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Mll-af4 and mll-mcef oncogenic fusion proteins show the identical protein interaction pattern

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Mixed-lineage leukemia (MLL) protein is a multidomain histone methyltransferase, which acts as transcriptional co-activator and plays an essential role in epigenetic gene regulation at early development and hematopoiesis. It is shown that MLL together with various nuclear proteins form numerous fusion proteins, which are enrolled in progression of similar malignant phenotypes of leukemia [5]. However, protein interaction model of different MLL fusions is still controversial.

To assess the pattern of protein interactions of MLL fusions, we performed protein-protein interaction (PPI) network analysis for two MLL chimera proteins, MLL-AF4 – t(4; 11)(q21; q23) and MLL-MCEF – ins(5; 11)(q31; q13q23), both of which are involved in acute leukemia progression [2,3]. Protein interaction data was extracted from text mining online software GPS-Prot v. 2.0 [4]. PPI network visualization and network parameters evaluation were performed using Cytoscape v. 2.8.3 software [7]. Cluster analysis was conducted by MCODE plug-in. The statistical significance of the cluster extraction was assessed as described in *Bader et al (2003).*

Our results show that each of the components of studied fusion proteins form highly interconnected distinct regions. MLL PPI network analysis reveals a clique cluster, indicating that MLL interacters are united in protein macromolecular complex, which is in accordance with previously published experimental data [6]. AF4 and MCEF proteins tend to form the same clique clusters, which also agree with experimental data [1]. It needs to be emphasized that the comparative interaction data taken from previously published papers were manually discarded from analyzed datasets.

In conclusion, we assume that the MLL-AF4 and MLL-MCEF fusion proteins tend to form identical PPI network, which can lead to the manifestation of similar malignancy, thus confirming that different fusions can cause the same disease network. Further detailed network analysis is required for obtaining more detailed pattern of protein interactions of MLL-caused leukemias.

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