

THE HUMAN LEUKOCYTE PROTEIN FORMIN (FMNL1) ASSOCIATES WITH KU-70 AND MAY PLAY A ROLE IN APOPTOSIS OF JURKAT CELLS

Kobarg, C.B., Favaro P., Costa, F. and Saad, S.T.

Centro de Hematologia e Hemoterapia e Departamento de Clínica Médica,
Universidade Estadual de Campinas, Brazil

The Human Leukocyte protein Formin (FMNL1) is over expressed in Jurkat cells and in peripheral blood leukocyte from chronic lymphocytic leukemia (CLL) patients. Our previous results of immunoprecipitation showed that FMNL1 associates with the protein kinase AKT, an important regulator of cell survival. AKT phosphorylates the protein BAD inactivating its pro-apoptotic function. We now found that FMNL1 associates with Ku70, a subunit of DNA Protein Kinase C (DNA-PK) that plays a crucial role in DNA repair and is activated by DNA breaks caused by radiation or chemotherapy. Ku-70 has also been shown to bind the pro-apoptotic protein BAX and to inhibit BAX-mediated apoptosis in vitro by preventing its re-localization to the mitochondria. Silencing of FMNL1 expression by RNAi experiments in Jurkat cells did not influence Ku70 mRNA levels measured by real time PCR and Western blot. However, preliminary results indicate that decreased FMNL1 expression leads to increased apoptosis in Jurkat cells as determined by measuring Annexin-V positive cells by flow cytometry. Together our results indicate that FMNL1 may play an important role in apoptosis of cancer cell lines mediated through its interaction with the two anti-apoptotic proteins: AKT and Ku70.