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From cytotoxic tumor-targeting to regulation of the tumor microenvironment: New considerations in pancreatic cancer chemotherapy

Current drug treatments for pancreatic cancer fail to effectively prolong survival and are often limited by dose-related toxicity in patients. Traditional school of chemotherapy focuses upon eradication of tumor cells, causing systemic side effects due to collateral damage in non-malignant normal cells of the host. Contemporary chemotherapeutic approach also considers the Tumor-Micro Environment (TME) when choosing new molecular targets, aiming to impede tumor progression by maintaining optimal tumor-microenvironment interactions. TME comprises tumor cells, endothelial cells, Tumor-Associated Macrophages (TAM), inflammatory and immune cells, as well as stromal factors such as Extracellular Matrix (ECM). Experimental data have demonstrated the role of these individual components in promoting tumor growth and progression. During epithelial-mesenchymal transition, cell-ECM interactions would reorganize the cytoskeleton to increase the migratory activity and invasiveness of cells, facilitating tumor progression and metastasis. Besides, macrophages in tumor inflammatory microenvironment could release vasoactive mediators like VEGF and chemokines that together promote tumor angiogenesis. In addition, tumor immunity could also be triggered due to anti-tumoral T cell responses that kill tumor cells by the CD8 cytotoxic T-lymphocyte recognizing major histocompatibility complex class I restricted antigens expressed on the surface of tumor cells. Here, the tumor-targeting ability of test drugs with the potential to induce tumor immunity reprogramming will be illustrated. Taken together, effective control of the tumor microenvironment may open up a brand new field for contemporary anti-tumor chemotherapy. Discovery of novel agents that possess target-specific anti-tumorigenic potential through distinctive mechanism while concomitantly modulating the tumor microenvironment would largely provoke pancreatic cancer chemotherapy efficacy.

Biography

Joshua K S Ko has completed his PhD in Pharmacology at the University of Hong Kong Medical School after completion of his undergraduate training at the University of Toronto, Canada with double specialists in Toxicology and Nutritional Sciences. He has been actively involved in many research projects, published over 100 papers in reputed journals. He is currently working as an Editorial Board Member of various journals including those of the Nature Publishing Group and also Member of the American Association for Cancer Research (AACR), European Association for Cancer Research (EACR) and International Union of Basic and Clinical Pharmacology (IUPHAR).

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