57th International Conference on the Bioscience of Lipids (ICBL)
Chamonix – Mont-Blanc, France, September 4-8, 2016
Scientific Report: "Lipidomics: from Structures to Functions"

The 57th ICBL was held in Chamonix, located at the extreme eastern part of the Auvergne-Rhône-Alpes region of France, very close to the Italian and Swiss borders. This ten thousand people city, just at the foot of Mont Blanc, the highest summit of Western Europe, is well equipped with hotels to receive the mountaineers and hikers from around the world, and the scientific delegates as well! The ICBL delegates met for four days at the Convention Centre LE MAJESTIC, facing the Mont Blanc massif, clearly visible due to the great weather this week.
The local Scientific Committee was representative of the French Institute for Multidisciplinary Biochemistry of Lipids mainly based in Lyon, with Michel Lagarde (Chair), Nathalie Bernoud-Hubac & Marie-Caroline Michalski (Co-Chairs), Catherine Calzada (Lyon), Frédéric Carrière (Marseille), Thierry Durand (Montpellier), Agnès Girard-Egrot (Lyon), Toshihide Kobayashi (Strasbourg/Tokyo).
The Conference was attended by around 150 scientists and accompanying persons from 35 countries, including 17 European Countries, the others being Japan, USA, Argentina, Canada, China, Australia, Korea, Taiwan, Armenia, Brazil, Chile, Iran, Israel, Koweit, Pakistan, Russia, Singapore, and Thailand, by decreasing numbers of delegates.

After a brief welcome address given by Professor Lagarde, the Conference opened on the evening of September 4th with the 20th Laurens van Deenen Lecture entitled "Resolving Inflammation in the 21st Century: Novel Lipid Mediators and Mechanisms", delivered by Professor **Charles N Serhan** from Harvard Medical School in Boston. Professor Serhan reported her research on oxygenated metabolites from the long-chain n-3 fatty acids DHA, DPA and EPA, so-called specialized pro-resolving mediators (SPM), and new glutathione conjugates like the well-known peptide-leukotrienes from arachidonic acid. All mediators were assessed with a metabololipidomics approach, and their pathophysiological relevance tested in various human tissues.
The award, sponsored by BBA Molecular and Cell Biology of Lipids, was presented by both the President of ICBL Laszlo Vigh, and Michel Lagarde.

This introductory lecture was followed by a welcome reception to all attendees.

The scientific program continued for the next four days with seven sessions similarly organized. Each one started with an invited lecture, followed by three or four oral communications selected from submitted abstracts, ending with a second invited lecture (14 invited lectures and 27 oral communications in total). A one-hour coffee break cut the session in two parts to allow visiting posters. Over 80 posters were continuously displayed to facilitate exchanges between presenters and attendees, then offering at least 12h for specific discussions. Among posters, 19 competed for the final 3 posters awarded to PhD students by a specific jury chaired by Professor Makoto Ito, from the ICBL Steering Committee. Also, 9 PhD students were selected for oral communications and were eligible for 2 awards after selection by a jury chaired by Professor Laszlo Vigh, President of ICBL.

Session 1 (Monday 5th morning): *"Membrane lipids"*. Chairs – Agnès Girard-Egrot (Lyon) & Gabor Balogh (Szeged).
The session started with an Invited Lecture from **Joke Bouwstra** (Leiden, Netherlands) who reviewed the function of various skin lipids, in the frame of inflammatory skin diseases. The numerous ceramides were enlightened as well as the major enzymes involved in sphingolipid metabolism. Then, **Ludovic D'Auria** (Chicago, USA) presented his work on erythrocyte plasma membrane subdomain re-organization in response to the neurotoxin psychosine. **Marielle Köberlin** (Vienna, Austria) talked about the perturbation of membrane lipid composition and organization related to Toll-like receptor (TLR)-induced inflammatory phenotypes. **Albert Maimo-Barcelo** (Palma, Spain) reported the profound impact of tumorigenesis on the lipidome in colorectal cancer and derived exosomes, especially at the phospholipid class level. **Gabor Balogh** (Szeged, Hungary) described the relationship between altered membrane and storage lipids in response to heat stress in yeast. He pointed out the lipid droplet biogenesis as a survival strategy. Finally, **Bruno Antonny** (Nice, France) in his Invited Lecture presented the specific role of phospholipid unsaturation in cell organelle function, discussing the impact of polyunsaturated phospholipids on membrane

curvature and fluidity of nanodomains. Synaptic vesicles were presented as a relevant situation.

Session 2 (Monday 5th afternoon): "*Plasma lipoproteins"*. Chairs – Catherine Calzada (Lyon) & Xavier Collet (Toulouse).
This session started by the Introductory Lecture from **Kazumitsu Ueda** (Kyoto, Japan) who reviewed the formation of nascent high-density lipoproteins (HDL), describing how the protein ATP binding cassette A1 (ABCA1) transiently stores lipids (essentially cholesterol and phospholipids) within its outer cell membrane domains to ultimately load these lipids onto apoliporotein A-1 (apoA-1). This was followed by **Evelyn Orso** (Regensburg, Germany) who reported on the reversal of platelet aggregation and release vesicles occurring during storage by mildly oxidized HDL. This protection might be associated with phospholipid and sphingolipid remodeling. Then, **Jerome Hendriks** (Diepenbeek, Belgium) discussed the loss of immunomodulatory effects of HDL in multiple sclerosis patients as an alteration of their apoA-1 aromatic amino-acid residues. **Gerhard Liebish** (Regensburg, Germany) presented the abnormal lipoprotein X found in cholestasis, and its various lipids. He pointed out the unusual high content of monounsaturated PC and PE. **Agata Sowinska** (Lodz, Poland) focused on the biological activity of different lysophosphatidylcholines (LPCs) acting through the G protein-coupled receptor 119 expressed in Langerhans islets, using oleoyl-LPC as a reference. Finally, the Invited Lecture from **Anatol Kontush** (Paris, France) discussed the multiple atheroprotective effects of HDL through several biological targets, likely due to HDL heterogeneity. However, he underlined the failure in decreasing the cardiovascular risk by raising HDL-cholesterol.

Session 3 (Tuesday 6th morning): *"Lipolytic enzymes"*. Chairs – Frédéric Carrière (Marseille) & George Carman (New Brunswick).
The first Introductory Lecture was given by **Dominique Langin** (Toulouse, France) who talked about the hormone-sensitive lipase (HSL), which degrades diacyl- and further monoacyl-glycerol, in the adipocyte and insulin sensitivity. A focus was done on the insulin sensitivity with a link between HSL, the carbohydrate response element binding protein (ChREBP) and the fatty acid elongase ELOVL6. **George Carman** (New Brunswick, USA) then reported on the regulation by phosphorylation (by several kinases)/dephosphorylation of the phosphatidate phosphatase, which produces DAG from PA, which is crucial for triacylglycerol accumulation and lipid droplet formation. **Margaret Holme** (London, UK) reported a colorimetric method to detect sphingomyelinase (SMase) activity at high sensitivity (pM range). The advantages for rapid measurements and application for screening SMases inhibitors were pointed out. **Kazue Kanehara** (Taipei, Taiwan), continued in presenting his research on plant phosphoinositide-specific phospholipase C2 (among 9 isoforms in Arabidopsis) acting upon several species of PIP and PIP_2 in response to tunicamycin-induced ER stress. **Vincent Rioux** (Rennes, France) reported on a preduodenal lipase releasing the medium chain fatty acid octanoic acid, then available for octanoylation of ghrelin to make it an active ligand of a hypothalamic growth hormone. The second Invited Lecture was given by **Gérard Lambeau** (Nice, France), talking about various secreted venom and mammalian PLA2 acting on specific membrane receptors together as phospholipid cleavage enzymes. Their number and complex activities allows them to exhibit several physiological and pathophysiological functions.

Session 4 (Tuesday 6th afternoon): *"Oxygenated metabolism of PUFA"*. Chairs – Nathalie Bernoud-Hubac (Lyon) & Hiroyuli Arai (Tokyo).
The Invited Lecture given by **Paula Patrignani** (Chieti, Italy) reviewed the last data available on cyclooxygenases (COX-1 and COX-2) and their inhibitors. These bifunctional homodimer enzymes generate prostaglandin H_2 in many animal cells. Among the well-known non-steroidal anti-inflammatory drugs acting upon COX, aspirin is the only irreversible inhibitor, acting by acetylation of the enzyme active site. Beyond that, aspirin is now recognized in preventing colon cancer, and to exhibit epigenetic action by acetylating histones. **Takehiko Yokomizo** (Juntendo, Japan) reported on the action of 12-HHT, the C_{17} PGH_2 cleavage product, especially formed in blood platelet by thromboxane synthase, through the leukotriene B_4 receptor BLT2 expressed in skin keratinocytes. 12-HHT accelerates skin wound healing *via* BLT2 activation. **Charlotte Jouvène** (Lyon, France) measured the various oxygenated metabolites of arachidonic and docosahexaenoic acids in rat brain by LC-MS/MS. The most representative are mono-hydroxylated derivatives followed by di- and tri-hydroxylated compounds, with around equal amounts in free form and esterified in phospholipids. **Magdalena Kiezel-Tsugunova** (Manchester, UK) reported a lipidomic assessment of long-chain omega-3 PUFA (DHA and EPA) in human skin. DHA and EPA supplementation increased production of anti-inflammatory oxygenated derivatives. DHA was preferentially metabolized in dermis and EPA in epidermis. **Wananit Wimuttisuk** (Pathum Thani, Thailand) talked about arachidonic acid-derived eicosanoids in shrimps. COX products (PGs), and lipoxygenase products were identified and found associated to the ovarian maturation, with the highest amounts at the early stages. Finally, **Hiroyuki Arai** (Tokyo, Japan) presented his Invited Lecture on Platelet-activating factor acetyl-hydrolases (PAF-AHs), of which three types have been identified in mammals. In addition of degrading PAF, these enzymes cleave the sn-2 position of oxidized phospholipids, then releasing oxygenated fatty acid products. It was reported that such products, characterized by a lipidomic approach, may be involved in IgE-mediated mast cell activation.

Session 5 (Wednesday 7th morning): *"Non-enzymatic lipid oxidation"*. Chairs – Thierry Durand (Montpellier) & Jetty Lee (Hong Kong).
Barry Haliwell (Singapore) started the session with his Invited Lecture. He reviewed the non-enzymatic lipid peroxidation process with the special role of "catalytic" iron. The classical deleterious lipid peroxidation was also mentioned regarding beneficial aspects reported for some stable end-products such as isoprostanes. The measurement of oxidative biomarkers was discussed relating to the numerous isomers requiring a specific lipidomic approach. **Jetty Lee** (Hong Kong, China) continued with the assessment of diverse non-enzymatic oxygenated products of n-3 and n-6 PUFA in food and tissues. Several isoprostanes/ dihomo-isoprostanes and isofurans/dihomo-isofurans were detected and measured by LC-MS/MS in the food chain. **Mikhail Shchepinov** (Los Altos, USA) spoke about lipid peroxidation-resistant PUFA. Interestingly, deuteration of PUFA at the bis-allylic positions slows down the rate limiting step of hydrogen abstraction required to initiate the peroxidation. **Kin Sum Leung** (Hong Kong, China) reported a mild effect of UVA on isoprostanes and isofurans formation (from arachidonic acid) in human keratinocytes, but the lipoxygenase products from DHA were measurable. It was supposed that the production of the latter could protect against that of the former. **Valery Bochkov** (Graz, Austria) reported anti-inflammatory and cell-protective action of oxidized phospholipids, contrary to the deleterious effects usually reported. Although Insights in

the mechanisms remain to be described, these results may explain some switch from acute to chronic inflammation. **Luisa Minghetti** (Rome, Italy) delivered her Invited Lecture on alpha-linolenic acid-derived phytoprostanes on the brain. The effect of such derivatives on undifferentiated nerve cells revealed some protective action against oxidant injury, likely through the activation of PPAR□ which could preferentially affect the brain cell maturation.

Session 6 (Thursday 8th morning): *"Lipid structures of nutritional interest"*. Chairs – Marie-Caroline Michalski (Lyon) & David Julian McClements (Amherts).
Charlotte Jacobsen (Lingby, Denmark) gave her Invited Lecture on functional lipid foods. Taking the example of n-3 PUFA that are susceptible to oxidation, she pointed out the role of the oil-water emulsions regarding the environmental factors involved in that oxidation. Controlling the homogenization and delivering conditions, together with appropriate antioxidants, are improvements to prevent lipid oxidation. **Sophie Ayciriex** (Dresden, Germany) exposed her results on the effect of food on the lipidome of Drosophila melanogaster eye. Saturated triacylglerols led to major phospholipids with less than 2 double bonds whereas highly unsaturated diet led to phospholipids with 3 to 5 double bonds. In contrast, sphingolipids were not affected. **Philippe Legrand** (Rennes, France) reported that intake of linoleic acid (LA) induced pro-inflammatory and steatogenic effects in rats. The LA-rich diet increased plasma interleukin 1 and tumor necrosis factor alpha, the expression of vascular cell adhesion molecules in aortas, and altered the stearoyl-CoA desaturase activity. **Valerija Vezocnik** (Ljubljana, Slovenia) showed her results in characterization of nanoemulsions of lipid droplets made of trioleoylglycerol coated with a sphingomyelin/cholesterol monolayer of different compositions in terms of size and shape. Finally the Invited Lecture from **David Julian McClements** (Amherts, USA) enlightened the various aspects related to bioavailability of oil-soluble agents, such as nutrients and vitamins, incorporated into nanoscale lipid droplets (d<200 nm) dispersed in water. These nanoemulsions increase the bioavailability of the considered bioactive agents. The physicochemical principles behind this was discussed.

Session 7 (Thursday 8th afternoon): *"Lipid imaging"*. Chairs – Toshihide Kobayashi (Strasbourg/Tokyo) & Donatienne Tyteca (Brussels, Belgium).
The session started with the Invited Lecture from **Christoph Thiele** (Bonn, Germany). He showed the use of alkyne labeled various lipids (fatty acids, glycerolipids, sphingolipids,…) to look at their localization in cultivated cells and tissues during cell metabolism. Highly sensitive and quantitative analysis of lipid turnover could be assessed by fluorescence. **Pooja Gusain** (Ishikawa, Japan) reported on the effect of chirality in membrane heterogeneity (especially lipid rafts), based on d- and l-menthol. The two chiral isomers clearly showed different affinities with membrane lipids, with d-menthol showing stronger affinity for unsaturated lipids. **Vivien Walter** (Strasbourg, France) focused on influence of the membrane charge on cell penetrating peptides. These short peptides may have drug delivery applications. It was shown that increasing both the temperature and membrane charge density facilitate peptide affinity. **Motohide Murate** (Saitama, Japan) reported the observation of trans-bilayer lipid distribution in plasma membranes by immune-electron microscopy. This was applied to confirm the asymmetric distribution of phospholipids in several cell types including erythrocytes, fibroblasts, neutrophils and thrombin-activated platelets. **Mélanie Carquin** (Brussels, Belgium) described the distribution of fluorescent Bodipy-ceramide in submicrometric domains of the yeast membrane. This revealed the presence of

sphingolipid domains in relation to specific membrane proteins. Then **Donatiene Tyteca** (Brussels, Belgium) delivered the final Invited Lecture. She focused on the role of membrane lipid heterogeneity in cell deformation, which is critical in many biological processes. Red blood cells were used as a model because of its unique deformability when passing through capillaries. The use of fluorescent toxin fragments and the atomic force microscopy allowed to evidence sphingomyelin- and cholesterol-rich submicrometric domains.

In addition to these sessions summarized above, three flash oral presentations were given by three of the most generous sponsors: delegates from Waters in session 4, from AB Sciex in session 5, and from Nutricia in session 6.
David Heywood, from Waters talked about: "Markers of health: molecular phenotyping unveils the healthy biosignature of "omega-3" transgenic mice"; **Cyrus Papan**, from AB Sciex presented "The lipidyzer^{TM} platform – a revolutionary tool for understanding the role of lipids in disease"; and **Dennis Acton**, from Nutricia reported "An innovative infant milk formula mimicking the human milk fat globule structure affects lipid hydrolysis and postprandial metabolism".

The three poster awards were given on Wednesday evening, in the course of the Conference Dinner. The awardees were:
- **Peter Tibor Dancs** (Budapest, Hungary): "Reconciliation of the vascular and vasoconstrictor actions of lysophosphatidic acid in the mouse aorta".
- **Francesca Di Bartolomeo** (Graz, Austria): "Functional characterization of the putative substrate recognition motif of phosphatidylserine decarboxylase 1 (Psd1P) from *Saccharomyces cerevisiae*".
- **Amanda Lo Van** (Lyon, France): "Study of the effects of docosahexaenoic acid (DHA) and a structured phospholipid containing DHA on an *in vitro* model of neurogenesis and stroke".

Two oral communication awards were given on Thursday evening at the end of session 7. The awardees were:
- **Mélanie Carquin** (Brussels, Belgium): "Segregation of fluorescent ceramide analogs into submicrometric domains at the yeast surface and relationship with proteins" (session 7).
- **Magdalena Kiezel-Tsugunova** (Manchester, UK): "Lipidomic assessment of oxygenated n-3 PUFA metabolites in human epidermis and dermis" (session 4).

Then Michel Lagarde concluded the Conference with many thanks to all the scientific contributors, presenters and discussants, to technicians for their help in logistics, and especially to Evelyne Roudier who managed with "fluidity" the relationships between all the attendees and the Convention Centre, and facilitated the social events, particularly on Wednesday afternoon with the excursion to the mount Brévent followed by the Conference Dinner to "La Cabane".
Sponsors of the Conference were once more acknowledged for their support, and Michel Lagarde wished all the best to delegates with hope to see them next year in Zurich for the 58th ICBL.