Author’s response to reviews

Title: Tumour Selective Nuclear Targeting In A Tumour Progression Model

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Dear Sir/Madam,

I am submitting a pdf version of the manuscript entitled:

“TUMOUR SELECTIVE NUCLEAR TARGETING IN A TUMOUR PROGRESSION MODEL”

by Michael S. Nastasie, Helmut Thissen, David A. Jans and Kylie M. Wagstaff,

for consideration for publication in BMC Cancer.

Cancer remains one of the most prevalent causes of morbidity and mortality worldwide, with an urgent need for new approaches to target bioactive molecules to cancer cells efficiently and specifically. Here we fuse the cancer cell specific nuclear targeting module of the Chicken Anemia Virus Apoptin protein to histones H2B and H3. By quantitating localisation of ectopically expressed protein in transfected isogenic human osteosarcoma and breast tumour progression models, we found 2-3 fold higher nuclear accumulation in tumour compared to normal cells, the first demonstration of enhanced nuclear targeting by Apoptin in a tumour progression model. Excitingly, we also identify for the first time an innate cancer targeting transduction ability for histone proteins that could be exploited synergistically with the Apoptin nuclear targeting module to affect an
overall 13-fold higher delivery of protein to osteosarcoma cancer cell nuclei compared to their isogenic normal counterparts.

This is the first report of innate cancer-cell specificity by a cell penetrating protein, with important implications for the use of protein transduction as a vehicle for gene/drug delivery in the future, and in particular in the development of highly specific and effective anti-cancer agents. Due to these novel aspects of the work, its quantitative nature, and its broad interest in terms of cancer cell specific targeting, we believe that this manuscript is of interest to the readership of BMC Cancer.

I thank you in anticipation of receiving an acknowledgement of receipt of the manuscript,

Yours sincerely,

Dr. Kylie M. Wagstaff