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In silico modeling of Bcr-Abl oncoprotein isoforms in chronic myelogenous leukemia

Chronic Myelogenous Leukemia (CML) is a cancer of the white blood cells. It develops, when a hematopoietic stem cell in the bone marrow acquires a Philadelphia (Ph) chromosome carrying the BCR-ABL fusion oncogene. The fusion of the ABL gene on chromosome 9 with the BCR gene on chromosome 22 results in the formation of two p210BCR-ABL onco-protein isoforms, b2a2 and b3a2, due to the head-to-tail fusion of p160BCR and p145ABL proteins. b2a2 and b3a2 differ in sequence by a 25 amino acid insertion and a Glu903Asp substitution. The oncogenic potential of p210BCR-ABL protein isoforms is due to the fact that the normally regulated tyrosine kinase activity of p145ABL becomes unregulated in both b2a2 and b3a2. p145ABL is a non-receptor tyrosine kinase that plays an important role in signal transduction and the regulation of cell growth. At the N-terminus, p145ABL contains the SH3, SH2 and SH1 domains. The SH2 and SH3 domains regulate tyrosine kinase function of p145ABL and the SH1 domain is responsible for the tyrosine kinase activity. The SH3 domain has a negative regulatory effect on the tyrosine kinase function. Deletion of SH3 or mutation in SH3 eliminates the tyrosine kinase activity of p145ABL. In silico modeling, using Psipred and ExPASy servers, was used to determine the secondary structural elements of these onco-protein isoforms. The structural elements of the two proteins were found to be different in the five □-helices (□25, □́, □26, □27 and □29) and nine β-strands (β12, β13, β15, β́, β17, β30, β□, β34 and β35) which comprise the SH1, SH2, SH3 and DNA-binding domains which can result in different roles played by the two isoforms in mediating signal transduction during the course of Chronic Myelogenous Leukemia. Both p210BCR-ABL proteins can cause pleiotropic effects on many signal transduction pathways that can affect cell survival, disease progression, genomic stability and hematopoiesis.

Biography

Entissar AlSuhaibani is a Professor of Genetic at King Saud University. Her research interest is the cytogenetic effect of radiation. She is involved in many research projects founded by many research institutions. In 2010, she was awarded as a Fellow for the 2010 L'Oreal UNESCO Pan Arab Regional Fellowships. She presented and participated in the various regional and international scientific conferences. She received gold and silver medals from different international expiations for the patent of the Invention of the Sister Chromatid Exchange staining SCE staining. She involved in many community activities to encourage Saudi females to engage in science field. Also, she is member of international and local scientific societies.

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