przybytkowska, E. Lewicka, A. Dabrowska-Kugacka, J. Antosiewicz.* ***The role of iron in marathon-induced changes on the EPO-erythroferrone-hepcidin axis***. Gdansk University of Physical Education and Sport, Poland

P.30.21. *E.E. Totu, D. Petre, D. Mănuc, C.M. Cristache.* ***Spectrophotometric procedure for melatonin detection***. University Politechnica of Bucharest, Romania

ABSTRACTS

L.30.1. About canonical and less canonical cell death induction by natural compounds with pharmacological potential

M. Diederich*

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Natural compounds are the fundament of pharmacological treatments and more than 50% of all anti- cancer drugs are of natural origins or at least derived from scaffolds present in Nature. Over the last 25 years, molecular mechanisms triggered by natural anticancer compounds were investigated. Emerging research showed that molecules of natural origins are useful for both preventive and therapeutic purposes by targeting essential hallmarks and enabling characteristics described by Hanahan and Weinberg. Moreover, natural compounds could change the differentiation status of selected cell types. One of the earliest response of cells treated by pharmacologically active compounds is the change of its morphology leading to ultra-structural perturbations: changes in membrane composition, cytoskeleton integrity, alterations of the endoplasmic reticulum, mitochondria and of the nucleus lead to formation of morphological alterations that are a characteristic of both compound and cancer type preceding cell death. Apoptosis and autophagy were traditionally considered as the most prominent cell death or cell death- related mechanisms. By now multiple other cell death modalities were described and most likely involved in response to chemotherapeutic treatment. It can be hypothesized that especially necrosis-related phenotypes triggered by various treatments or evolving from apoptotic or autophagic mechanisms, provide a more efficient therapeutic outcome depending on cancer type and genetic phenotype of the patient. In fact, the recent discovery of multiple regulated forms of necrosis and the initial elucidation of the corresponding cell signaling pathways appear nowadays as important tools to clarify the immunogenic potential of non-canonical forms of cell death induction.

L.30.2. Oleacein, translation from Mediterranean diet to preventive medicine.

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In preventive medicine, substances, that would be applied to the treatment of chronic inflammation accompanying a progression of atherosclerosis, are searched. Such a biological active compound seems to be secoiridoid, such as oleacein, often occurring in the plants from the family of Oleaceae. Oleacein (dialdehydic form of decarboxy methyl elenolic acid linked to hydroxytyrosol;3,4-DHPEA- EDA) is structurally derived from a glucoside oleuropein, which is predominant compound of extra virgin olive oil, as well as leaves of Ligustrum vulgare*.*

In our recently publish study we were able to show that oleacein together with complexes of haemoglobin (Hb) and haptoglobin (Hp) may enhance change of macrophage phenotype from pro-inflammatory to anti- inflammatory. This effect has been related to increased expression of CD163 and IL-10 receptor, as well heme oxygenase 1.

Further study indicates that oleacein possesses a unique ability to prevent destabilisation of carotid atherosclerotic plaque induced by acute inflammation. It was related to the attenuation of plaque cells apoptosis and necrosis induced by the free radicals and cytokines. Additionally, we have noticed that oleacein in the dose-depend manner decreases secretion of proteases such as MMP-9 and MMP-9/NGAL complex. The recent study showed that these biomarkers are acutely induced after ischemic stroke.

These preliminary studies still require confirmation in an animal model, however we point out that in the future oleacein may play a significant role in early prevention of ischemic stroke, particularly in patients with arterial hypertension.

L.30.3. Antioxidant activity of alcohol extracts from some plants of Armenian flora: the highest level and its possible nature

N. Sahakyan, M. Petrosyan, A. Trchounian*

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Plant origin secondary metabolites have served as antioxidants in medicines against various diseases. They have anticancer, anti-inflammatory and anti-aging properties and may reduce oxidative stress through a number of different mechanisms. In addition they can be used as effective natural additives in cosmetics.

The purpose of this research was to test biological activity of alcohol extracts obtained from the leaves of Morus alba, Primula veris L., Malva sylvestris L. and Bryonia alba L. roots which are used in Armenian folk medicine and have been included in some cosmetic formulations, as antioxidants. Plant material was harvested from Kotayk region (Armenia, 1700-1800 m above sea level). Antioxidant activity of extracts was measured through DPPH-assay (2,2-diphenyl-1-picrylhydrazyl), TBARs-assay (thiobarbituric acid reactive substances), metal-chelating and tyrosinase inhibitory ability determination. The concentration of total phenolics was determined using Folin–Ciocalteu reagent and external calibration with GA (gallic acid).

Our investigations have shown that M. sylvestris had the highest free radical reducing ability (IC50 = 7.44 µg/ml), while IC50 value of P. veris, M. albaand B. alba were 87.5, 259.6 and 470 µg/ml, respectively. Fe^{2+} and Cu^{2+} ions could support the formation of free radicals via Fenton reaction. So, plant extracts ability of metal ion chelating is of great value. Our studies showed that P. veris had the highest metal-chelating power (56.0%), but M. albaand M. sylvestris had the similar activity, their percentage of metal ion inhibition was 29.9% and 29.6 %, respectively. B. alba had the lowest activity (5.6%). Plant extracts tyrosinase inhibitory activity is of special interest in cosmetic industry due to its skin lightening ability. M. sylvestris, P. veris and B. alba possessed almost the same ability to inhibit tyrosinase with 56.4, 58.2 and 58.6% inhibition, respectively. And only M. alba inhibited the 38.25% of tyrosinase in stock solution. In order to minimize the quantity of applicable laboratory animals, only one extract with the highest antiradical activity (M. sylvestris) had been chosen for TBARs assay. Lipid peroxidation was significantly inhibited in the presence of M. sylvestris extract when compared to the control ($P < 0.05$). The TBARs assay indicated that AI% was 89.2% in comparison to the same concentration of positive control – α-tocopherol, where this parameter was 91.1%. Total phenolic content of B. alba extract was 139.8, M. sylvestris extract - 152.81, P. veris extract – 308 and M. alba extract – 343.92 µg/ml GAE.

Thus, obtained data indicate that plants extracts investigated could be used as the positive sources of substances with antioxidant activity.

L.30.4. Whey Protein: Can it boost cellular antioxidant processes?

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Cellular metabolic processes inherently produce free radicals. In healthy cells, antioxidant mechanisms function to neutralise these free radicals. Dietary antioxidants can help to boost cellular antioxidant processes. Bovine whey proteins are prized for their bioactivity and recently have received considerable attention for their antioxidant potential.

The objectives of this research were (1) determine antioxidant activity of whey products and individual whey proteins, (2) to investigate whether this antioxidant activity survived upper gut transit, (3) to examine the bioavailability of whey peptides across the intestinal barrier and (4) to assess health benefits of transported peptides on downstream target cells. Initially, all commercial whey samples were subjected to a static simulated gastrointestinal digestion (SGID). The antioxidant activities of SGID whey samples were evaluated using inhibition of peroxyl radicals (ORAC), reduction of ferric ion (FRAP) and scavenging of synthetic radicals (ABTS).

SGID whey boosted antioxidant markers in intestinal cell lines and protected them against oxidative stress. Individual whey peptides were transported across using the intestinal barrier co-culture model, Caco-2/HT-29 and assisted muscle and liver cells to counteract/nullify free radicals. In conclusion, consumption of a whey based beverages are likely to boost antioxidant status of muscle and liver cells.

L.30.5. Modulation of Wnt signaling by natural and synthetic compounds in cancer cells

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The aberrations in canonical Wnt signaling have been attributed to the development of several types of cancer, including colorectal and head and neck cancers and also glioblastoma. This pathway regulates the expression of several important genes responsible for the regulation of cell proliferation and apoptosis, e.g. BIRC5, CCND1, c-MYC*. A complex regulatory network modulates the activation of β-catenin-dependent transcription making it amenable to the search of inhibitors with anti-cancer activity. The analysis of the activity of several lichen-derived compounds revealed that polyphenolic depsides and depsidones may decrease Wnt signaling in colorectal cancer and glioblastoma cell lines. Such an activity was also observed in a group of resveratrol analogues and the inhibitory activity of 3,4,4'-tri-methoxy-stilbene and 3,4,2',4'-tetra-methoxy-stilbene in glioblastoma cell lines was strongest. Their activity can be compared to the action of several synthetic compounds which target different proteins in the Wnt pathway. The inhibitors of Porcupine or CBP have been shown to robustly decrease β-catenin-dependent transcription in colorectal and head and neck cancer cell lines. On the other hand, the activity of epigenetic modulators targeting histones deacetylases or histone methyltransferases and demethylases have been found weak suggesting that targeting a single epigenetic protein may not effectively block β-catenin transcriptional activity.*

Acknowledgements: The studies were supported by grants from the Polish National Science Centre – 2014/13/D/NZ7/00300 (JP) and 2017/01/X/NZ7/00673 (AMC) and research funding from Poznań University of Medical Sciences, Poznań, Poland.

L.30.6. Natural Redox Modulators in Cancer Therapy

***T. Ozben*[1]*, A. Cort*[2]**

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The roles of oxidative stress in physiology and pathology have been intensively studied over the last decades, but the problem is still far beyond our full comprehension. The roles of free radicals and antioxidants have been entirely redefined recently. Free radicals widely recognized as absolute evils causing damage to biologically important molecules and structures, have been recently transformed into positive actors, in the appreciation of their essential impact in the intracellular signaling and regulation of apoptosis. In contrast, the great hope that antioxidants could be the panacea resolving practically many health problems has vanished, due to the growing number of inconclusive or negative data from studies. Multiple drug resistance (MDR) may develop against chemotherapeutic agents with unrelated chemical structure and mechanism of action used for the treatment of cancer, reduces the efficacy of drugs, and remains as a major challenge in the treatment of cancer. A complex redox pattern underlies MDR problem. Natural product modulators of MDR are used as low toxicity chemosensitizers to enhance the efficacy of anticancer protocols and to overcome MDR. Redox active drugs could provide a valid and promising way to overcome MDR in cancer therapies via targeting an axis consisting of drug transporters, aryl hydrocarbon receptor, phase I/II metabolic enzymes, and the inducible Nrf2-linked pathway. The mechanism underlying the MDR inhibition by natural products obtained from plants and fungi lies in the blockade of the drug binding site, interference with the ATP hydrolysis process, alteration in integrity of cell membrane lipids, and decrease in Pgp or/and MRP1 expression. During coadministration, natural modulators compete with cytotoxic agents for binding to the active site of the transporters and reduce drug efflux. However, beneficial versus deleterious effects of these substances must be well evaluated in chemoresistance and cancer therapy.

References:

Current Topics in Medicinal Chemistry. 15 (2): 170-178, 2015, 2016.
Oxidative Medicine and Cellular longevity. Article Number: 4251912, 2016.
Oxidative Medicine and Cellular longevity. Article Number: 6023417, 2016.
Nutrition and Cancer. 67 (3): 411-423, 2015.
Molecular Medicine Reports. 5(6): 1481-1486, 2012.
Journal of Physiology and Biochemistry. 68(4): 555-562, 2012.
Journal of Pharmaceutical Sciences. 96(9): 2181-2196, 2007.

L.30.7. The interplay of desaturase enzymatic activities and the first observation of a de novo *synthetic pathway to PUFA in human cancer cell line*

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Desaturase enzymatic pathways are key steps in fatty acid biosynthesis, but the de novo *synthesis of unsaturated fatty acids in human cells occurs only at the level of one double bond insertion (monounsaturated fatty acids - MUFA - biosynthesis), starting from the saturated fatty acid structures of palmitic acid and its elongation product stearic acid. The biosynthetic pathways leading to polyunsaturated fatty acids (PUFA) in humans so far are known to require the dietary intakes of essential fatty acids of the omega-6 (linoleic acid) and omega-3 (alfa-linolenic acid) series, as the necessary substrates to produce other PUFAs and lead to the fatty acid molecular diversity which is observed in eukaryotic cells.*

In connection with our studies on fatty acid-based membrane lipidomic profiles in health and diseases, we examined the effects of saturated and monounsaturated fatty acid supplementations in Caco-2 cells, a cancer cell model used to estimate nutritional and metabolic transformations. We showed for the first time the formation of a de novo synthesized PUFA and followed-up its incorporation in the Caco-2 cell line, evaluating also the differences in the fatty acid membrane remodeling determined by the supplemented fatty acids.

Acknowledgement: This work is supported by a donation from the Di Bella Foundation, Italy.

O.30.1. Acetyl-L-carnitine (ALCAR) inhibits angiogenesis, migration and macrophage recruitment in prostatic cancer cells

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Many efforts have been addressed on the identification of novel active compounds from natural sources, endowed with anti-proliferative, anti-oxidant, chemopreventive properties, and their ability to target the tumour microenvironment (TME). Through metabolomics approaches we previously found that in serum samples from prostate cancer (PCa) patients, three carnitine family members were significantly decreased, suggesting a potential protective role of carnitine against PCa. Acetyl-L-carnitine (ALCAR) is an acetic acid ester of carnitine with high bioavailability and is involved in the transport of fatty acids across the inner mitochondrial membrane. We have showed that ALCAR was able reduce angiogenesis in vitro*, acting on the VEGF/VEGFR2 and CXCR4/CXCL12 axes. We also found that ALCAR inhibits inflammatory angiogenesis* in vivo*, by reducing endothelial cells and macrophage recruitment in the matrigel plugs.*

Here we investigated the ability of ALCAR to interfere with key functional steps of prostate carcinogenesis and identified the molecular mechanisms involved. The effects of ALCAR on PCa cells were investigated in vitro *by functional assays (adhesion, migration and invasion assays), molecular and biochemical approaches (RT-PCR, FACS, Byoplex western blot).*

We found that ALCAR reduces apoptosis on PCa cells (PC3, Du-145, LNcap) and inhibits crucial tumorigenic steps such as adhesion, migration and invasion. We than confirmed the results from functional assays at molecular levels, and we found that ALCAR blocks CXCR4/CXCL12 axes, a key regulator of malignant migratory/aggressive phenotype. In accordance with our published paper, we confirmed the anti-angiogenic and ant-inflammatory properties of ALCAR, that we found to lower VEGF and CXCL8 production in PCa cell lines. Furthermore, we found a significantly reduced expression of inflammatory-related chemokines/cytokines involved macrophage recruitment such as CCL2, IL-6 and TNFα in PCa cells.

Our results highlight the angio/chemopreventive and anti-inflammatory properties of ALCAR and allow the identification of multiple and overlapping mechanisms of action through which ALCAR inhibits PCa progression/metastasis. Our findings provide the rational for the employment of ALCAR, as a possible supplement for approaches of chemoprevention in subjects at high risk to develop cancer.

O.30.2. Nrf2 and the intestine: chemical and physical regulators to highlight the difference between non-transformed intestinal epithelial cells and colorectal adenocarcinoma

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Management of redox homeostasis is of crucial importance for the correct function of the intestinal tract. In fact, through dietary intake intestinal cells are continuously challenged by the presence of pro- and/or anti- oxidant compounds. Cancer cells are known to "exploit at their need" the cellular redox system with complex metabolic changes associated to the loss/gain of functional modifications that characterizes the progression of the disease [1]. In this light, the comprehension of mechanistic changes sustaining the differential sensitivity of tumor cells in comparison to healthy ones is of paramount importance for a correct therapeutic approach, as well as for the selection of the most appropriate nutritional scheme.

For the purpose of this study non-transformed intestinal epithelial cells HCEC-1CT were compared to HT-29 cells, a widely used colon epithelial cell line derived from colorectal adenocarcinoma. Nrf2 (Nuclear factor erythroid-derived 2-like 2) was chosen as one of the most important regulator of cellular antioxidant response, as well as in light of its prominent role in cancer progression [2].

Our approach revealed differential reactivity (i.e. nuclear/cytosolic localization) of Nrf2 in HT-29 cells in comparison to HCEC-1CT cells. This effect was visible upon incubation with the food contaminant mycotoxin ATXII (chemical challenge), as well as upon application of shear stress (1dyn/cm^2) mimicking the movement of the intestinal lumen (physical challenge). Overall, combinatory physical/chemical challenge revealed complex responses of the two cell types that can greatly enhance the comprehension of influence of food constituents and contaminants at intestinal level [3].

References:

[1] Panieri E, Santoro MM. ROS homeostasis and metabolism: a dangerous liason in cancer cells. Cell Death Dis. 2016 doi: 10.1038/cddis.2016.105

[2] Taguchi K, Yamamoto M. The KEAP1-NRF2 System in Cancer Front Oncol. 2017 doi: 10.3389/fonc.2017.00085. eCollection 2017.

[3] Del Favero et al. Functional impairment triggered by altertoxin II (ATXII) in intestinal cells in vitro: cross talk between cytotoxicity and mechanotransduction under revision.

O.30.3. Antioxidant and cytotoxic activity of cocoa powders

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Cocoa powder is an industrial product obtained by processing cocoa beans. High content of biologically active compounds allows various physiological effects of cocoa powder that exceed its nutritional role, so it is often classified into a very popular group of "functional foods". The aim of this study was to evaluate the influence of alkalization process on cocoa powder's functionality in terms of antioxidant and cytotoxic properties.

This investigation was conducted on five natural and eight alkalized cocoa powders. Antioxidant activity was determined by HPLC postcolumn derivatization with ABTS. In vitro *cytotoxicity against HT29 cell line after 24 h exposure was measured by MTT assay.*

Alkalized cocoa powders showed significantly lower ($p<0.05$) antioxidant activity (128.3 µmol TE/g) compared to group of natural cocoa powders (230.8 µmol TE/g). Considering dose response curves expressed as % of control versus samples, we did not observed significant impact on cell growth. Survival index, calculated as area under curve, for all samples ranged from 930 to 1131. In addition, we figured out that alkalized cocoa powders have had less cytotoxic activity ($p<0.05$). Based on these results, it can be concluded that kind of cocoa powders in regard to different processing conditions influenced tested biological activities. Taken together, the present study suggests that antioxidant activity could be reliable ground for potential health benefits of cocoa powder.

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O.30.4. Role of the Parkinsons Disease-related protein DJ-1 in redox control and neuronal protection

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DJ-1 is encoded by the park7 gene and mutations eliminating DJ-1 function is associated to familiar type of early onset Parkinson´s Disease (PD). Additionally, postmortem analysis of brain samples from both idiopatic PD and Alzheimer´s Disease patients reveal an increased level of oxidized DJ-1. DJ-1 is a redox sensitive protein that mediates neuroprotection and cell stress in general and is strongly up-regulated in astrocytes of PD patients although the mechanisms are largely unknown.

We have generated a transgenic zebrafish line that mirrors the astrocytic DJ-1 up-regulation observed in PD in addition to a DJ-1 knock-out line in order to understand the function of DJ-1.

We show that by increasing solely astrocytic DJ-1, zebrafish larvae can be protected by PD-related insults as induced by MPP^+ or rotenone. Proteomic profiling of the astrocytes suggests that DJ-1 regulates both Nrf2-dependent and -independent pathways. The CRISPR/cas9-based knock-out line of DJ-1 shows that loss of DJ-1 can be partly compensated by other antioxidant-related protein, but that loss of DJ-1 makes the zebrafish larvae more vulnerable to oxidative stress. Our findings show that these transgenic lines can be highly useful animal models to understand the role of DJ-1 in neuroprotection.

O.30.5. Gut microbiota is differentially affected by distinct weight loss strategies

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Obesity is a metabolic disease that has reached the epidemic level worldwide. Gut microbiota is a key factor within the homeostasis of the host, with a role in weight loss. However, different interventions for weight loss could have a different response in the gut microbiota. Thus, the aim of the current study is to study different interventions for weight loss in patients with a different degree of obesity: bariatric surgery, Mediterranean diet and ketogenic diet.

Stool and blood were sampled before and after the interventions for the bacterial 16 rRNA sequencing by NGS (Ion S5, Thermofisher) of the stool samples. Biochemical and anthropometrical variables of routine were measured in blood. QIIME2 was used for the sequences analysis and translation into bacteria, PICRUSt for their functional inference and MicrobiomeAnalyst and STAMP, respectively, for their statistical analysis.

There were interesting differences between the analyzed procedures. Bariatric surgery, which obtained the highest weight loss, was not able to radically change the gut microbiota profile, but changed its functionality. Mediterranean diet, which obtained the least weight losses, registered a significant increase of the diversity and SCFAs producers. The ketogenic diet, which was in an intermediate point about the weight loss, produced a drastic change in the gut microbiota profile and its potential functionality. This study could open new research in obesity therapies targeting gut microbiota.

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P.30.1. Biosynthesis of silver nanoparticles using plant extracts as reducing/capping agents

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Searching for and developing of non-toxic, clean and ecofriendly methods for synthesis of nanoparticles (NPs), intended for medical application, is a scientific topic permanently attracting attention due to the great impact of biomedical applications in tissue engineering, bioanalytical diagnostics, cancer therapy and new drug delivery systems. A variety of physical, chemical or hybrid methods for synthesis of metal NPs exist, but in general, they are toxic, expensive, with low yield and with limitations for use in medicine (e.g. contamination from precursors, etc.).

Thus, the aim of our study was to design "green" method for synthesis of AgNPs compatible for pharmaceutical formulation, by using capping agent from natural source. Plant extracts are rich in enzymes and variety of phytochemicals that can reduce metal (silver) salts. Since many plant species are well-known, and have wide spread traditional use, there is a perspective for new, non-traditional uses because of the already reported antioxidative, antibacterial, antifungal, bioenchancing activity, etc. Plant extracts with antioxidative properties are also suitable to be incorporated into or be deposited on the surface of AgNPs, while at the same time serving as a reagent for NPs synthesis.

We used plant extracts for biosynthesis of AgNPs. The obtained AgNPs have to be thoroughly characterized using different and suitable analytical techniques to reach final formulation, which will confirm the possible synergistic effects of AgNPs and antioxidative compounds with plant origin.

P.30.2. The influence of catechins and phenolic acids on the redox balance of cells.

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To pinpoint actual role of dietary antioxidants in supporting endogenous antioxidant defence system in cells, the relation between their physicochemical, electrochemical and biological properties must be revealed. The aim of our study was to clarify these relationships for catechins and phenolic acids as well as to determine the molecular implications resulting from exposure to the tested compounds for oxidative stress response system in HT29 cell line.

Reduction potentials of antioxidants were determined by potentiometric titration. The biological tests embraced determinations of cytotoxicity and antioxidant activity in cell culture assessed by CAA assay. Genomic studies concerning modulation of expression of genes involved in oxidative stress response employed RT-PCR array-based technologies.

Our studies showed correlation between chemical properties and biological potential of polyphenols. This influence was accompanied with regulated expression of genes involved in antioxidant defence system of cell. The set of regulated genes was dependent not only on structure of investigated compounds, but also on their standard reduction potentials.

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P.30.3. Antioxidants protect overexpression of Nurr1 *in stressed dopaminergic cells*

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The nuclear receptor NR4A2 (Nurr1) is induced by stress and injury in brain; Nurr1 *is a transcription factor necessary for the maintenance of the midbrain dopaminergic neurons because it regulates the dopaminergic synthesis and it has a key role in the protection against oxidative and inflammatory stress associated to neurodegeneration.*

Permethrin (PERM), a member of the family of synthetic pyrethroids, can induce dopaminergic damage. In particular, impairment of Nurr1 *and tyrosine hydroxylase (*TH*) gene expression has been observed in animal models.*

The aim of this study was to evaluate in vitro*, through PC12 dopaminergic cells used as paradigm of neurodegeneration in neurobiological and neurochemical studies, if the overexpression of Nurr1 induced by PERM can be counterbalanced by antioxidants. The expression of two of the main transcription factors regulating the genes involved in pro-inflammatory and anti-inflammatory responses Nrf2 and NF-kB respectively are also analyzed.*

Results show that the incubation of PC12 cells with 1mM PERM for 72 hours, leads to over expression of Nurr1 *gene. This effect occurs with both corn oil and EVO used to solubilize the toxicant even if the cell viability and the Nrf2 expression were increased by the presence of EVO respect to corn oil. RT-PCR of* Nurr1 *showed that its up-regulation was significantly reduced in the presence of antioxidants glutathione (GSH), tocotrienols (TOC) and Electrolyzed reduced water (ERW), but the effect was more pronounced with the addition of ERW. Since ERW resulted from RT-PCR analysis the most efficient among the compounds used, western blotting was performed on PC12 cells treated with PERM or with PERM plus ERW. Nurr1 protein expression increased by PERM exposure was down-regulated in the presence of ERW while non-significant changes were observed for TH.*

In conclusion, the protective effect of antioxidants in this in vitro model suggests that PERM toxicity could be linked to the redox system imbalance. Even if EVO is not able to counterbalance Nurr1 *expression impairment, improved cell viability and anti-inflammatory properties suggest a potential beneficial effect of this component of Mediterranean diet.*

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P.30.4. Homocysteine-induced changes in iron metabolism in HUVEC cells are mediated by Akt-FOXO3a signalling pathway

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Hyperhomocysteinemia is a risk factor for cardiovascular diseases and many others. There is evidence that iron can mediate homocysteine (Hcy) toxicity. Thus, the aim of this study was to investigate the effect of Hcy on iron metabolism in HUVEC and SH-SY5Y cells. We demonstrate that Hcy induced upregulation of ferritins L and H in HUVEC cells in a time dependent manner and had no effect on ferritins in SH-SY5Y cells. The change in ferritin expression was preceded by a significant decrease in the cellular level of the active form of Akt kinase (p-Akt) in HUVEC but not in SH-SY5Y cells.

In order to confirm the involvement of Akt kinases and FOXO3a in ferritins upregulation, the HUVEC cells were transfected with siRNA against Akt1, Akt2, Akt3 and FOXO3a respectively. A significant increase in ferritin L and H protein levels was observed in Akt siRNA transfected cells, while in cells transfected with FOXO3a siRNA decrease in ferritins level was notice. Moreover, in the HUVEC cells treated with Hcy for 6 days active form of kinase Akt return to control value and it was accompanied by drop in ferritin L and H protein levels. Cytotoxicity of hydrogen peroxide (H_2O_2) significantly decreased in HUVEC cells pre-treated with Hcy for 24 h while in SH-SY5Y cells did not change.

Our results provide new mechanistic insight into the possible role for insulin signalling in Hcy-induced changes in iron metabolism. These data indicate that Hcy induces an adaptive increase in cellular ferritin level, and the process is mediated by alterations in Akt-FOXO3a signalling pathway.

P.30.5. Cancer inhibitory activity of dietary berries

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Regular consumption of particular foods, may confer specific molecular and cellular protection. A plethora of in vitro, in vivo as well as human studies has suggested as a diets rich in fruits and vegetables have been associated with a reduced risk of cancer. Mounting evidence reports a variety of health benefits of berry fruits that are usually attributed to their non-nutritive bioactive compounds, mainly phenolic substances such as flavonoids or anthocyanins. Although it is still unclear which particular constituents are responsible for the extended health benefits, it appears that whole berry consumption generally confers some anti-oxidant and anti-inflammatory protection to humans and animals. In this context, there has been an increasing interest in the role of polyphenols and other phytochemicals in cancer, particularly for their anti-oxidant and anti-inflammatory properties.

The aim of this study was to assess the antitumor activity of raspberry extract.Cell growth inhibition was evaluated using a standard colorimetric MTT assay, flow cytometry was introduced to investigate cells antioxidant and apoptosis effect of different human cancer cells: MDA-MB-231 (estrogen-negative breast carcinoma cells), MCF-7 (estrogen-positive receptor breast carcinoma cells), A549 (adenocarcinomic human alveolarbasalepithelial cells).

P.30.6. Effect of whey proteins on the immune system and its relation to examination stress

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Milk contains casein, which is the main protein of milk, as well as the soluble proteins which are also called whey proteins. It is known that whey proteins have a number of positive effects on human health. In this study, we aimed to evaluate the relationship of whey protein supplementation with examination stress and effects on antioxidant capacity, glutathione and the immune system.

The study was approved by the institutional ethics committee. It included 36 participants, who were third grade students at Marmara University School of Medicine. The participants were divided into three groups: control, casein and whey. The control group did not receive any nutritional supplementation, while the other two groups were supplemented with either casein (33g) or whey protein (44g) once daily for 15 days in addition to their normal diet. Blood samples were obtained at the beginning of the study (day 0), on the examination day (16th day) and after the examination (21st day). Serum cortisol and cytokine levels (TNF-alfa, IL-6, IL-12) were measured by ELISA. Antioxidant capacity and glutathione levels were measured by spectrophotometric methods.

No significant difference was observed in terms of their age, body mass index, nutrition, physical activity, tobacco and/or alcohol use when the three groups were compared. An increase in antioxidant capacity and glutathione levels of the participants using whey protein was observed whereas there was no change in control and casein groups at the end of two weeks. Whey protein supplementation did not affect cortisol levels, but participants taking whey protein showed an increase in serum TNF-alfa and IL-6 levels. A slight decrease was observed in cortisol levels after the examination, but no significant change was found in other parameters.

It is suggested that the use of whey protein strengthens the response to oxidative stress by increasing the antioxidant capacity and glutathione levels while supporting the immune system by affecting the cytokine response.

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P.30.7. Effect of the kinetic of protein digestion on sarcopenia inhibition

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Today we can observe growing number of people who have problems correlated with improper diet. These problems include for example: obesity, diabetes, cardiovascular diseases or sarcopenia. During my PhD studies I am going to identify colloidal food structures which probably will be used for preventing sarcopenia. Sarcopenia is the age-associated loss of skeletal muscle mass and function. This is important problem because of booming aging population and economic costs on health care for people over 65 [1]. Optimal nutritional status in combination with physical activity are key factors in preventing this syndrome. Older people ingest 5-10 g proteins per meal. To obtain good protein muscle synthesis they should ingest 20-25 g per meal [2]. Because it is hard to convince older people to excersises and changing their nutritional habits, there is a need to find innovative strategies to limit body protein loss during aging. Increasing of bioaccessibility of protein in food is an option. According to ex vivo studies muscle from old rats Essential Amino Acids (EAAs) are required for an optimal stimulation of muscle protein synthesis [3]. EAAs cannot be synthesized de novo by the organism, so they must be supplied in diet. Whey Proteins (WPs) contain a high concentration of EAA, particulary leucine. Whey protein gels can meet the requirements for quick transport to small intestine, high bioaccessibility of AAs in small intestine and probably good anabolic response in muscle.

*The aim is to identify microstructure of colloidal systems which could possibly give good anabolic answer in muscle of sarcopenic people. These systems will be digested under simulated conditions (*in vitro *digestion models) to find structures which can give high bioacessibility of amino acids in small intestine. This high bioacessibility is correlated with proper anabolic mechanisms in muscles [4][5].*

References:

[1] J. E. Morley et al., Prevalence, incidence, and clinical impact of sarcopenia: facts, numbers, and epidemiology—update 2014, J Cach. Sarc. Muscle, (2014) 5:253–259.
[2] A. Laviano et al., Sarcopenia and Nutrition, Adv. Food Nutr. Res., Volume 71 (2014) 101-136.
[3] J.E.Tang et al., Ingestion of whey hydrolysate, casein, or soy protein isolate: effects on mixed muscle protein synthesis at rest and following resistance exercise in young men. J. Appl. Physiol. (2009) 107: 987-992.
[4] W.L. Hall et al., Casein and whey exert different effects on plasma amino acid profiles, gastrointestinal hormone secretion and appetite, Brit. J. Nutr. (2003), 89, 239–248.
[5] D.H.P. Guimaraes et al., Whey proteins solubility as function of temperature and pH, LWT - Food Scien. Tech. 38 (2005), 77-80.

P.30.8. Nucleic acids as food components and they impact on epigenome

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Nucleic acids (DNA and various forms of RNA), are present in every living cell of animal and plant organisms as well as in microorganisms, therefore in most foodstuffs consumed by humans their presence is expected. Next to proteins, fats, vitamins and carbohydrates, they are a natural component of food products, primarily of those containing cellular structures. In the case of consumption of foods, a certain amount of NA, including double-stranded RNA, can be introduced into the human gastrointestinal tract, where they can survive the digestion process in alimentary tract, pass through the intestinal barrier and circulate in the blood system. Nucleic acids play an important role as a source of nucleotide-related molecules and participate in many biosynthesis pathways, like enzyme-precursors, as well as, as a nitrogen and phosphorous source. The major role of dietary nucleic acids is to provide building blocks for the synthesis of cellular DNA and RNA by the salvage pathway, as well as to facilitate the de novo *nucleic acid synthesis.*

With the development of studies on low molecular weight NA, for example various types of RNA the ability to transfer the particles from the ingested food to cells of the intestinal tract and more in the bloodstream has been demonstrated, and suggested that it could affect the expression of genes of the consumerThe small regulatory nucleic acids – RNAs – are presumed to regulate gene expression in the consumer's body, to influence epigenome and, in consequence, to affect metabolism. In the contexts of epigenetics the role of ingested DNA fragments seems to be an important subject. It is the part of the sentence "We are what we eat".

In our study, the presence of nucleic acids in high and low processed food products after thermal treatment was investigated. Both long-chain, non-degraded fragments with an average length of 20,000 bp and short-chain nucleic acid fragments were found in investigated meat samples. In the context of nucleic acid migration from the intestine to the blood stream, their presence is an important point for further investigations on their possible impact on human epigenome.

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P.30.9. The role of S6K1/2 kinases in the process of lysosomal membrane permeabilization and cell death induced by sulforaphane – a natural anticancer agent

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The increase in morbidity and mortality due to oncological diseases obliges to search for new therapies. Recent research has shown that an effective mechanism triggering cancer cell death is the induction of lysosomal membrane permeabilization (LMP). This process results in a destabilization of lysosomal membranes and a release of lysosomal enzymes – cathepsins - into the cytosol. Released cathepsins are involved in cell death, by necrosis or apoptosis, and the resulting type of cell death depends on the degree of lysosome membrane damage. The mutual superiority between LMP and apoptosis is complex, depending on the inducing factor as well as its intensity. In the light of published research, cancer cells appear to be particularly predisposed and sensitive to LMP induction compared to normal cells. This feature is associated with the high rate of the metabolism of these cells, increased volume of lysosomes and high levels of reactive oxygen species (ROS), although the exact mechanism of this relationships has not been fully understood.

Our results show that in mouse embryonic fibroblasts (MEF) devoid of S6K1/2 kinases - proteins commonly overactivated in cancers - there is no lysosomal degradation of autophagosomes during stress induced by sulforaphane (SFN). SFN is a natural anticancer agent present in cruciferous plants inducing autophagy and apoptosis in cancer cells by, in a large extent, an increase in the level of ROS of mitochondrial origin and permeabilization of mitochondrial outer membrane (MOMP). Analysis of the lysosome morphology during SFN-induced stress showed that this compound in wild-type cells causes an increase in the number of lysosomes stained with LysoTracker Red - a lysosomotropic fluorescent dye accumulating in organelles with an acidic pH. At the same time, in SFN-treated cells lacking S6K1/2 kinases, the number of stained lysosomes did not increase. This resulted not due to the reduced number of lysosomes in these cells but from the permeabilization of the LMP. Because MEF devoid of S6K1/2 also exhibit reduced viability and increased susceptibility to induction of apoptosis by SFN compared to wild type cells, the question arises whether LMP is the primary cause leading to induction of apoptosis in these cells or vice versa *- is the result of increased activation of caspases/MOMP (apoptosis), or whether these are two independent phenomena. The next steps of the project will aim to explain the interrelations between LMP and apoptosis in cells lacking S6K1/2 kinases during SFN-induced stress and explain the mechanism causing increased susceptibility to permeabilization of lysosomes, in particular the analysis of the ROS level .*

The results will allow us to clarify whether the permeabilization of lysosomes observed during the SFN treatment of cells lacking S6K1/2 kinases contributes to cell death. In addition, they should allow to determine the mechanism that sensitizes lysosomes to permeabilization in the absence of S6K1/2 kinases in the cell. The obtained

results may have a high scientific value, as there have been no reports on the influence of S6K kinases on lysosomal function so far.

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P.30.10. ROS scavengers modulate anthrapyridazones activity

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An anthraquinone moiety is present in multiple highly active anticancer drugs widely used in treatment of a broad spectrum of malignancies. One class of such compounds are anthracyclines, including doxorubicin, daunorubicin, mitoxantrone and others. They are believed to act through topoisomerase II inhibition, and with structurally-unrelated compounds such as etoposide or amsacrine constitute a family of topoisomerase II poisons.

Over 20 anthrapyridazones, imino analogues of anthraquinone, have been synthesized in our department in search for a highly potent anticancer drug lacking typical characteristics of ABC-transporter substrates.

In the family of anthrapyridazones, a strong correlation between DNA binding affinity and anticancer activity is observed. Although this suggests a common mechanism of action, a closer look at the molecular level has revealed a considerable variety of modes of action. Of importance, some anthrapyridazones are capable of generating significant amounts of ROS, which may contribute to their DNA double strand breaks-inducing property. ROS-generation ability was noted particularly for HL-60 cell line, an acute myeloid leukemia model.

In the present work, we explore the possibility of modulating the activity of anthrapyridazones activity with common ROS scavengers, superoxide scavenger vitamin C and hydroxyl radical scavenger N-acetylcysteine. Particularly, N-acetylcysteine is able to supress ROS generation of selected anthrapyridazone derivatives.

P.30.11. Catechins as epigenetic modulators

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Flavonoids, a group of abundant food polyphenols, support the endogenous antioxidant system and maintenance of redox homeostasis by scavenging reactive oxygen species. This group of flavonoids includes catechins - antioxidants present in green tea, known for providing numerous health benefits. Recently green tea catechins have been reported to affect DNA methylation. Regarding the reversible nature of epigenetic modifications, deeper insight into relationship between cellular redox state and DNA methylation may contribute to a better comprehension of the role of antioxidants in chemoprevention and treatment of chronic diseases

Our previous results have showed that the low (1 µM) and the high (10 µM) doses of catechins applied to human colon adenocarcinoma cell line (HT29) induce different changes in the expression of some redox-related genes [1]. Based on this, we aimed at examining the methylation profiles in the promoter areas of the up-regulated HSPA1A and the down-regulated SRXN1 using Methylation-Specific PCR and Methylation-Sensitive High Resolution Melting. The objective of the research was to find out whether the observed dose dependence was caused by epigenetic modulation of gene expression.

In the case of HSPA1A, methylation level within examined CpG island was not significantly affected by catechins, regardless of concentration. Conversely, the methylation level within SRXN1 CpG island was significantly increased when cells were exposed to the high concentration of catechins.

In conclusion, the methylation levels of CpGs located in the promoter area of SRXN1 and HSPA1A can be modulated by catechins exhibiting strong antioxidant activity, therefore the observed modulation seems to be redox-sensitive. Moreover, catechins so far have been considered as inhibitors of methylation, whereas they can also act as methylation inducers. This dual function may derive from their ability to influence cellular redox homeostasis.

References:

[1] Baranowska M. et al. The relationship between standard reduction potentials of catechins and biological activities involved in redox control. Redox Biol. *2018: 17, 355-366*

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P.30.12. Transcriptional acitivity of epigenetic remodelling genes in human skin and regenerative capacity

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Epigenetic regulation determines the development of organisms, cell differentiation as well as the differentiation potential of stem cells, thus suggesting an important role of epigenetic mechanisms in regeneration capacity. Genes involved in DNA methylation/demethylation processes, histone modifications and other regulators of chromatin remodelling could be considered as the markers of epigenetic remodelling and their transcriptional activity can be regarded as an estimate of cellular plasticity and regenerative potential. Surgical skin wounds of patients receiving neoadjuvant therapy prior to abdominal surgery are known to show delayed healing, which complicates further therapy.

The aim of this study was to investigate the transcriptional activity of genes involved in epigenetic remodeling in the skin samples collected from neoadjuvant patients.

We performed qPCR quantification of transcript levels for a selection of genes involved in different epigenetic mechanisms including DNA methylation, histone modifications and chromatin structure regulation.

In the predominant part of examined genes, we observed statistically significant 2-5-fold decreases in expression in the skin of neoadjuvant patients in comparison to other oncological patients who received no neoadjuvant treatment prior to surgery. In addition, we found that the expression levels of the same epigenetic markers in in vitro *expanded human epidermal progenitor were markedly, 2-16-fold lower than in the skin samples and non-cultured epidermal cells collected from the patients.*

Significant reduction in the activity of epigenetic markers in the skin after neoadjuvant therapy indicates the importance of epigenetic remodelling in wound healing and suggests novel therapeutic directions for skin wound treatment.

Acknowledgements: This work was supported by the National Science Centre – Poland grant no. 2011/03/D/N25/00555 (MP) and grant no. 2011/2012/05/D/NZ5/01224 (AW).

P.30.13. Novel technology of preparation liposomes with antioxidant vitamins to treat age-related diseases

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The novel nanotechnology was used to encapsulate vitamins (C, E) into the DPPC liposomes. Proportions of vitamins and DPPC lipids were selected as one vitamin per one lipid molecule. In liposome structure the hydrophobic vitamin E was placed inside the hydrophobic part of liposome and the hydrophilic vitamin C were located on the surface of liposomes. The formation of the complexes were confirmed by calorimetric and biological experiments. In particular, calorimetric curve of complex liposomes are considerably different from the calorimetric peak profiles of the pure DPPC liposomes. Biological experiments reveal that complex nanoparticles (vitamin E and DPPC lipid complex) are more effective against tumorous Jurkat cells than adding the same amount of pure vitamin C and E, which is a quite significant result.

As we know, with age increasing, the concentration of radicals in the human body increases, and health problems of older people are due precisely to the presence of a large amount of these radicals. Therefore, the presence of antioxidant molecules in the body compensates the impact of harmful radical groups, which should reduce age-related health problems. It is well known that vitamins C and E are harmless medicines and are strong antioxidants. Incapsulation of these molecules inside the liposomes makes it possible to deliver them to the needed tissue, which makes them more effective for solving age-related problems.

P.30.14. The impact of redox active compounds belonging to different flavonoid groups on the antioxidant activity system of HT29 cells.

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All multicellular organisms for energy production use the commonly occurring element in nature, which is oxygen. During metabolic processes, and especially during respiration, side products are created, which are referred to as reactive oxygen species (ROS). Due to their high reactivity, they may have a significant impact on the functioning of the whole organism. When there is an imbalance between the amount of ROS and the possibility of their neutralization, oxidative stress occurs in the body, which may lead to damage to cellular structures. The most important line of defense is a set of enzymes capable of neutralizing ROS. Some of them use the most common antioxidant in the body – glutathione – and other endogenous antioxidants. However, antioxidant defense system of cell is not always sufficient. Thus, to protect cells from oxidative stress, dietary supplementation with antioxidants appears to be a reasonable approach to maintain proper redox balance.

The aim of this research was to examine the selected biological activities for representatives of redox active compounds belonging to different flavonoid groups. Four antioxidants belonging to flavonols (quercetin and its glycoside) or to flavanons (naringenin and its glycoside) were selected for the study. The experiments performed included determination of cytotoxicity of the tested compounds by MTT test, determination of cellular antioxidant activity by CAA test, and determination of the influence of the above-mentioned compounds on DNA integrity in HT29 cells by comet assay.

The obtained results indicated that the tested compounds in the concentration range used are non-toxic to HT29 cells. Neither they caused DNA damage. Significant differences in the biological properties of the tested compounds were seen in cellular antioxidant activity. In the case of quercetin and rutin, antioxidant activity increased with increasing concentration of those compounds. However, stronger reducing activity was observed for the aglycone – quercetin. For naringin possesing a sugar residue, CAA values oscillated around zero for all concentrations tested. Naringenin, which is an aglycone, exhibited antioxidant activity at physiologically available concentrations, but at higher concentrations had pro-oxidative activity.

The results of the research indicated that the physiological concentrations of naringenin and naringin undergoing deglycosylation during transport to cells may be of great importance for maintaining the redox homeostasis. Increasing the dose of antioxidants did not lead to better protection against ROS and changed the redox status of the cell from reduced to oxidative.

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P.30.15. On possible mechanisms of resistance of bacteria to antibiotics and phages - ways to overcome them

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Nowadays, studying antibiotics, germs and their resistance has reached the highest level in the scientific world. Because around us an amount of microbes are huge, so their influence on living system are very important. Not only health depends on them, but also a creation of sterility area, for example food produced stuffs. After many various experiments and measurements scientists predicted, that using antibiotics (regarded as "world savers") in a couple of years, will be totally in vain, because germs will gain resistance towards antibiotics. As it seems, without any doubt, dilemma may cause lethal and fatal results for the whole humanity, but there is always a hope, isn't there?!

To study the process of bacterial growth, it is important to determine how the timing of bacterial growth changes in response to variability of composition of media, or if we introduce an antimicrobial drug or bacteriophage into the media. Using the method of turbidimetry, we showed that bacterial growth pattern is influenced not only by just presence of the antimicrobial drug, but also the concentration of the drug into the medium, as different concentrations of the drug showed different patterns of growth. The bacterial proliferation is ceased at certain ratio between bacterial cells and antibiotics' molecules, and this ratio in microbiology has got a special term- minimum inhibitory concentration, MIC.

The experiments held by us concerns the dependence of bacteria E. coli proliferation on the miscellaneous external conditions. The roles of these conditions were played by various antibiotics, particularly by Ampiox and Gentamycin. We used to conduct our experiments on E.coli C bacteria. The effect of these antibiotics' action was determined according to bacterial proliferation. It was found out that bacterial proliferation depends on the amount of antibiotics, more precisely the bacterial proliferation is ceased at certain ratio between bacterial cells and antibiotics' molecules, and this ratio in microbiology has got a special term- minimum inhibitory concentration, MIC.

It was used the turbidimeter in our experiments that enabled us to observe the variability of bacteria by means of measuring the turbidity of the solution real-time mode and exactly this method enabled us to define the MIC for these both antibiotics. In addition, by means of using the turbidimeter we observed a very important case of interaction between bacteria and antibiotic such as acquired resistance when adding the same antibiotic the second times to bacteria which could not affect the bacterial proliferation any more. Moreover, this methods enabled us ascertain that the autocrine

signaling is responsible for this acquired resistance. It is interesting that turbidimeter also showed that heating the solution by 20 degrees forced this resistance to vanish. According to our results, receptor proteins on the bacterial cell membrane are not saturated with antibiotics or bacteriophages fully and there are free unbound membrane receptors, which we hypothesize is the reason for uninhibited bacterial growth.

To determine the resistance of the bacteria, experiments were conducted involving Ampiox and Gentamicin antibiotics. We showed those conditions when the bacteria developed resistant to antibiotics. It was interesting to show mechanisms when the bacteria revolved back to sensitivity to antibiotics.

P.30.16. Caffeine – new insight of known antioxidant

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Oxidative stress is an intrinsic process, plays a pivotal role in the pathogenesis of many dread diseases, including cancer. In an organism, most of the reactive oxygen species (ROS) formed are removed during natural biochemical processes. The long-lasting weakening of the antioxidant barrier in cells or production too many ROS can lead to damage to the genetic material, cell structure or enzymes contributes to the carcinogenesis process. Antioxidants, natural ROS scavengers, protect telomeres and delay cellular aging in normal somatic cells. However, in cancer cells occurs the reverse effect through existing a higher redox homeostasis threshold.

This study presents the impact of caffeine, known antioxidant on telomerase activity and a probable explanation for this phenomenon by generating ROS.

P.30.17. Dietary oxidized phospholipids: from digestion to biological effect

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The results of numerous epidemiological studies indicate that the type, quality and intake of food-delivered lipids contribute to the prevention or promotion of diet related and metabolic diseases such as: type 2 diabetes, obesity or atherosclerosis. Among the food-delivered lipid compounds, phospholipids (PLs) attract increasing attention due to their high nutritional value and functional properties. PLs, especially those containing essential unsaturated fatty acids (FAs) exhibit a number of key biological activities. At the same time, polyunsaturated FAs incorporated in the structure of natural occurring PLs are particularly susceptible to oxidation.

Oxidized phospholipids (OxPLs) delivered with food and products of their digestion can be potentially toxic molecules for to the epithelial cells of digestive tract. Accumulation of OxPLs can lead to gut pathologies as a result of cell membrane modifications as well as DNA and protein damage. Additionally, OxPLs may lead to pathological conditions in cells by aberrant regulation of numerous genes implicated in cell proliferation, differentiation, cellular stress, inflammation and lipid metabolism. Among transcription factors activated by OxPLs are such important gene expression regulators as PPARs, Nrf-2 or ATF4.

Long-chain oxidized PLs generated by LOX-1 catalyzed oxidation were characterized using offline two-dimensional liquid chromatography coupled with DAD, CAD and MS detection. Kinetics of non-oxidized PLs (n-OxPLs) and OxPLs digestion by porcine pancreatic phospholipase A2 were studied using pH static method (pH=8). Effect of n-OxPLs and OxPLs on human colon adenocarcinoma cell line (HT-29) growth was determined using MTT test.

Our research suggests that OxPLs are digested slower by porcine pancreatic phospholipase A2 in comparison with their native counterparts. This may result from a decreased phospholipase A2 activity towards its substrates when chemically modified, e.g. by oxidation as is the case with OxPLs. In addition, OxPLs exhibited higher toxicity against model cells of the gastrointestinal tract.

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P.30.18. Rationale of MaPLE project focused on intestinal permeability in the older subjects

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The increase in the aging population is a great worldwide challenge by considering the impact on health care system due to the burden of chronic degenerative diseases. Ageing is often associated to systemic inflammation and recent findings suggest that also intestinal permeability (IP) could be increased in the older subjects contributing to a low-grade chronic inflammation. The intestinal microbiota seems to be a significant IP regulator and the age-related microbial dysbiosis has been showed to promote IP in the animal model [1]. Dietary intervention strategies could modify the relative abundance of specific bacterial groups and consequently affect the maintenance of normal intestinal barrier function. In this context, food bioactives such as polyphenols can have a regulatory role.

MaPLE project aims to test the hypothesis that altering the diet of older subjects with established IP by increasing polyphenol intake will lead to beneficial changes at intestinal and systemic level. Through a controlled randomised cross-over dietary intervention study (8-week polyphenol-rich diet versus 8-week control diet), MaPLE project investigates the efficacy of a polyphenol-rich dietary pattern in older people (>60 y), living in a well-controlled defined setting. Numerous biomarkers related to IP with specific attention to zonulin, oxidative stress, inflammation, vascular function, microbiota ecosystem, blood bacterial and LPS loads and serum/urine metabolomics has been considered.

Data from MaPLE project will provide new perspectives for the implementation of a polyphenol-rich dietary pattern able to promote a protective metabolic phenotype in the older subjects.

References:

[1] Thevaranjan N, et al. Cell Host Microbe. 2017.

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P.30.19. Prevention of 7β-hydroxycholesterol-induced mitochondrial dysfunction and cell death by dimethylfumarate and monomethylfumarate on 158N murine oligodendrocytes

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Multiple sclerosis (MS) is a highly debilitating and often fatal demyelinating disease. There is currently no efficient treatment for this disease. However, several molecules can slow the progression of MS which is associated with oxidative stress and increase of oxidized cholesterol derivatives (oxysterols) such as 7β-hydroxycholesterol (7β-OHC). It is therefore necessary to better know the biological activity of 7β-OHC and to identify natural or synthetic molecules capable to prevent its side effects.

For this, we studied the effects of dimethyl fumarate (DMF), the active compound of Tecfidera (Biogen) used for the treatment of relapsing-remitting MS, and of its major metabolite monomethyl fumarate (MMF) on a model of murine oligodendrocytes (158N) grown under conditions of oxidative stress. The 158N cells were cultured in the presence or absence of 7β-hydroxycholesterol (7β-OHC, 50 µM for 24 h), with or without DMF and MMF, used at 25 µM, introduced in the culture medium 2 h before the addition of 7β-OHC. Cell viability and / or mitochondrial succinate dehydrogenase activity were assessed by the MTT assay. Measurement of mitochondrial transmembrane potential (Δψm) was performed by flow cytometry using $DiOC_6(3)$. Membrane integrity was evaluated by flow cytometry using propidium iodide (PI) and fluorimetry using fluorescein diacetate (FDA).

A significant attenuation of the cytotoxic effects of 7β-OHC was observed with DMF and MMF: decrease in the number of non-adherent and dead cells; decrease in the number of cells having an impaired plasma membrane (IP (+) cells, FDA (-) cells). DMF and MMF also prevented the mitochondrial alterations induced by 7β-OHC: recovery of Δψm and increase of mitochondrial succinate dehydrogenase activity. These results demontrate cytoprotective effects of DMF and MMF towards 7β-OHC: prevention of mitochondrial dysfunctions and cell death. These results support the interest shown in DMF and MMF not only in the treatment of MS but also for all diseases where increases of 7β-OHC are observed.

P.30.20. The role of iron in marathon-induced changes on the EPO-erythroferrone-hepcidin axis

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The aim of this study was to investigate whether a marathon affects changes in key hormones responsible for iron metabolism: Erythroferrone (ERFE) and Hepcidine (Hpc). Moreover, we assessed if bearing mutations of the *HFE* gene, responsible for controlling the absorption of iron, would influence iron metabolism.

Twenty-nine healthy man (mean age 38± 5), who took part in the Gdansk marathon were studied. HFE gene mutation using PCR technique was evaluated. Blood iron, ferritin, ERFE, and Hpc level were assessed before, immediately and 9±2 days after the marathon.

ERFE increased after the marathon and remained elevated one week later, but only in the runners whose hepcidin decreased ($p<0,05$). Athletes characterized by low blood iron concentration before the marathon (<105 µg/dl) presented with a significant increase in ERFE after the marathon, while those with high blood iron (>105 µg/dl) had a stable ERFE concentration ($p<0,05$). Blood ferritin concentration had no effect on changes in ERFE induced by the marathon. Despite high prevalence of *HFE* gene mutation (11 out of 29 runners) no differences in all study parameters (iron, ferritin, Hpc, ERFE) were observed.

In the presented study, we demonstrate that alterations in hormones regulating iron metabolism (ERFE, Hpc) induced by a marathon are significantly dependent on blood iron concentration at baseline. Contrary to our expectations, athletes who were HFE heterozygotes demonstrated similar changes in iron metabolism to wild type ones.

P.30.21. Spectrophotometric procedure for melatonin detection

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Melatonin has been and still it is used in various clinical trials for different therapeutic approaches. Melatonin, known as a hormone of the pineal gland, could be also found in the gastrointestinal tract containing significant more melatonin that could be released into the blood stream following food intake. Its specific actions as an antioxidant agent are related to direct radical scavenging, playing a role in upregulation of antioxidant and downregulation of pro-oxidant enzymes. In addition, melatonin is able to potentiate the efficacy of other antioxidants, such as ascorbate, through direct radical scavenging leading to an important radical detoxification.

The work focused on the demonstrated antioxidant properties is dedicated especially for the treatment of neurodegenerative disorders, such as Alzheimer's disease. Therefore, high interest is directed towards melatonin dosage. However, the precise melatonin contents are sometimes affected by uncertainties that result from sampling particular methodological problems, as melatonin can be easily destroyed by oxidants and then, erroneous data are easily obtained due to the presence of compounds mimicking melatonin or interfering with it.

In present work, it is introduced an assessment procedure for melatonin dosage based on spectrophotometric methods, derivative spectrophotometry and fluorescence. The fluorescence method presented a quantification limit of 0.7 x 10^{-12} mol/L and a determination limit of 1.10 x 10^{-12} mol/L. The application of derived spectrophotometric UV-Vis method could be very useful for spectra with overlapping or interfering signals. Applying this versatile and effective method LOQ = 9.83 x 10^{-12} mol/L and LOD = 29.81 x 10^{-12} mol/L have been obtained, for a regression coefficient of 0.9987. The measurements were performed at pH=7.2. Detection of melatonin in various pharmaceutical, synthetic or biological samples based on proposed spectrophotometric methods have the advantages of high sensitivity, selectivity and simplicity.

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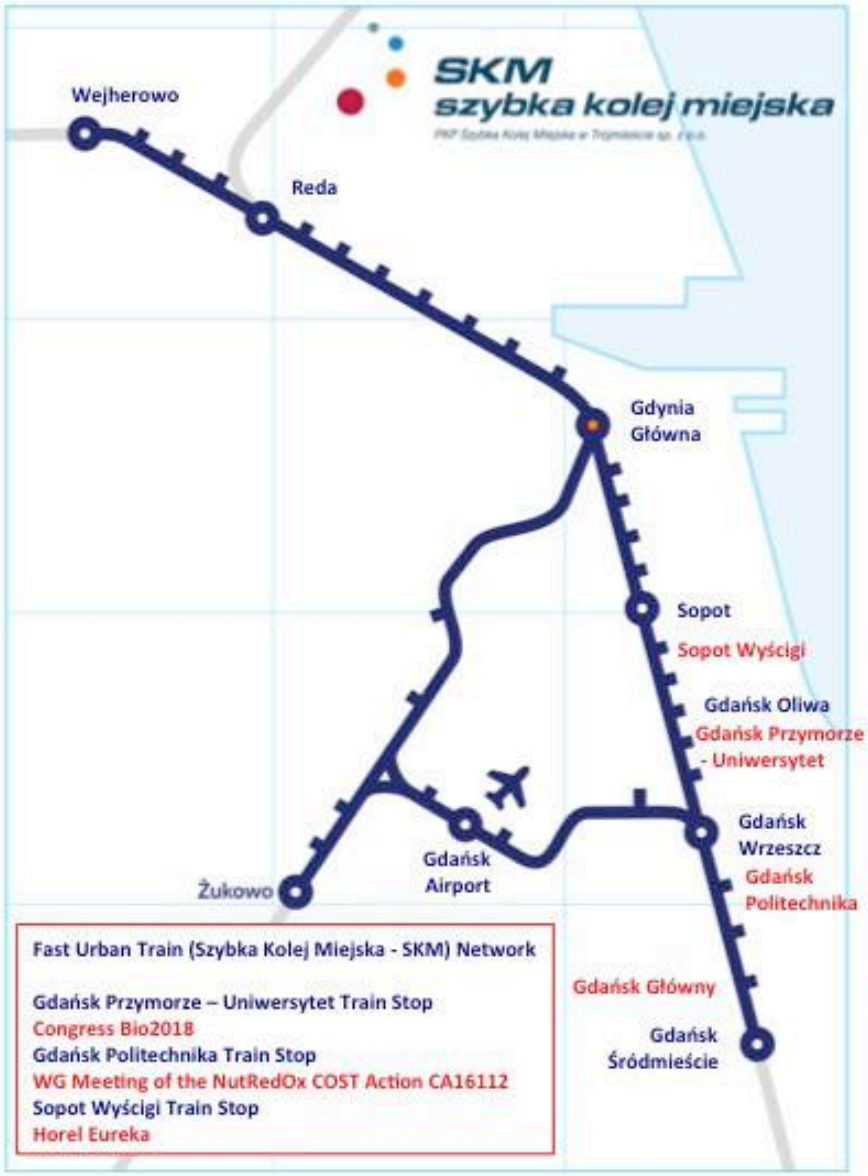

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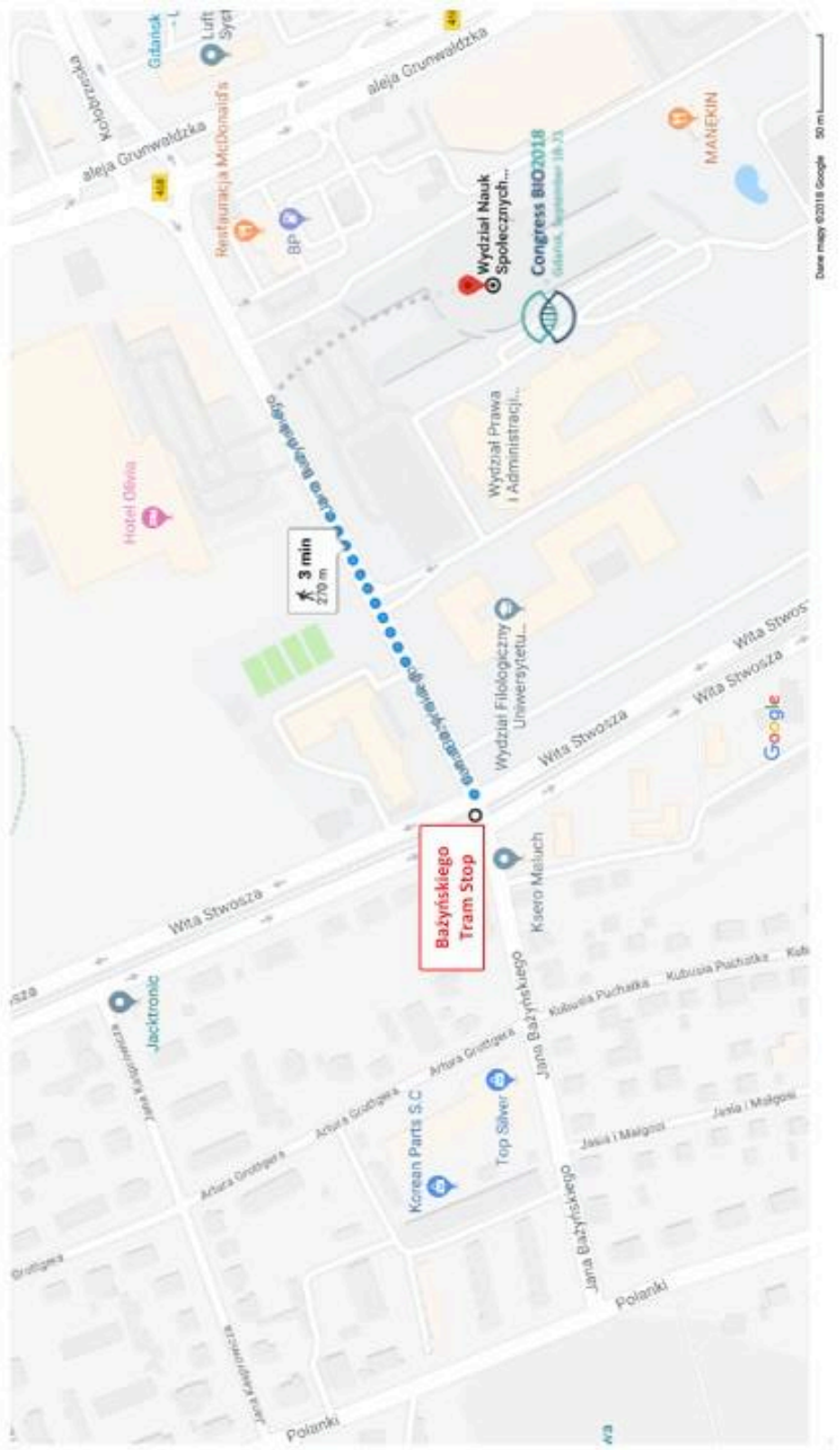

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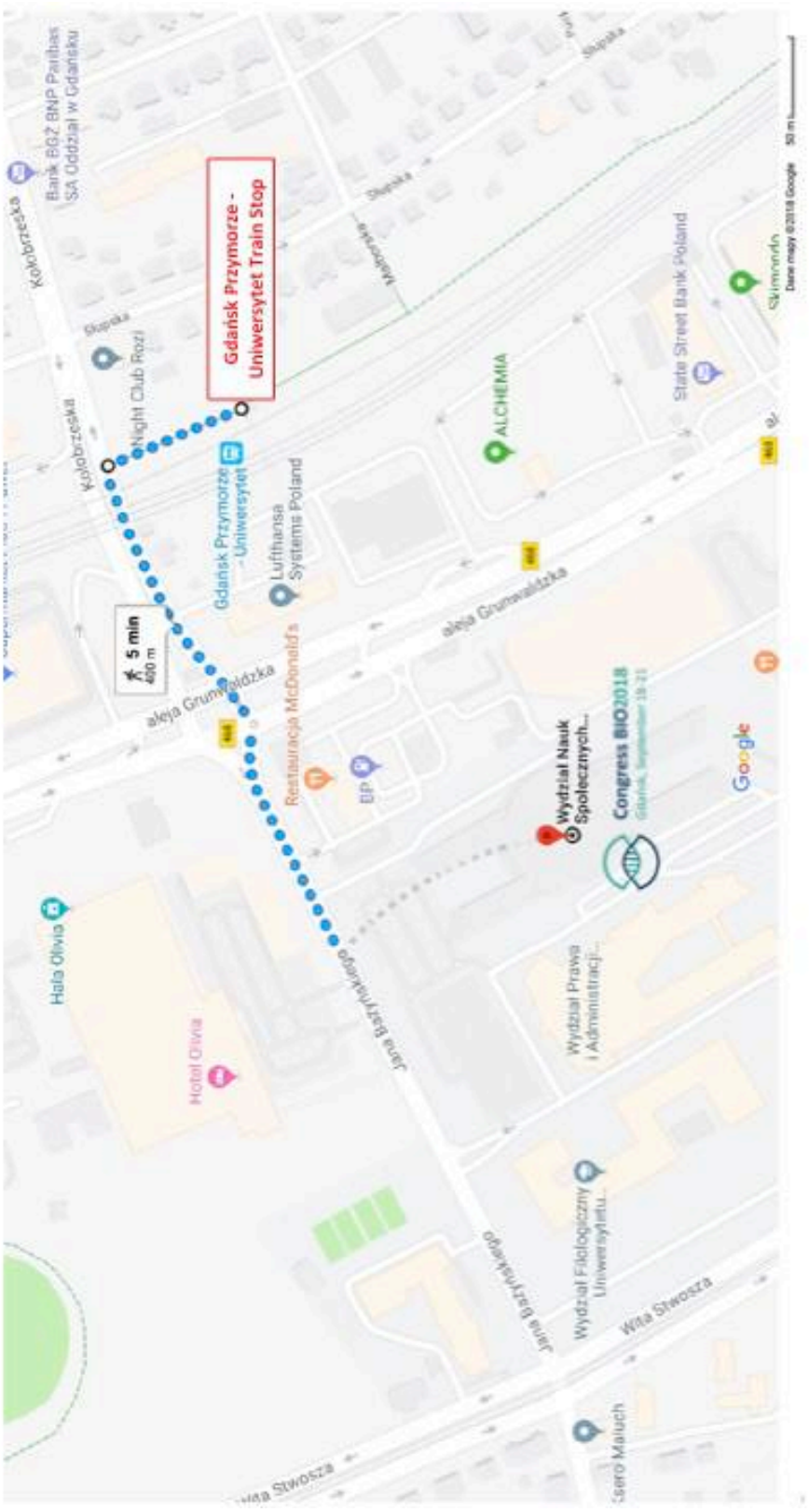

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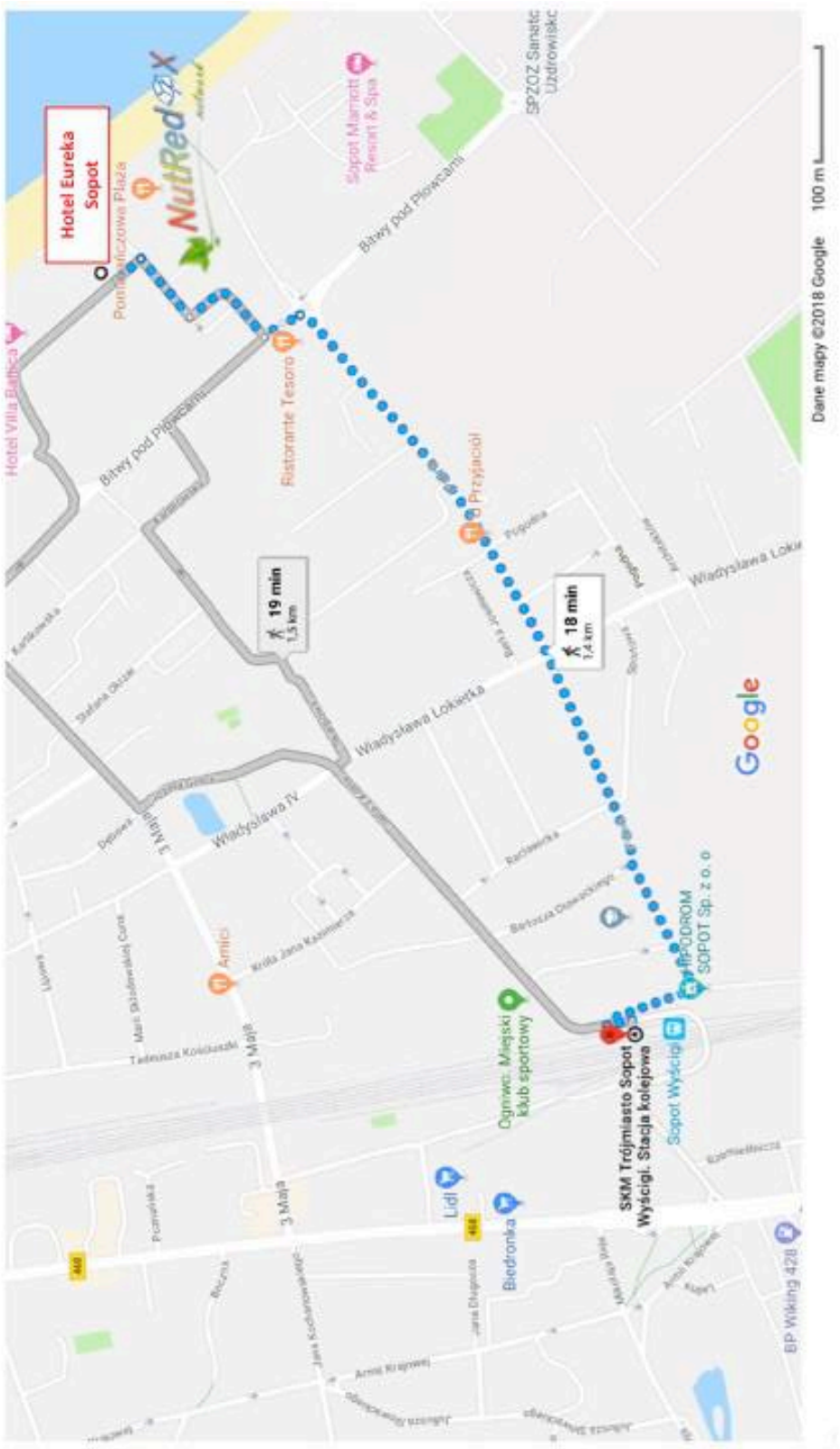

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