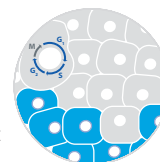


The Challenge of Treatment Resistance

Diversity, or heterogeneity, among cancer cells within and between tumors is a major cause of treatment resistance. Some examples of heterogeneity are as follows:

Some cancer cells in a tumor may not be rapidly dividing, thus becoming insensitive to treatments that target rapidly dividing cells, such as cytotoxic chemotherapeutics.



Some cancer cells in a tumor may have or may acquire mutations in the target against which the drug is developed, thus rendering the treatment ineffective.



Some cancer cells in a tumor may have or may acquire molecular or cellular differences other than changes in the treatment target, thus rendering the treatment ineffective.



Some cancer cells in a tumor may leverage redundancies in signaling networks that help them proliferate uncontrollably, thus becoming resistant to a treatment targeting a signaling protein.



In addition, differences in tumor microenvironmental components can render a treatment ineffective.