Nature Reviews Urology | Published online 8 Nov 2016; doi:10.1038/nrurol.2016.230

PROSTATE CANCER

On target — theranostic imaging for aggressive disease

> "...phage particles displaying the SNTRVAP motif specifically targeted GRP-78-expressing, DU145-derived xenografts"

A targeted theranostic agent for aggressive prostate cancer has been described in *Proceedings of the National Academy of Sciences*. GRP-78 — a glucose-regulated cell surface protein — can be effectively targeted for imaging and therapy delivery and could be translated into clinical applications for patients with this disease.

Renata Pasqualini, one of the corresponding authors, told *Nature Reviews Urology* "In essence, we use combinatorial library selection to discover, validate, and exploit the biochemical diversity of tumour and endothelial cells for developing targeted pharmacology." She explained "In this proof-of-concept endeavour, our criteria included finding the optimal signal-to-background attributes and determining the best correlation between the imaging signal and GRP-78 expression levels for the detection of prostate cancer."

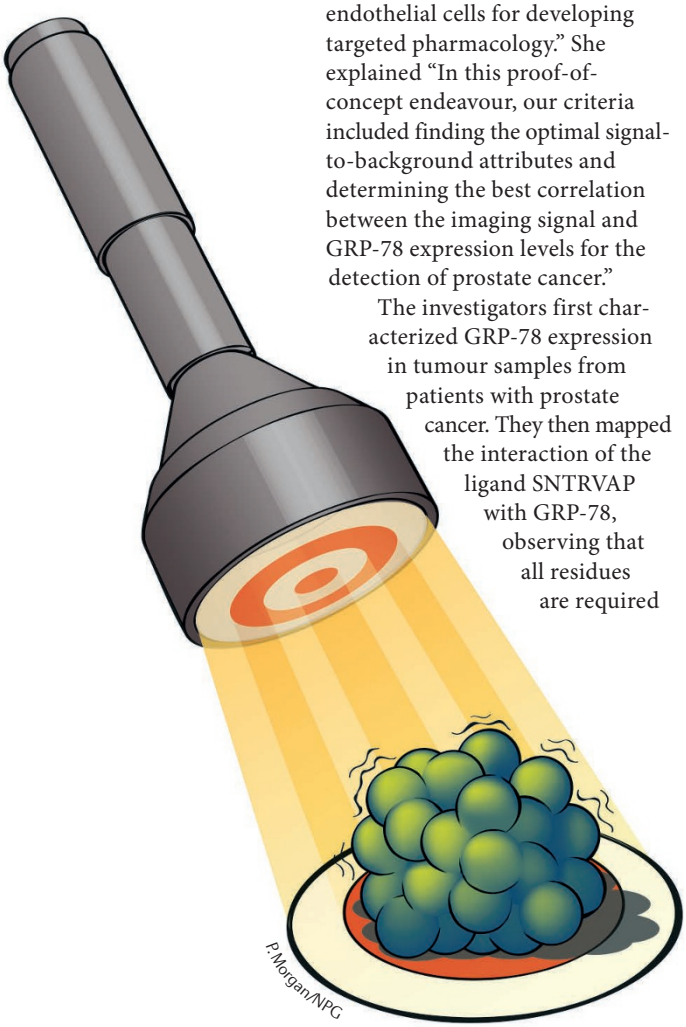
The investigators first characterized GRP-78 expression in tumour samples from patients with prostate cancer. They then mapped the interaction of the ligand SNTRVAP with GRP-78, observing that all residues are required for complete binding and that the interaction is specific.

In vivo, phage particles displaying the SNTRVAP motif specifically targeted GRP-78-expressing, DU145-derived xenografts. Moreover, coupling of SNTRVAP with a small interfering RNA for GRP-78 effectively downregulated GRP-78 expression.

The theranostic capacity of *HSVtk*, which can be used for noninvasive imaging in the presence of a radiolabel substrate and a cell-suicide-inducing transgene in the presence of ganciclovir (GCV), was analysed *in vivo* using patient-derived xenografts. PET imaging using ^{18}F-FDG or ^{18}F-FEAU showed that *HSVtk*-containing targeted particles specifically localized at metabolically active tumour sites. Furthermore, ^{18}F-FEAU–PET–CT imaging revealed that delivery of *HSVtk* plus GVC significantly inhibited tumour growth in these mice.

Wadih Arap, another corresponding author, explained "This work substantially accelerates plans for the translation of molecular–genetic imaging and therapy for advanced prostate cancer into the clinic. Our long-term goals are to change the management of patients with prostate cancer by enabling noninvasive, systemic, targeted monitoring through imaging of reporter genes. The much-heralded era of precision medicine has the potential to bring therapeutic and molecular-genetic imaging strategies together." He concluded "Translational clinical trials will ultimately determine the value of this strategy."

Louise Stone



ORIGINAL ARTICLE Ferrara, F. *et al.* Targeted molecular-genetic imaging and ligand-directed therapy in aggressive variant prostate cancer. *Proc. Natl Acad. Sci. USA* http://dx.doi.org/10.1073/pnas.1615400113 (2016)