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Role of epigenetics-microRNA axis in drug resistance of multiple myeloma


Despite administration of novel therapies, multiple myeloma (MM) remains incurable with resistance to drugs leading to relapse in most patients. Thus, it is critical to understand the mechanisms underlying the drug resistance of MM and develop more effective therapeutic strategies. Genetic abnormalities are well known to play a central role in MM pathogenesis and therapy resistance, however, epigenetic aberrations mainly affecting the patterns of DNA methylation / histone modifications of genes (especially tumor suppressors) and miRNAs have also been shown to be involved. Importantly, while epigenetic silencing of miRNAs in MM is well documented, some epigenetic markers are known to be direct targets of miRNAs particularly the recently described “epimiRNAs”. Drugs targeting epigenetic modifiers (e.g. HDACs, EZH2) can sensitize MM resistant cells to anti-myeloma drugs and reversibility of epigenetic changes makes these drugs promising therapeutic

agents. Therefore, combination of miRNA mimics with inhibitors of epigenetic modifiers would be a more potent therapeutic strategy in MM patients in relapse or refractory to treatments. We will discuss the findings of recent investigations on epigenetics/miRNA regulatory axis in development of drug resistance in MM and highlight possible approaches for therapeutic applications of such interaction.

Speaker Biography

Hong Chang is a laboratory physician in Hematology and Oncology at Toronto General Hospital/ University Health Network and a Full Professor at the University of Toronto, Canada. His research has mainly dealt with the characterization of genetic events for initiation and progression of multiple myeloma (MM) as well as identification of prognostic factors and therapeutic targets in MM. Dr. Chang serves on the Editorial Board of several scientific journals and has published over 140 peer-reviewed scientific manuscripts. He has received many research and educational awards such as the TransAmerica Life Canada Award from Leukemia and Lymphoma Society of Canada (LLSC), the Excellence in Life Sciences Teaching Award, University of Toronto.

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