Learning Track 5: AMR in Cancer

Stage 0 (Writing)

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Drug Resistance in Cancer

Drug resistance is a pervasive issue in cancer treatment, significantly complicating the effectiveness of various therapeutic strategies. It is defined as the capability of cancer cells to evade the effects of pharmacological agents, which can be either intrinsic (present before treatment) or acquired (developing in response to therapy). The complexity of drug resistance arises from multiple factors such as genetic mutations, tumor heterogeneity, and the dynamics of the tumor microenvironment.

A critical mechanism of drug resistance is genetic alteration. Cancer cells can undergo mutations that modify drug targets, reducing drug binding and efficacy. For example, the threonine to isoleucine mutation (T315I) in the BCR-ABL kinase domain exemplifies this mechanism, where the mutation impairs the binding of the tyrosine kinase inhibitor imatinib, commonly used in the treatment of chronic myeloid leukemia (CML) (Wang et al., 2019). Such genetic changes necessitate the development of second-line therapies.

Epigenetic alterations also play a significant role. Changes like DNA methylation can silence tumor suppressor genes or activate oncogenes, promoting resistance. For instance, hypermethylation of specific gene regions has been linked to diminished sensitivity to common chemotherapeutic agents like cisplatin (Khan et al., 2024). These epigenetic modifications can lead to drug-tolerant persister cells that survive treatment and contribute to relapses.

According to Walcher *et al.* (2020) Cancer Stem Cells (CSCs) further complicate drug resistance. With their ability to self-renew and differentiate, CSCs contribute to tumor heterogeneity and the persistence of resistant subpopulations. CSCs often express high levels of drug transporters, such as ABC transporters, which expel drugs from cells, reducing their effectiveness. As a result, although therapies may initially shrink tumors, surviving CSCs frequently lead to recurrence and further challenges.

The impact of drug resistance on cancer treatment outcomes cannot be overstated. Statistics indicate that up to 90% of cancer-related deaths are attributable to drug resistance (Si *et al.*, 2019). Recognizing the mechanisms of drug resistance is crucial for developing innovative therapeutic strategies. Emerging approaches include combination therapies that simultaneously target multiple pathways to counteract resistance mechanisms, precision medicine that tailors therapies to individual patient profiles, and the development of inhibitors specifically designed to overcome resistant mutations.

In summary, drug resistance is a formidable barrier to successful cancer treatment, necessitating a multifaceted understanding of its mechanisms, implications, and underlying biological processes. Ongoing research aimed at deciphering these complex interactions is essential in paving the way toward more effective cancer therapies, novel therapeutic approaches, and improved patient survival rates.

References

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