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Deciphering the Links Between the Variations in Plasma Lipid Profiles of AML Patients and the Metabolic Reprogramming of Leukemic Cells: A Proof of Concept of the Impact of Dietary Habits on the Prognosis of Cancers

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Abstract

The concept of one health emphasizes the role of the environment and the ecosystem in which individuals live on the development of diseases. In particular, the food environment and the nutrition of individuals is a well-identified major element in the increase of the frequency of cancers that represent one a of the first cause of death worldwide. Indeed, numerous studies have highlighted the link between obesity and "western diet" with the frequency of cancers in the world. This suggest that the availability of nutrients which is completely shaped by the environment plays a dominant role in cancer cell metabolism and should impact significantly the prognosis of cancer patients. In this context, we compared the quantity and the profile of lipids present in the plasma of patients for whom acute myeloid leukemia (AML) was newly diagnosed among two subgroups with high and low prognosis (according to ELN 2017). An increase quantity of neutral lipids (FFA), which are storage lipids, in patients with an unfavorable prognosis, suggesting that the mobilization of these storage lipids improve viability and chemoresistance of leukemic cells. Moreover, we observed a significant increase of some phospholipids, sphingomyelin (SM) and PhosphoCholine (PCh) in patients with an unfavorable prognosis, suggesting that these PL are markers of aggressiveness and tumor progression associated with a poor prognosis in AML. The fact that we observed the increase of PCh was as a common mechanism of survival against starvation in leukemic cell lines strongly suggest that PCh has a protective role which could increase the resistance of leukemic cells in stressful situations. In addition, we have shown that the metabolite composition of leukemic cells from AML patients varies according to the cytogenetic and molecular status of the patients and we have confirmed that the variations of certain phospholipids, including phosphocholine, significantly influence the prognosis and the chemosensitivity of the patients. In conclusion, our work shows that leukemic cells develop molecular mechanisms that allow them to use lipids from plasma and from the tumor environment to generate lipid mediators that increase their survival and their resistance to chemotherapy. Since this flow of nutrients is directly dependent on the dietary environment of

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individuals, it demonstrates the interest of global strategies integrating the nutritional ecosystem of patients for improving the prognosis of cancers.