Identification and Characterisation of Anti-N-CoR Protease in Acute Myeloid Leukemia

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Acute myeloid leukemia is a malignant cell disorder of myeloid lineage that mostly affects children and young adults. Normal maturation of myeloid cell lineage is widely due to the transcriptional repression played by the nuclear receptor co-repressor (N-CoR). The deregulation of N-CoR mediated transcriptional repression due to misfolded N-CoR confirmation shown to contribute to the transformation of myeloid cells in AML through the de-repression of growth-promoting genes. Further demonstration has also shown that the specific loss of N-CoR in AML was caused by a heat-labile protease known as O-sialoglycoprotein endopeptidase (OSGEP). These findings suggest that the proteases that promote the degradation of N-CoR may impart a key role in the growth and transformation of AML cells. The AML specific anti-N-CoR proteases has been purified from AML cell lines through HPLC-based size exclusion chromatography and confirmation of their role in N-CoR degradation was carried out by in-vitro N-CoR degradation assay using recombinant N-CoR protein as a substrate. The resulting purified proteases showing optimal degradation activity will undergo mass spectrometry to confirm their identity. Transfection has been carried out on HEK293 cells and the cultured cells were extracted for Western blotting assay to detect the levels of N-CoR protein. The identification and characterization of anti-N-CoR proteases and defining their role in AML pathogenesis will contribute to better understanding of molecular mechanisms underlying the transformation of AML cells.

Keywords: Acute myeloid leukemia, N-CoR, Protein Misfolding, Heat Labile Protease, OSGEP, High Performance Liquid Chromatography

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