

Lysophospholipid signaling in cancer and immunity at a glance

Lysophospholipids (LPLs), including lysophosphatidic acid (LPA) and sphingosine-1-phosphate (S1P), are low molecular weight lipid metabolites derived from enzymatic processing of membrane phospholipids. These compounds bind to multiple G protein-coupled receptors and transduce many different intracellular signaling events. LPA and S1P receptors were originally identified as a family of orphan *endothelial differentiation gene* (*EDG*) receptors, and subsequently expanded into a larger group of receptors with important physiological functions. To date 6 LPA receptors and 5 S1P receptors are known. These receptors mediate survival, migration, and differentiation of cells, which are also important characteristics of tumors.

This focused issue of the *Translational Cancer Research* journal is dedicated to seven review articles focused on the current understanding and processes of the regulatory roles of LPLs on cancer and cancer-related immunity. S1P is predominantly known to induce the egress of lymphocytes from lymphoid organs like thymus and spleen, but also has many additional functions in other physiological systems. The role of S1P in cancer immunity and development is discussed with the particular focus on different mechanistic concepts. In addition, the role of S1P in colitis-associated colon cancer (CAC) is highlighted. S1P can activate nuclear factor kappa B (NF- κ B) and signal transducer and activator of transcription 3 (STAT3), two important signaling pathways in both, inflammation and carcinogenesis. Modulation of S1P metabolism by dietary sphingolipids may therefore influence onset and progression of cancer. While S1P is known for its pro-survival activity, its relative ceramide induces apoptosis. Both molecules are metabolites of sphingosine and can rapidly be converted into each other. The metabolism of ceramide and S1P influences cell fate, and their roles in cellular processes in cancer are outlined.

LPA induces similar functions as S1P like angiogenesis, which is an important process in the development of cervical cancer. LPA can be produced by autotaxin, which removes the choline headgroup from lysophosphatidyl choline. The activity of autotaxin and the impact of LPA on cervical cancer are discussed. In addition, LPA also mediates prostate cancer progression via increased cell proliferation, survival, and migration. The expression pattern of LPA receptors and metabolic enzymes involved in LPA generation in prostate cancer are outlined. Similar to S1P, LPA also influences lymphocyte migration in lymph nodes. Production of LPA by vascular endothelial cells and stromal cells of the lymph nodes and the expression of LPA receptors on stromal cells and lymphocytes are important factors for transendothelial and interstitial lymphocyte migration, which is described in detail. Finally, the role of lysophospholipid signaling in zebrafish development is reviewed. Since both LPA and S1P receptors are expressed in zebrafish, this model system provides a good basis for the rapid analysis of S1P and LPA receptor function and their pharmacological modulation.

We hope this collection of articles can provide comprehensive background information for clinicians and scientists for a better understanding of current advancements in the LPL research field.

As guest editors for this focused issue, we thank all the contributors for their excellent articles and also for their efforts to submit on time. We also thank the editor and staff of the *Translational Cancer Research* journal for their constant help during the past year making this focused issue possible.

Acknowledgments

Funding: None.

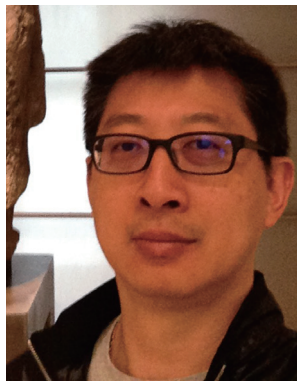
Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Translational Cancer Research* for the series “Lysophospholipids on Immunity and Cancer”. The article did not undergo external peer review.

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.3978/j.issn.2218-676X.2015.10.02>). The series “Lysophospholipids on Immunity and Cancer” was commissioned by the editorial office without any funding or sponsorship. HL and MHG served as the unpaid Guest Editors of the series. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Hsinyu Lee



Markus H. Gräler

Hsinyu Lee, Ph.D, Professor

Department of Life Science, National Taiwan University, Taipei, Taiwan

(Email: Hsinyu@ntu.edu.tw.)

Markus H. Gräler, Ph.D, Professor

SG Sepsis Research, Department of Anesthesiology and Intensive Care Medicine, Center for Sepsis Control and Care (CSCC), and

Center for Molecular Biomedicine (CMB), University Hospital Jena, 07740 Jena, Germany

(Email: Markus.Graeler@med.uni-jena.de.)

Submitted Sep 30, 2015. Accepted for publication Oct 01, 2015.

doi: 10.3978/j.issn.2218-676X.2015.10.02

View this article at: <http://dx.doi.org/10.3978/j.issn.2218-676X.2015.10.02>

Cite this article as: Lee H, Gräler MH. Lysophospholipid signaling in cancer and immunity at a glance. *Transl Cancer Res* 2015;4(5):451-452. doi: 10.3978/j.issn.2218-676X.2015.10.02