Study unveils SINE's potential of re-activating tumour fighting proteins within a cell

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New study suggests that selective blockade of CRM1-dependent nuclear export represents a completely novel, tumour metastasis-selective approach for the treatment of advanced metastatic prostate cancers.

According to the researchers, the human nuclear export protein chromosomal region maintenance/exportin 1/Xpo1 (CRM1) is the sole exportin mediating transport of many multiple tumor suppressor proteins out of the nucleus. Their study aimed to verify the hypothesis that CRM1 inhibition could be beneficial for the treatment of prostate cancer metastases, which was achieved by testing the effects of the orally available, potent and selective, clinical stage SINE compound KPT 330.

"Although the class of compounds used in our studies—SINEs or Selective Inhibitors of Nuclear Export—have just recently entered early clinical testing, our results suggest that these agents could be active in patients with androgen-independent prostate cancer," commented study's lead author Dr. Claudio Festuccia, of the University of L'Aquila in Italy.

"Most of the current treatments for prostate cancer work by reducing the levels or blocking the receptors for a set of hormones called androgens. These SINE compounds act through an entirely new mechanism by re-activating a cells own tumor fighting proteins. These tumor fighting proteins, called tumor suppressor proteins, act as a guardian against the development of cancers by detecting damage to a cell's DNA and if

DNA damage is found, activating the cell's own suicide program," he explained.

"Since all cancers have a great deal of DNA damage, re-activation of tumour suppressor proteins could cause the cancer to commit suicide. We observed just such an effect with these new SINE drug candidates."

According to the authors, the study also showed that these new SINE drug candidates prevented prostate cancer cells from causing damage to bones.

"The mechanisms of preventing the damage are now being worked out, but it appears that these new SINE drug candidates can suppress a type of bone cell called an osteoclast," said Festuccia.

Osteoclasts are activated by prostate cancer cells to destroy bone, and play an important role in prostate cancer-associated bone disease.

The results of this study will be presented at the 5th European Multidisciplinary Meeting on Urological Cancers in Marseille, France, on 15-17 November 2013.

More information: Festuccia, C. et al. "Crm1-selective inhibitors of nuclear export (sine) reduce the incidence of tumor spreading and improve overall survival in preclinical models of prostate cancer," Abstract O10, 5th EMUC.

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