Next Generation Sequencing Analysis of Mesenchymal Stem Cells in a Sri Lankan Cohort of Myelodysplastic Syndromes Patients

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Abstract

Background/Objectives: Mesenchymal stem cells (MSCs) are precursors of marrow stromal cells which interact with the haematopoietic compartment and are implicated in the pathogenesis of Myelodysplastic Syndromes (MDS). The molecular profiles of MDS-MSCs have not been extensively studied; and may provide insights into MDS disease biology.

Methods: DNA was isolated from bone marrow MSCs from 11 newly diagnosed *de novo* MDS patients. Next Generation Sequencing was performed on an Illumina(R) MiSeq NGS platform, using a gene panel consisting of 54 genes that are frequently mutated in myeloid malignancies.

Results: Mutations in 37 genes were identified in 11 MDS-MSC samples. All patients carried at least one mutation in their MSC compartment. MDS-MSCs demonstrated frequent mutations in epigenetic regulators (*DNMT3A,TET2,EZH2,ASXL1,BCOR/BCORL1,KDM6A*) and genes in signaling pathways (*KIT,NRAS,PDGFRA*). *KIT* and *PDGFRA* genes were co-mutated in two patients. RAEB-MSCs showed the highest number of mutations and *KDM6A* and *KIT* mutations were present all RAEB patients. Fifteen previously reported mutations were identified. Out of these T665P in PDGRFA, H1367P in BCOR and M541L in KIT were observed in ≥2/11

patients. The recurrent novel mutations included H485P of KIT, L1742W of TET2, H588P of DNMT3A and T181P & T833P of KDM6A.

Conclusions: Both novel and reported mutations in myeloid malignancies were present in the MDS-MSCs studied. Mutations mostly affected epigenetic mechanisms and signaling pathways of MDS-MSCs. These changes may be an indication of a possible role of MSCs in MDS disease pathogenesis or progression. Further bioinformatics analysis will be done to determine the pathogenic role of these mutations.

Keywords: Myelodysplastic syndromes (MDS), mesenchymal stem cells (MSCs), mutations, next generation sequencing