Tumor ecosystem

The tumor ecosystem refers to the complex and dynamic interactions between a tumor and its surroundings microenvironment. This ecosystem includes not only cancer cells but also various other cellular and non-cellular components that influence tumor growth, progression, and response to treatment.

Key Components of the Tumor Ecosystem

Cancer Cells

The primary malignant cells that drive tumor growth.

They exhibit heterogeneity, meaning different subpopulations may have distinct genetic and phenotypic characteristics.

Tumor Microenvironment (TME)

Cancer-Associated Fibroblasts (CAFs): Support tumor growth, produce extracellular matrix (ECM), and secrete signaling molecules that promote invasion. Immune Cells: Includes tumor-infiltrating lymphocytes (TILs), macrophages, dendritic cells, and natural killer (NK) cells. Some immune cells can suppress tumor growth, while others (e.g., tumor-associated macrophages, Tregs) may promote it.

Blood Vessels (Angiogenesis): Tumors induce the formation of new blood vessels via VEGF to ensure a supply of nutrients and oxygen.

Extracellular Matrix (ECM): A structural scaffold that provides biochemical and mechanical support.

Metabolic and Hypoxic Niches

Tumors reprogram metabolism (e.g., Warburg effect) to adapt to low oxygen and nutrient availability. Hypoxic regions within tumors trigger pathways like HIF-1α, promoting angiogenesis and metastasis. Neural and Endocrine Interactions

Neural innervation of tumors can influence their growth, with stress-induced signaling pathways playing a role. Hormonal changes can impact certain cancers (e.g., estrogen in breast cancer, and testosterone in prostate cancer). Microbiome Influence

The gut microbiome and local microbiota can influence immune responses and therapy resistance. Therapeutic Implications

The tumor ecosystem affects drug penetration, immune evasion, and resistance to therapy. Strategies targeting the ecosystem include immune checkpoint inhibitors, anti-angiogenic drugs, and microenvironment-modifying therapies. Understanding the tumor ecosystem is crucial for developing personalized oncology strategies, as disrupting these interactions can improve treatment efficacy.

Would you like me to focus on a specific aspect, such as immune interactions or metabolic reprogramming?

The glioma tumor immune microenvironment (TIME) is a complex ecosystem comprising tumor cells, stromal cells, immune cells, and extracellular matrix components. This microenvironment plays a critical role in glioma progression, immune evasion, and resistance to therapies, particularly in aggressive types like glioblastoma.

Preclinical translational research studies

Peng et al. developed a fast, efficient, and complex culture system (IPTO, individualized patient tumor organoids) that accurately recapitulates the cellular and molecular pathology of human brain tumors. Patient-derived tumor explants were cultured in induced pluripotent stem cell (iPSC)-derived cerebral organoids, thus enabling the culture of a wide range of human tumors in the central nervous system (CNS), including adult, pediatric, and metastatic brain cancers. Histopathological, genomic, epigenomic, and single-cell RNA sequencing (scRNA-seq) analyses demonstrated that the IPTO model recapitulates cellular heterogeneity and molecular features of original tumors. Crucially, they showed that the IPTO model predicts patient-specific drug responses, including resistance mechanisms, in a prospective patient cohort. Collectively, the IPTO model represents a breakthrough in the preclinical modeling of human cancers, which provides a path toward precision oncology [1].

[1] Peng T, Ma X, Hua W, Wang C, Chu Y, Sun M, Fermi V, Hamelmann S, Lindner K, Shao C, Zaman J, Tian W, Zhuo Y, Harim Y, Stöffler N, Hammann L, Xiao Q, Jin X, Warta R, Lotsch C, Zhuang X, Feng Y, Fu M, Zhang X, Zhang J, Xu H, Qiu F, Xie L, Zhang Y, Zhu W, Du Z, Salgueiro L, Schneider M, Eichhorn F, Lefevre A, Pusch S, Grinevich V, Ratliff M, Loges S, Bunse L, Sahm F, Xiang Y, Unterberg A, von Deimling A, Platten M, Herold-Mende C, Wu Y, Liu HK, Mao Y. Individualized patient tumor organoids faithfully preserve human brain tumor ecosystems and predict patient response to therapy. Cell Stem Cell. 2025 Feb 5:S1934-5909(25)00002-5. doi: 10.1016/j.stem.2025.01.002. Epub ahead of print. PMID: 39938519.