

Transcriptomic Landscapes of Cancer Progression and Therapeutic Resistance

Elena Petrova*

Department of Cancer Genomics, Saint Petersburg State University, Petersburg, Russia

DESCRIPTION

Transcriptomic landscapes of cancer progression and therapeutic resistance represent a comprehensive view of how gene expression programs evolve during tumor development, metastasis, and treatment failure. Cancer is not a static disease but a highly dynamic and heterogeneous process driven by continuous genetic and transcriptional alterations. While genomic mutations provide the foundational alterations that initiate cancer, transcriptomic changes reflect the functional consequences of these mutations and the adaptive responses of tumor cells to environmental pressures, including therapeutic interventions. The study of transcriptomic landscapes has therefore become central to understanding tumor biology and improving clinical outcomes. At the core of cancer transcriptomics is the analysis of gene expression patterns that distinguish normal cells from malignant cells. These patterns are shaped by oncogene activation, tumor suppressor gene inactivation, epigenetic remodelling, and micro environmental interactions. Transcriptomic profiling using high-throughput Ribonucleic acid (RNA) sequencing allows researchers to capture these changes at a global scale, revealing dysregulated pathways involved in proliferation, apoptosis evasion, angiogenesis, immune modulation, and metabolic reprogramming. These alterations collectively define the transcriptomic signature of cancer progression.

Cancer progression is series of evolutionary stages, each accompanied by distinct transcriptomic changes. As tumors advance, transcriptomic profiles become increasingly complex, reflecting increased heterogeneity and the emergence of sub clonal populations. These subpopulations often exhibit distinct gene expression programs that confer survival advantages under selective pressures such as hypoxia, nutrient deprivation, and immune surveillance. One of the most important features of cancer transcriptomic landscapes is intratumoral heterogeneity. Tumors are composed of diverse cell populations that differ in their transcriptional states, even when derived from a single ancestral clone. This heterogeneity contributes to functional diversity within tumors, enabling some cells to proliferate rapidly while others adopt invasive or drug-resistant phenotypes. Single-cell RNA sequencing has been instrumental in uncovering this

heterogeneity, revealing rare subpopulations that drive metastasis and therapeutic resistance. Metastasis is a complex, multi-step process that involves extensive transcriptomic reprogramming. Cancer cells undergoing epithelial-to-mesenchymal transition (EMT) exhibit dramatic changes in gene expression, including downregulation of epithelial markers and upregulation of mesenchymal genes. This transcriptional shift enhances cell motility, invasiveness, and resistance to apoptosis, facilitating dissemination from the primary tumor to distant organs. Transcriptomic studies have identified key regulators of EMT, including transcription factors and signaling pathways that coordinate this process. Cancer cells can adapt to chemotherapy, and immunotherapy through dynamic changes in gene expression. These adaptations may involve activation of drug efflux pumps, reactivation of survival pathways, metabolic rewiring, or suppression of apoptotic signaling. Transcriptomic profiling before, during, and after treatment has revealed that resistant tumors often exhibit distinct gene expression signatures compared to sensitive tumors.

Another important mechanism involves tumor microenvironment interactions. Cancer cells exist within a complex ecosystem of immune cells, fibroblasts, endothelial cells, and extracellular matrix components. Transcriptomic profiling has revealed that interactions between tumor cells and stromal cells can promote resistance by creating protective niches. Cancer-associated fibroblasts can secrete growth factors that support tumor survival, while immune cells may be reprogrammed into immunosuppressive phenotypes. Metabolic reprogramming is another hallmark of cancer progression and therapeutic resistance. Cancer cells often shift their metabolism to support rapid growth and survival under stress conditions. Transcriptomic analysis has revealed upregulation of glycolytic enzymes, lipid metabolism pathways, and amino acid transport systems in resistant tumors. Epigenetic regulation plays a central role in shaping transcriptomic landscapes in cancer. Deoxyribonucleic Acid (DNA) methylation and histone modifications can silence tumor suppressor genes or activate oncogenes, leading to persistent changes in gene expression. These epigenetic alterations are often reversible, making them attractive targets for therapy. Single-cell transcriptomics has provided unprecedented insight into the dynamic nature of

Correspondence to: Elena Petrova, Department of Cancer Genomics, Saint Petersburg State University, Petersburg, Russia, E-mail: elena.petrova@spbu.ru

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cancer progression. By analyzing gene expression at the individual cell level, researchers can track the evolution of tumor subpopulations over time. This approach has revealed that

resistant cells often pre-exist in small populations within untreated tumors, rather than arising solely in response to therapy.