1276-1293. e11.

[71] HU C, QIAO W, LI X, et al. Tumor-secreted FGF21 acts as an immune suppressor by rewiring cholesterol metabolism of CD8$^+$ T cells[J]. Cell Metabolism, 2024, 36(3): 630-647.e8.

[72] ZHANG Y, VU T, PALMER D C, et al. A T cell resilience model associated with response to immunotherapy in multiple tumor types[J]. Nature Medicine, 2022, 28(7): 1421-1431.

[73] LU Z, MCBREARTY N, CHEN J Y, et al. ATF3 and CH25H regulate effector trogocytosis and anti-tumor activities of endogenous and immunotherapeutic cytotoxic T lymphocytes[J]. Cell Metabolism, 2022, 34(9): 1342-1358. e7.

[74] BENSINGER S J, BRADLEY M N, JOSEPH S B, et al. LXR signaling couples sterol metabolism to proliferation in the acquired immune response[J]. Cell, 2008, 134(1): 97-111.

[75] XU J, WAGONER G, DOUGLAS J C, et al. Liver X receptor agonist regulation of Th17 lymphocyte function in autoimmunity[J]. Journal of Leukocyte Biology, 2009, 86(2): 401-409.

[76] TAKAHASHI H, NOMURA H, IRIKI H, et al. Cholesterol 25-hydroxylase is a metabolic switch to constrain T cell-mediated inflammation in the skin[J]. Sci Immunol, 2021, 6(64): eabb6444.

[77] ALROSAN A Z, HEILAT G B, AL SUBEH Z Y, et al. The effects of statin therapy on brain tumors, particularly glioma: A review[J]. Anticancer Drugs, 2023, 34(9): 985-994.

[78] CAO D, LIU H. Dysregulated cholesterol regulatory genes in hepatocellular carcinoma[J]. Eur J Med Res, 2023, 28(1): 580.

[79] CORADINI D. Impact of De Novo cholesterol biosynthesis on the initiation and progression of breast cancer[J]. Biomolecules, 2024, 14(1).

[80] HE X, LAN H, JIN K, et al. Cholesterol in colorectal cancer: An essential but tumorigenic precursor?[J]. Front Oncol, 2023, 13: 1276654.

[81] KUZU O F, NOORY M A, ROBERTSON G P. The role of cholesterol in cancer[J]. Cancer Res, 2016, 76(8): 2063-2070.

[82] REBELO A, KLEEFF J, SUNAMI Y. Cholesterol metabolism in pancreatic cancer[J]. Cancers(Basel), 2023, 15 (21): 5177.

[83] BAEK A E, NELSON E R. The contribution of cholesterol and its metabolites to the pathophysiology of breast cancer [J]. Horm Cancer, 2016, 7(4): 219-228.

[84] SNAEBJORNSSON M T, JANAKI-RAMAN S, SCHULZE A. Greasing the wheels of the cancer machine: The role of lipid metabolism in cancer[J]. Cell Metabolism, 2020, 31(1): 62-76.

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封面故事

免疫学的重要性不容忽视。面对日益严峻的感染、肿瘤和自身免疫疾病等人类健康难题，免疫学为我们提供了探索和开发有效治疗手段的理论基础和方法路径。通过深入研究和理解免疫机制，我们有望找到应对这些健康挑战的新策略，提供更为可靠和持久的健康保障。

免疫疗法在晚期肿瘤治疗中展示了巨大潜力，带来了令人振奋的希望。然而，肿瘤免疫机制的复杂性使其仍然面临巨大挑战。人体抗肿瘤免疫反应与肿瘤逃逸机制之间的斗争是决定肿瘤命运的关键。免疫细胞可以在非淋巴器官内形成异位淋巴组织，即三级淋巴结构。这些三级淋巴结构及肿瘤微环境的变化与患者预后和治疗效果密切相关。因此，深入探讨三级淋巴结构的抗肿瘤免疫机制，对于研发有效的肿瘤免疫疗法至关重要。

在抗肿瘤免疫过程中，三级淋巴结构发挥了重要作用。环形涡流图直观地展示了这一过程的关键步骤：肿瘤相关抗原释放；树突状细胞捕获抗原并呈递给 CD8$^+$ 和 CD4$^+$ T 细胞；CD8$^+$ 和 CD4$^+$ T 细胞活化并分化为细胞毒性T细胞和辅助性T细胞；活化的T细胞浸润到肿瘤组织内，并在趋化因子的作用下聚集形成三级淋巴结构；在三级淋巴结构中，B 细胞、T 细胞和 DCs 等免疫细胞之间的相互作用，最终促进抗肿瘤免疫反应。三级淋巴结构提供了一个有利于免疫反应的局部微环境，从而形成一个正向反馈循环，进一步增强抗肿瘤免疫。针对这一免疫循环的每个节点，提出针对性的治疗方案，可为肿瘤治疗提供新的思路和目标，进一步推动肿瘤免疫疗法的发展和应用。