

## Molecular Mechanisms of Drug Resistance in Hematological Malignancies

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Chemotherapy is the most widely used treatment strategy for cancer which is the highest second reason for human death after heart related diseases. However, cellular resistance mechanisms developed by cancer cells and tissues to applied anticancer agents at the beginning or during therapy are a significant problem preventing successful therapy. Resistance developed by cancer cells to structurally and functionally different cytotoxic agents is called multi drug resistance. The resistance can be observed at the beginning of the treatment or during treatment and these are known as intrinsic or acquired resistance respectively. The resistance phenotype is associated with the tumor cells that gain a cross-resistance to a large range of drugs that are structurally and functionally different.

Drug resistance mechanisms have different molecular genetics and biochemical factors depending on the drug applied and the type of cancer. Secondary genetic alterations and disorders in cancer cells may also result in drug resistance. That is why it is of vital importance to study and consider all the signaling pathways, in multidrug resistance of cancer.

Multidrug resistance can operate *via* many unrelated mechanisms, such as overexpression of energy-dependent efflux proteins, decrease in uptake of the agents, increase or alteration in drug targets, alterations in cell cycle checkpoints, inactivation of anticancer agents or their compartmentalization, inhibition of apoptosis, enhancement of DNA repair mechanisms, problems related to drug metabolism and aberrant metabolism of bioactive sphingolipids. The elucidation of the actual resistance mechanism and the employment of molecular and biochemical approaches to overcome multidrug resistance have been a major goal in cancer research. This presentation will describe and explain the mechanisms contributing to multidrug resistance in cancer chemotherapy and touch on the possible approaches for reversing resistance.