Cell Communication and Signaling BioMed Central

Meeting abstract

Open Access

CNK1 controls invasiveness of breast cancer cells via transcriptional regulation of MT1-MMP through the PI3K-Akt-NF-κB signalling axis

RD Fritz*[1], Z Varga[2] and G Radziwill[1]

Address: [1]Institute of Medical Virology, University of Zurich, Zurich, Switzerland and [2]Institute of Clinical Pathology, University Hospital Zurich, Zurich, Switzerland

* Corresponding author

from 12th Joint Meeting of the Signal Transduction Society (STS). Signal Transduction: Receptors, Mediators and Genes
Weimar, Germany. 29–31 October 2008

Published: 26 February 2009

Cell Communication and Signaling 2009, **7**(Suppl 1):A30 doi:10.1186/1478-811X-7-S1-A30

This abstract is available from: http://www.biosignaling.com/content/7/S1/A30

The scaffold protein CNK1 was described to be involved in protooncogenic signalling pathways utilising protein kinases Raf-1 and Src and the small GTPase Rho. Deregulation of these molecules is clearly correlated with cancer. Nonetheless, a direct impact of CNK1 on cancer cell behaviour was not investigated so far. To address this question we analysed the function of CNK1 in a highly invasive breast cancer cell line MDA-MB-231.

Downregulation of CNK1 by retroviral shRNA delivery reduced cell proliferation and this effect was even more pronounced under serum starvation. Furthermore, knockdown of CNK1 impaired the invasion of Matrigel by MDA-MB-231 cells without affecting cell migration, suggesting a defect in proteolytic activity in these cells. In agreement with this observation, expression of several matrix metalloproteinases was diminished in CNK1 knockdown cells. In particular the promoter of membrane type 1 matrix metalloproteinase (MT1-MMP) was shown to by less active upon CNK1 downregulation. Conversely, CNK1 overexpression stimulated the MT1-MMP promoter. This stimulatory effect was sensitive to the IKK inhibitor BAY11-7082 and the PI3K inhibitor LY294002. CNK1 was found to influence the alternative NF-κB pathway through regulation of the processing step from p100 to p52. Moreover, phosphorylation of Akt on Ser 473 was reduced in CNK1 knockdown cells, a result which is consistent with Akt's importance in p100 processing. Importantly, analysis of human cancer samples by immunohistochemistry revealed that CNK1 can be overexpressed in breast cancer samples compared to healthy tissue.

Taken together, these results provide evidence that CNK1 is a part of the invasion-promoting machinery in breast cancer cells and may be considered as a potential therapeutic target.