

SCIENTIFIC REPORT

Biomimetic Radical Chemistry **1st Annual Meeting of COST Action CM1201** **Bologna, May 6-7, 2013**

The meeting has been held in the Research Area of the Consiglio Nazionale delle Ricerche in Bologna for two days (May 6 and 7, 2013).

Dr. Chatgililoglu, the Chair of the CM1201 Action, did the opening of the meeting on May 6 at 9:30 am. He described the COST system and the finalities to the audience that was composed by the COST participants and MC members, plus local participants as scientists in chemical and biological research working in the CNR Research center. Also he gave a general overview of the Action, and for this first scientific meeting he underlined the importance of mixing the expertise of the four working group participants, in order to get the best interaction possible. Also he encouraged the Early Stage Researchers present at the meeting to establish fruitful discussions with the other scientists and individuate the common research activities to be developed in the Action. There were more than 60 participants, which included also the local participants. Both days were organized with the lectures of participants to the 4 working groups, in order to give the possibility to know the research fields of all scientists participating to the Action.

On May 6, Session 1 started with the WG2 (*Models of DNA Damage and Consequences*) and Dr. Jean-Luc Ravanat (France) gave a talk on "Recent aspects of radiation-induced DNA lesions", with interesting results on the discovery of a new lesion in the DNA sequence due to the connection between sugar and base damage. The second speaker was Dr. Martine E. Lomax (Great Britain) on "*Processing AP sites as single lesions and within clustered damaged sites when present in mononucleosomes*", which described the methodologies to assess the activity of endogenous repair systems on the DNA damages. In the program there was the absence of Dr. Gantchev that could not participate for personal reasons. Prof. Leif A. Eriksson (Sweden) gave an interesting talk on "*Computational Modeling of ROS/Radical-induced DNA Damage Processes*" describing his potentiality to interact with several Action members in order to apply his computational facilities to the study of the DNA conformational changes due to the modification of base and sugar units. Also he underlined that he can do modelling also for membrane and protein structures and his group has a very large access and working hours at the computer facility of his organization.

After the coffee break, the session of the WG1 on Radical Enzymes started with Prof. Bernard Golding (Great Britain) giving an interesting talk on "*How do microbes degrade hydrocarbons in the oxygen-free biosphere?*", which showed the high potential of environmental applications of the

scientific results of the Action. Also he showed that chemical research are very important to assess the mechanistic steps of enzymatic activities and to use at the best the enzyme functioning in synthetic, environmental and biotechnological fields. The session 2 proceeded with the talks of Prof. Jerzy L. Gebicki (Poland) on *"Inhibitory effect of flavonoids on catalase: structure-activity relationship"*, Dr. Aleksandra Jankovic (Serbia) on *"Impacts of manganese (II) pentaazomacrocyclic superoxide dismutase mimic in diabetes"*, Prof. Matthias Boll (Germany) on *"Reduction of aromatic rings by dearomatizing arylcarbonyl-CoA reductases"* and Prof. Myriam Seemann (Germany) on *"GcpE and LytB, two Fe/S enzymes involved in the biosynthesis of isoprenoids"*. A large scenario of the activity of antioxidant enzymes came from these lectures, including the role of metal coordination in the enzymatic structures, which has to be still fully elucidated, together with the importance of structural and chemical requirements for the enzymatic active sites. A lively discussion involved all participants, also because the presented enzymatic activities can be easily connected with bio-inspired synthesis, biotechnological applications, membrane functioning and free radical processes.

The morning session ended at 13:30.

The meeting restarted at 14:30 with the WG3 (*Membrane Stress, Signalling and Defences*) session took place. Prof. Sasson (Israel) gave a lecture on *"The impact of nutritional overload-induced phospholipid remodeling on pancreatic β -cell function and dysfunction"* showing the collaboration between Israeli and Italian scientists that has already started in the field of cell signalling and connection with lipidomics in diabetes. He spoke about the collaboration with the CNR group of Dr. Ferreri which allowed two events of the cell metabolism, lipid remodelling and cell signalling, to be connected, thus showing the importance of interdisciplinary research for obtaining fundamental cell biology discoveries. Prof. Pohl (Austria) gave a lecture on *"Protein activation by reactive aldehydes"* showed her methodology of studying protein functions connected with membrane lipid asset, which was appreciated from many participants and several collaborations were already envisaged. Dr. Aoun (France) gave a lecture on *"Novel biomarkers for radical stress attack in mitochondria and plasma: mtDNA lesions, trans-PUFA in membrane phospholipids and isoprostanes"*, showing the ongoing collaboration with Dr. Chatgililoglu on the mitochondrial DNA isolation for studying the ROS damages, and also results from the collaboration with the Italian team on the detection on trans-PUFA and isoprostanes as marker of free radical damage in lipoproteins. The two other contributions came from Dr. Branka Mihaljevic (Croatia) on *"Radical scavenging activity of trans-resveratrol: photophysical and photochemical properties of resveratrol"* and Dr. Michele Melchiorre (Italy) on *"Free radical stress and fatty acid-based lipidomics"* which gave an overview of methodologies and molecular libraries to be shared and implemented during the COST Action activities.

The last session of the day started after the coffee break, with representative scientists of the WG 4 *Bio-Inspired Synthetic Strategies*. Prof Studer (Germany) gave a seminar on the carbene catalysis which was inspired from biological enzymatic functioning. The activity of antioxidants was presented by Prof. Engman (Sweden) which contributes to the Action with synthetic methodologies

in connection to the development of efficient antioxidants. The other two lectures from Dr. Guillaume Povie (Switzerland) on *“Catechol derivatives in radical chain reactions”* and Dr. Angeles Martin (Spain) on *“New synthetic strategies based on C-, O- and N-centered radicals”* indicated bio-inspired synthetic strategies and their potential to be developed within collaborative projects of the Action.

The first day of the Scientific Meeting ended at 18:30.

The second day of the Meeting (May 7) started at 9:30 with the WG2 session. Dr. Terzidis (Italy) spoke on *“Purine 5',8-cyclo-2'-deoxynucleoside lesions”* describing the methodology of oligonucleotide synthesis and incorporation of the cyclonucleoside lesion, together with the development of the analytical protocols to examine DNA damages of biological samples. This talk showed that the collaborations with several groups of the Action, also for the study of the enzymatic process of the DNA damage, can be successfully implemented. The presentation of Dr. Krzysztof Bobrowski (Poland) on *“Pulse radiolysis: a tool for investigating radical processes in biological molecules”* was oriented to the description of the facility in Poland that is very sophisticated tool for investigation of mechanistic and kinetic steps of radical transformation. He declared his interest to have collaborations with the Action participants applying pulse radiolysis studies in several fields. The talk of Prof. Massimo Bietti (Italy) on *“Laser flash photolysis as a tool for the study of hydrogen atom transfer and electron transfer reactions of oxygen centered radicals”* again gave the overview of a methodology that is very useful to determine kinetics and mechanistic aspects of free radical and electron transfer reactivity. The lectures of Prof. Dimitar Angelov (France) on *“Nucleosome remodeling and base excision repair”* and Prof. Alexandros G. Georgakilas (Greece) on *“Radiation-induced clustered DNA lesions: induction and repair”* gave a very interesting overview of the consequences of DNA damages and described the methodologies that can be applied to discover the biological importance and consequences of this damages. A lively debate went on the different aspects and methods available in the Action, that can be utilized in a coordinated way in order to give an important contribution to the understanding of the mechanisms involved in free radical damages and repair, also for potential health and diagnostic applications.

After coffee break, the WG1 session started with Dr. Frank Dekker (The Netherlands) that spoke on *“Novel inhibitors and activators of lipoxygenases and their role in NF- κ B signalling”* showing the effect of an interesting enzymatic cascade and related inhibitors on the signalling from one of the most important signalling for DNA activation. Prof. Athanassios Nicolaides (Cyprus) spoke about *“High- and room-temperature isomerizations of dimers of highly pyradalized alkenes”* with computational studies important for their contribution to fundamental mechanistic investigations. Prof. Tamis Darbre (Switzerland) gave her lecture on *“Peptide dendrimers with bipyridine at the core as models of metalloenzymes: pH-tuned metal coordination and peroxidase activity”* which involved synthetic and mechanistic studies on enzymatic activities connected also with metalloenzymes. Prof. Radu Silaghi-Dumitrescu (Romania) gave a talk on *“Computational approaches on two free radical generating systems: the peroxide chemistry specific to bleomycin*

and P450, and the cobalt corrins” and also gave an overview of several projects carried out at his Institute which can be interesting for many Action participants. The morning session was close by Prof. Ioulia Smonou (Greece) on *“Biocatalysed reactions and one-pot synthesis of pharmaceutical precursors”* showing the powerfulness of enzymatic activity to carry out stereoselective processes. The morning session ended at 13:30.

The afternoon session started with WG4 representatives and prof. Ullrich Jahn (Czech Republic) gave a talk on *“New catalytic electron transfer- induced and thermal radical cyclizations”* with interesting application to the omega-6 fatty acid transformations and action of prostaglandin synthase enzyme. Prof. Gabor Speier (Hungary) spoke on *“Radical chemistry of a flavin coenzyme mimic”* giving some insights on mechanistic aspects of electron transfer reactivity. Prof. Ioannis N. Lykakis (Greece) gave a talk on *“Green photocatalytic organic transformations using mesoporous-metal-oxide-supported gold nanoparticles and polyoxometalates”* with interesting application in functionalized materials with bio- and nano-technological applicability. Dr. Cyril Ollivier (France) showed an overview of his research on *“Bio-inspired electron transfer processes for fine chemical synthesis”* and Dr. Jozsef Kaizer (Hungary) spoke on *“Iron complexes as functional models for the soluble methane monooxygenase enzyme”*.

After coffee break, the last session of the meeting started with the WG3 representatives. Prof. Tomris Ozben (Turkey) spoke on *“Bleomycin increases trans lipid isomers in human testicular cancer cell membrane”* showing results of her collaboration with Dr. Ferreri on the radical stress produced by the antitumoral agent bleomycin, which resulted in the cis-trans isomerisation of membrane lipids. Dr Ivana Tartaro Bujak (Croatia) spoke about *“The influence of natural occurring antioxidants on lipid peroxidation and isomerization processes in model micellar system”* showing the study on micelles that allowed the isoemrization and peroxidation processes to be studied on linoleic acid as substrate. Dr. Naila Rabbani (Great Britain) spoke about her studies on *“Glycation of HDL and LDL by methylglyoxal causes structural remodelling linked to increased atherogenicity”* and Prof. Kyriakos E. Kypreos (Greece) talked on *“Novel causative relationship between low HDL and diet-induced nonalcoholic fatty liver disease”*, both giving relevance to the lipoprotein chemistry and analytical methodologies in the discovery of biomarkers and the inspiration for protective strategies against free radical damages.

At 18:30 the Scientific Meeting was closed by the words of the Chair Dr. Chatgililoglu, wishing the successful start of collaborative projects and short term missions among the Action participants.