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Identification of new microRNA biomarkers in drug-insensitive cancer stem cells in human leukemia

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ABL tyrosine kinase inhibitor (TKI) therapies have had a major impact on treatment of chronic myeloid leukemia (CML) worldwide. However, TKI monotherapies are not curative and initial and acquired TKI resistance, as well as relapse, remain challenges. To identify miRNAs in TKI-insensitive CD34+ stem/progenitor cells that might serve as potential biomarkers and/or therapeutic targets; we have used Illumina sequencing to create absolute miRNA expression profiles from treatment-naive CD34+ cells obtained at diagnosis from TKI-responders and non-responders, and normal bone marrow (NBM) as controls. DESeq analysis revealed 66 differentially expressed miRNAs between CML and NBM samples ($P<0.05$); and 12 between TKI-responders and non-responders. 21 differentially expressed miRNAs were confirmed in CD34+ cells from IM-responders (n=12), non-responders (n=10) and normal individuals (n=11). Importantly, significant changes in some of these miRNAs were detected in CD34+ cells from CML patients (n=65) after 3-month nilotinib (NL) treatment; 19 normalized after NL therapy, whereas 10 showed little change. We also identified differently expressed mRNAs that are predicted targets of the deregulated miRNAs, by comparing RNA-Seq data from the same CML and NBM samples. Strikingly, only 7 differentially expressed mRNAs were predicted targets of the deregulated miRNAs when comparing TKI-responders and non-responders. These miRNAs and their target genes may serve as useful biomarkers to predict clinical response of patients to TKIs and may point to novel therapeutic targets.

Biography

Xiaoyan Jiang is a distinguished Scientist in the BC Cancer Research Centre, a Professor in the Department of Medical Genetics and an Associate Member in the Department of Medicine at the University of British Columbia, Vancouver, Canada. Her research interests are focused on basic and translational research of molecular properties of leukemic stem cells that contribute to the development of leukemia and drug resistance. She has been invited to present her work at national and international conferences (>120), to join Editorial Boards of 20 reputed journals and has published more than 100 peer-reviewed publications, review articles and book chapters.

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