[S2-4] [4/18/2002(Thur) 16:00-16:30/Hall B]

Functional Study of Fas Associated Factor 1, an Nm23-Binding Protein, in Apoptotic Execution

Eunhee Kim

Research Center for Biomedicinal Resources and Division of Life Science, PaiChai University, Taejon 302-735, Korea

Non-metastatic protein 23 (Nm23), has been implicated in a wide variety of biological processes including suppression of metastasis, regulation of proliferation and differentiation, and apoptosis. We have screened human Nm23 interacting proteins using yeast two hybrid assay and found that Nm23-H1 was interacting with human Fas associated factor 1 (hFAF1). FAF1 was previously known to enhance but not able to initiate apoptosis on its own. However, we found that hFAF1 could initiate apoptosis in the absence of any extrinsic death signals when overexpressed in BOSC23 cells. The apoptotic potential of hFAF1 required amino acid 181-381 region (hFAF1(181-381)) containing downstream ubiquitin homologous domain (UB2) and adjacent nuclear localization signal. Based on the fact that caspase-8 is recruited to Fas upon Fas activation, we questioned if FAF1 interacted with caspase-8. FAF1 could interact with caspase-8 *in vivo* as well as *in vitro*. The amino acid 181-381 region of hFAF1 capable of apoptotic execution, was mapped as the caspase-8 binding region and the DED (death effector domain) of caspase 8 was responsible for the interaction with FAF1. Apoptosis in HeLa cells by caspase 8 DED increased significantly when cotransfected with hFAF1(181-381). Moreover, we found that hFAF1(181-381) as well as hFAF1 enhanced the formation of death effector filaments (DEFs) formed by caspase-8 DED and was colocalized with caspase-8 DED in the DEFs. Thus, our data provide one of molecular mechanisms for the pro-apoptotic function of FAF1 i.e. enhancing the DEF formation via direct interaction with caspase-8.