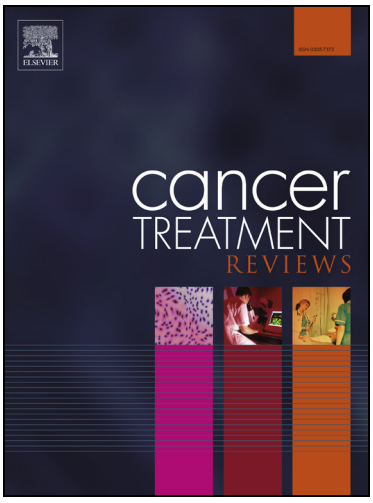

Anti-Tumour Treatment

Drug resistance in multiple myeloma

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Drug resistance in multiple myeloma

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Abstract

Multiple myeloma (MM, plasma cell myeloma) is a malignant hematologic disease characterized by the clonal proliferation of malignant plasma cells. The treatment of MM has changed dramatically in recent years, with the introduction of new drugs into therapeutic strategies, both in the front line setting and in relapsed refractory disease. However, most patients eventually relapse and often demonstrate multiple drug resistance. Therefore there is still an urgent and unmet need to define the molecular mechanisms of resistance for available drugs in order to enhance the use of existing treatments and design more effective therapies. Genetic abnormalities are well known to play a central role in MM resistance to available drugs, and epigenetic aberrations mainly affecting the patterns of DNA methylation and histone modifications of genes, especially tumor suppressors, can be involved in the resistance mechanism. Moreover, defects in the mechanisms of apoptosis, senescence and DNA repair could also contribute to drug resistance. In addition, mutations or alterations in the expression of the drug target can influence response to therapy. Achieving a better understanding of the pathways and protein expression involved in MM drug resistance and the development of novel therapeutic strategies are important goals for further progress in the treatment of MM. This review gives a critical overview of the role of cellular, microenvironmental and molecular mechanisms of drug resistance in MM.