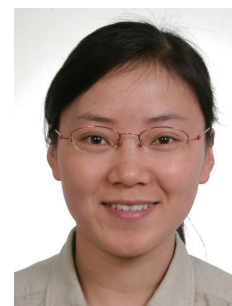


HETEROGENOUS NULCEAR RIBONUCLEOPROTEIN K (HNRNPK) IS A POTENTIAL TARGET OF METASTASIS

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Instruction: Cancer is emerging as a leading cause of death and still awaits effective therapies. One of the reasons, many cancers fail therapy is the metastasis property of cancer cells by which they travel through the blood stream, invade various tissues and escape local therapy. Identification of the factors leading to metastasis hence is highly important in designing of effective and novel anti-cancer therapeutics.

Background: In a study by Inoue et al (2007) PNAS 104:8983-8988, randomized intra-cellular antibody library was used for functional silencing in conjunction with chemotaxis assay to identify genes involved in metastasis in human HT1080 fibrosarcoma. Cell clones that lost chemotaxis characteristics were seen to harbor intracellular antibodies to hnRNP K protein. Based on this, it was suggested that hnRNP K is a candidate target metastatic activity of cells. hnRNP K is a multifunctional signaling protein. It has been found in the nucleus, cytoplasm and mitochondria and is involved in transcription, splicing, chromatin remodeling, translation and DNA damage processes.

Purpose: We undertook a study to investigate the effect of hnRNP K on proliferation and metastatic properties of cancer cells in in vitro and in vivo.

Method: We established stably overexpressing hnRNP K derivative cell lines of mouse (NIH3T3) and human (U2OS) nonmalignant transformed cells. In malignant human HT1080 fibrosarcoma, hnRNP K was compromised by intracellular antibody described in Inoue et al (2007).

Conclusions: Our study on hnRNP K overexpression and silencing in animal model of cancer using xenograft and tail vein tumor cell injections in nude mice revealed that (i) hnRNP K is a potential target of metastasis and (ii) intracellular antibody of hnRNP K has antitumor and anti-metastasis activity.