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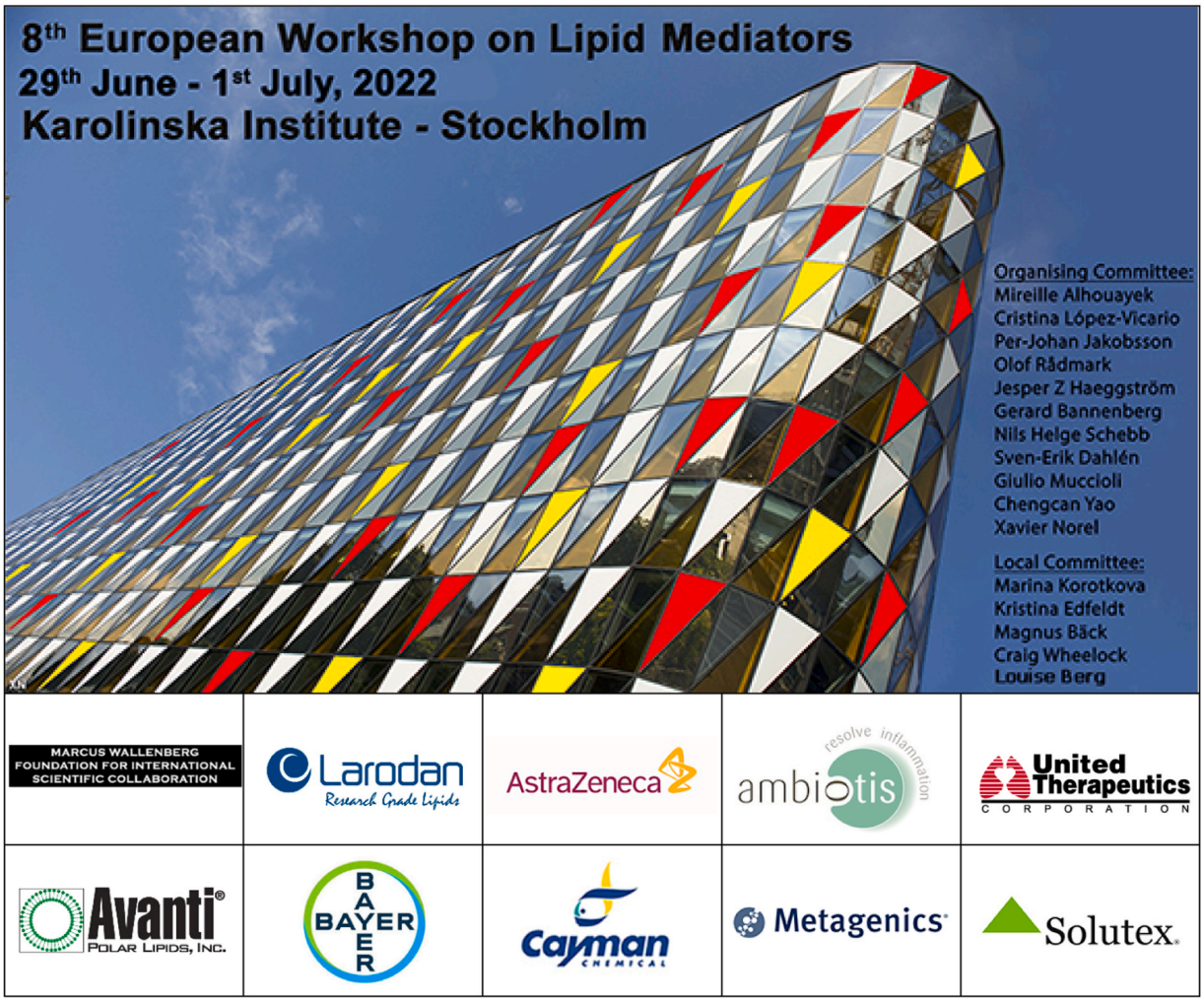
Editorial – Special issue of the 8th European Workshop on Lipid Mediators



The eight European Workshop on Lipid Mediators (8EWLM) was held at the Karolinska Institute in Stockholm, Sweden June 29th – July 2nd, 2022. The aim of the workshop was to bring together those researchers and students interested in the field of bioactive lipid mediators.

The eight edition of this biennial workshop was organized by Mireille Al Houayek, Gerard Bannenberg, Sven-Erik Dahlén, Jesper Haeggström, Per-Johan Jakobsson, Cristina López-Vicario, Giulio G. Muccioli, Xavier Norel, Olof Rådmark, and Chengcan Yao with local assistance by

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Magnus Bäck, Louise Berg, Kristina Edfeldt, Marina Korotkova, and Craig Wheelock. The three-day event provided a good opportunity for participants to present their work and enjoy a variety of presentations by experts. In addition, a dedicated session allowed 11 young scientists to present their work and an educational session was organized to focus on key aspects of enzyme kinetics, oxylipin biology and analysis and well as the role of prostaglandin E_2 (PGE_2) in lung inflammation. The full program (and downloadable abstract book) is available at https://workshop-lipid.eu/8EWLM/. More than 200 scientists from across and outside Europe attended the workshop in the beautiful Sune Bergström aula within the Karolinska University Hospital building. The workshop placed special focus on the following themes: i) Prostacyclin analogs, ii) the resolution of inflammation, iii) lipid mediator research at the Karolinska Institute, iv) enzymatic formation, receptors and signal transduction, v) lipid mediator classes and structural chemistry, and vi) therapeutic approaches.

Here, we present to you this Special Issue of Prostaglandins and Other Lipid Mediators with a total of fourteen publications equally comprised of reviews and original publications by speakers who presented at the 8th EWLM. This Special Issue is neither a systematic nor comprehensive review of all the topics and presentations delivered at the 8EWLM, but rather highlights the voluntary contributions of the participating scientists and their research colleagues.

Bouhadoun and colleagues [1] studied the vascular pharmacology of several DHA-derived specialized proresolving mediators (SPMs). Resolvin D1 (RvD1), resolvin D5 and maresin 1 were found to reduce PGE_2-induced contractions of human coronary artery preparation. The expression of various receptors for SPMs, FPR2/ALX, GPR32 and LGR6, was confirmed in human coronary artery tissue. The vasorelaxant effect of RvD1 pretreatment was shown to be mediated by nitric oxide.

Serhan and Chiang [2] reviewed the more recent aspects of specialized pro-resolving mediators (SPM) biology. First, they review the current knowledge on SPM production and actions. Then they discuss the stereochemical assignment and the current knowledge on the biosynthesis of the more recently described cysteinyl-SPMs (cys-SPMs). These peptide-lipid molecules can be regrouped into three series of derivatives, i.e., maresin conjugates in tissue regeneration (MCTRs), protectin-CTR (PCTRs) and resolvin-CTR (RCTRs). Serhan and Chiang conclude their manuscript by describing the current knowledge on the actions of the cys-SPMs.

Kahnt and colleagues [3] review the formation of specialized pro-resolving lipid mediators (SPMs) in leukocytes. They summarize the enzymatic prerequisite for the production of SPM, including the importance of 5-lipoxygenase activating protein (FLAP) for the biosynthesis of most of the lipoxins and resolvins. They also discuss the current knowledge on the biosynthesis of SPM in granulocytes and macrophages. Having summarized the evidence supporting a low production of trihydroxylated oxylipins (e.g. lipoxins, RvE1, RvD2 and RvD3) by human leukocytes, Kahnt and colleagues summarize the biological activities of the dihydroxylated SPMs (e.g. 5,15-diHETE, RvE2, RvE4, RvD5) as these are reported to be released in higher amounts from human leukocytes.

Liu and colleagues [4] report original data supporting the presence of a shunt in arachidonic acid metabolism during in vitro inflammatory responses upon microsomal prostaglandin E synthase-1 inhibition (mPGES-1). mPGES-1 is the key enzyme for the generation of PGE_2. Liu et a. compared the eicosanoid profiles in four in vitro inflammation models during mPGES-1 inhibition and cyclooxygenase-2 (Cox-2) inhibition. While COX-2 inhibition depressed all the prostanoid productions in the four models, mPGES-1 inhibition shifted PGE_2 production towards PGD_2 production in three models but one (i.e. rheumatoid arthritis synovial fibroblasts) in which prostacyclin production was favored. The work by Liu et al. has implication in the understanding of the therapeutic effects of mPGES-1 inhibition.

Hakobyan and colleagues studied the effect of cis-platin and progesterone exposure on nuclear phospholipids. The antagonistic effect of progesterone on cis-platin-induced changes in the levels of various nuclear phospholipids is thought to be of relevance in the regulation of nuclear functions of cell such as replication, DNA transcription, DNA remodeling and epigenetic regulation of gene expression [5].

Hammoud and colleagues presented a new methodological approach validated with rapid screening and UPLC-MS/MS validation to make a rapid and highly affordable diagnosis of different types of sphingolipidosis. This analytical process offers rapid and appropriate patient management in settings with reduced resources where sphingolipidoses are most relevant [6].

Teder and colleagues have reviewed the literature on the topic of the crosstalk between the unfolded protein response (UPR) and bioactive lipid mediator formation and activity in the context of ischemic stroke. Endoplasmic reticulum stress-related UPR is one of the causes of neuronal and glial cell loss after stroke. The review provides a good overview of lipid mediators in stroke pathophysiology, the biochemical changes in the UPR, modulation of UPR, and connections to lipid mediator formation, which are instructive to future research in alleviating stroke outcome [7].

Belikova and colleagues [8] report here their findings on the prostanoid component of the exercise-induced bronchoconstriction (EIB) obtained using intact segments of human bronchi. Hyperosmolar mannitol was used to mimic ex vivo EIB. In their model constriction is mediated by histamine, cysteinyl leukotriene and thromboxane (TP) receptors. They found that inhibiting prostaglandin D synthase and TXA synthase has similar effects than blocking the TP receptor. Overall the data Belikova et al. report in their paper suggests that the EIB component mediated by the TP receptor is induced by COX-1-generated PGD_2 and TXA_2.

Ferri and colleagues address in their review the relevance of specialized pro-resolving mediators (SPM) in the context of viral infections. After summarizing the inflammatory events during viral infections, they discuss the current knowledge on the production and effects of SPM in the context of important viral diseases such as Influenza A virus, Respiratory syncytial virus, SARS-CoV-2, Herpes viruses and Kaposi's sarcoma-associated herpesvirus. While the COVID-19 pandemic rebooted research on viruses, the crosstalk between viruses and SPM was and remains an active research field as summarized in the review by Ferri et al [9].

Paquot and colleagues made a significant advance in the analytical capabilities for quantitative measurement of prostaglandin-glycerol esters and prostaglandin-ethanolamides, their precursors, as well as classical prostaglandins, by validating a new and sensitive UPLC-MS/MS method. Femtomole sensitivity was exemplified in a murine colitis model and in activated macrophages [10].

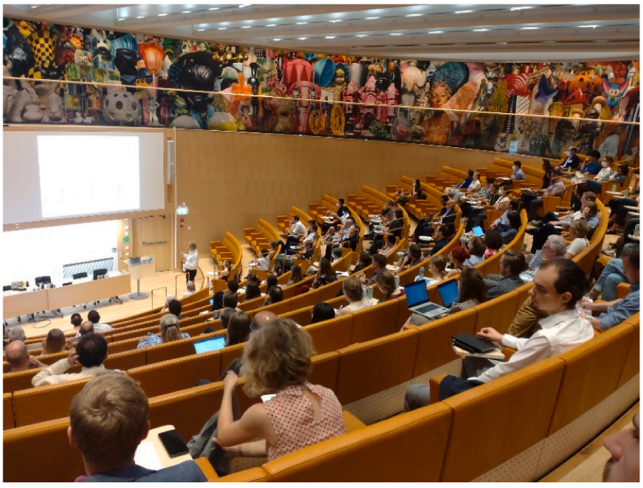
Biagini and colleagues presented new research findings documenting the effects of distinct SARS-CoV 2 variants on the PUFA and plasma oxylipin levels in COVID-19 patients. A comparison of plasma samples of patients infected with wild-type, Alpha (B.1.1.7), Delta (B.1.617.2), and Omicron (B.1.1.529) variants led to the conclusion that the Alpha and Delta variants induced a comparable lipid profile alteration upon infection, which differed significantly from Omicron. The latter variant increased the levels of pro-inflammatory mediators and decreased the levels of omega-3 PUFA in infected patients [11].

Birkic and colleagues used a molecular dynamics approach to explore the interactions of 13 endogenous lipid mediators with the transient receptor potential vanilloid 1 (TRPV1) channel. TRPV1, a ligand-gated cation channel, plays a role in nociception. The authors report in their paper that the lipid mediators binding TRPV1 can be grouped based on their structure and affinity for the vanilloid pocket. They also found that the position and number of polar groups on the lipid mediator ligand impact the binding stability due to polar interactions with the protein. The binding interactions observed by Birkic et al [12]. in their MD study may be useful for the interpretation of in vivo and in vitro pharmacodynamics studies.

Sieminska and colleagues developed a 96-well format extraction

protocol for the quantification of urinary eicosanoid (e.g. prostaglandins, thromboxanes, isoprostanes, etc) together with cortisol/cortisone and exogenous steroids. Indeed, urinary eicosanoid concentrations are thought to reflect inflammatory processes in multiple diseases. As reported by the authors, the developed single solid-phase extraction of 300 μL urine proved to have satisfactory analytical performance. The method described in their manuscript by Sieminska et al [13] should simplify the implementation of urinary eicosanoid quantification in large-scale screening.

Ramström and collaborators investigated oxylipin changes in serum and plasma of dogs related to ovulation by LC-MS/MS-based profiling of sixty-seven lipid mediators. Several putative biomarkers were identified that signal the period before, during and after ovulation, which can be informative to determine ovulation in dogs which is otherwise not always easily determined [14].



The 8th EWLM organizers would like to acknowledge the contributions of both the young and senior researchers who presented their work in Stockholm. We also thank the local staff at the Karolinska Institute who helped to organize the workshop logistics and made the event a wonderful experience for all participants. We would also like to sincerely acknowledge the generous sponsors of the 8th EWLM: The Marcus Wallenberg for International Scientific Collaboration, Larodan, AstraZeneca, Ambiotis, United Therapeutics, Avanti Polar Lipids, Bayer, Cayman, Metagenics, Solutex, Idorsia, Lipidomix, ONO Pharmaceutical, Gesyntha Pharma, Sciex, Echelon Biosciences, Tebubio, Lab Supplies Nordic BB, GOED and Elsevier. Without their generous support this workshop would not have been possible.

We are pleased to announce that the next edition of this workshop, 9th EWLM, will be held at the University of Edinburgh, United Kingdom from June 26–28, 2024. For more information on our next event and to view the scientific program and list of invited speakers, see our website: https://workshop-lipid.eu/index.php?cat=Program. A special session for young researchers, and a session of educational presentations, will also be organized.

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