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Preface

Lipid metabolism in cancer

Dysregulated lipid metabolism is an established hallmark of cancer. Lipids play diverse roles in maintaining cellular structure, forming membrane microdomains for functional scaffolding of protein complexes, serving as fat storage depots, and acting as signaling molecules. All of these processes are critical in cancer not only for generating the membrane constituents necessary for proliferating cells, but also for the energetic, biophysical, and signaling pathways that drive diverse aspects of tumorigenesis. Consistent with the importance of lipids in cancer, regulatory factors, enzymes, and transporters involved in lipid transport, lipid synthesis, and lipid degradation are dysregulated in cancer cells. There are also well-established epidemiological links between obesity and a higher incidence of developing certain cancers, suggesting that the physiological alterations resulting from excessive weight gain and resulting co-morbidities also influence cancer pathogenicity. This Special Issue on Lipid Metabolism in Cancer includes several reviews and articles highlighting the importance of lipid metabolism in both cancer cells and host tissues in cancer pathogenesis.

While the link between obesity and cancer has been historically attributed to factors such as inflammation and heightened adipokine and insulin signaling, this Special Issue includes several reviews and articles that highlight the role of both endogenous and exogenous sources of lipids for meeting the energetic, structural, and oncogenic signaling requirements of cancer cells. Louie et al. review the mechanisms linking obesity and cancer and how dysregulated whole-body physiology and metabolism in obesity influences cancer pathogenicity. Included in this review is also an emphasis on either exogenously or endogenously produced oncogenic signaling lipids that can fuel tumor growth and metastasis. Baumann et al. review the diverse roles of lipids in cancer. The authors introduce the various lipid species either exogenously produced or generated de novo that influence breast cancer pathogenesis. They also delve into the regulatory mechanisms underlying heightened de novo lipogenesis in breast cancer, and review the role of endoplasmic stress and the unfolded protein response to lipogenic hepatic steatosis and the parallels with HER2/neu-positive breast cancer fat storage phenotypes. Zadra et al. discuss alterations of lipid metabolism in prostate cancer and its regulation by oncogenic signaling, diet, and lifestyle, as well as how we can take advantage of this understanding to develop novel diagnostic tools and therapeutic strategies to combat prostate cancer. Nieman et al. also discuss the mechanisms underlying obesity and cancer, focusing on exciting discoveries that show how surrounding adipose tissue and adipocytes can promote cancer cell initiation and progression. Zhang and Saghatelian discuss how seemingly inert structural lipids and their metabolism can exert key points of control over the BCL-2 family-regulated apoptotic program. The authors highlight two key cases of ceramide and cardiolipin and their connection between lipid metabolism and the cellular decision to undergo apoptosis versus proliferation.

This Special Issue also features several primary articles highlighting the important role of lipid metabolism in cancer. Huang et al. show that tumors arising from Bcr/Abl-transformed B cells trigger lipid mobilization of white adipose tissue to the liver causing dyslipidemia that promotes B-cell proliferation and tumor growth. The authors also show that the PPAR-alpha agonist and lipid-lowering drug fenofibrate suppresses B-cell lymphoma growth. Louie and Roberts use metabolomic profiling and isotopic fatty acid tracing to globally map alterations in fatty acid and lipid metabolism that underlie cancer progression. The authors show that aggressive cancer cells exhibit heightened incorporation of exogenous free palmitate into glycerophospholipids, sphingolipids, and ether lipids compared to less aggressive cancer cells, with increased generation of several tumor-promoting lipid signaling molecules. Salazar et al. demonstrate a potential mechanism for the anticancer action of cannabinoids, which include tetrahydrocannabinol and the endogenous cannabinoid lipids 2-arachidonoylglycerol and anandamide. The authors show that TRIB3 plays a crucial role in the anti-cancer actions of cannabinoids and suggest that this effect is based on the ability of this protein to interact with AKT and inhibit its full activation by mTORC2. Fowler et al. uncover a unique relationship between the components of the endocannabinoid system and markers of angiogenesis. The authors find that the association of the endoglin score with tumor stage at diagnosis and disease-specific survival is modulated by the expression levels of endocannabinoid markers, thus potentially informing future diagnostic tests for prostate cancer.

This Special Issue on Lipid Metabolism in Cancer highlights the intricate interplay between cancer cell and whole body lipid metabolism that collectively fuels cancer initiation and progression and provides unique insights into the vast and diverse role of various lipid species in cancer. This issue also suggests potential nodes in lipid metabolism that may be targeted for future cancer diagnosis or therapy.

Daniel Nomura is an assistant professor in the Department of Nutritional Sciences and Toxicology at the University of California, Berkeley. Dr. Nomura's research group is interested in mapping dysregulated lipid metabolism in human diseases, such as inflammation and cancer, towards identifying, characterizing, and developing novel therapeutics strategies for combatting human disease. His group utilizes functional proteomic and metabolomic approaches towards achieving these goals.

Ben Cravatt is a professor in and chair of the Department of Chemical Physiology at The Scripps Research Institute in La Jolla, California. Dr. Cravatt's research group is interested in understanding the roles that enzymes play in physiological and pathological processes, especially as it pertains to the nervous system and cancer. To address this challenge, his group develops and applies advanced chemoproteomic and metabolomic platforms.

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