> This metabolic imaging approach has considerable potential for monitoring treatment response in patients receiving PI3K–mTOR-targeted therapies

showed that a single dose of rapamycin (15 mg/kg) 24 h before imaging resulted in a significant decrease in metabolism in JHRCC228 xenografts compared with nonresponding JHRCC12 xenografts, and lactate levels in dissected tumours corresponded with these imaging data.

This metabolic imaging approach has considerable potential for monitoring treatment response in patients receiving PI3K–mTOR-targeted therapies. "We are looking to not only further pursue this in more models of ccRCC with more targeted therapies but also to interrogate other metabolic pathways," commented corresponding author Kayvan Keshari. "The potential for use in clinical management is high, as hyperpolarized MRI has recently been translated to patients".

Annette Fenner

ORIGINAL ARTICLE Dong, Y. et al. Hyperpolarized MRI visualizes Warburg effects and predicts treatment response to mTOR inhibitors in patient-derived ccRCC xenograft models. *Cancer Res.* https://doi.org/10.1158/0008-5472.CAN-18-2231 (2018)

> compound 28 acts via a different mechanism to enzalutamide

by assessment of senescence-associated β-galactosidase (SA-β-Gal) activity. Furthermore, expression of endogenous AR target genes was suppressed. "It seems these classes of compounds inhibit nuclear translocation and chromatin accessibility of the AR," comments corresponding author Aria Baniahmad; "Of further interest, these compounds induce cellular senescence, which has been shown ex vivo in patient prostate cancer samples for atraric acid."

The use of novel chemical platforms enables development of AR antagonists that act via different pathways and might help overcome the problem of therapy resistance. The team are now analysing some of the compounds in xenograft mouse models and microspheroids, either alone or in combination with other inhibitors of pathways known to activate the AR.

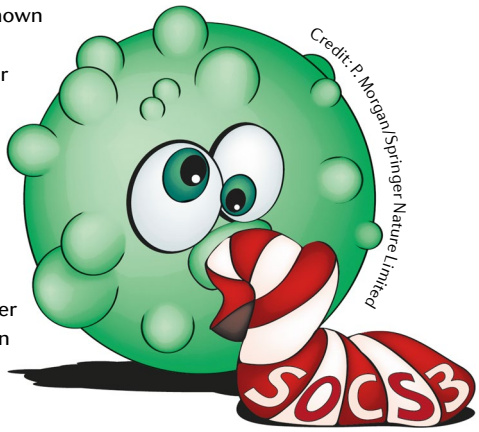
Annette Fenner

ORIGINAL ARTICLE Roell, D. et al. Halogen-substituted anthranilic acid derivatives provide a novel chemical platform for androgen receptor antagonists. *J. Ster. Biochem. Mol. Biol.* https://doi.org/10.1016/j.jsbmb.2018.12.005 (2019)

PROSTATE CANCER

Putting a SOCS in prostate cancer

New preclinical data have shown the potential of inducing overexpression of suppressor of cytokine signalling 3 (SOCS3) in castration-resistant prostate cancer (CRPC) using gene therapy. This therapy probably works by attenuating the IL-6–Janus kinase (JAK)–signal transducer and activator of transcription (STAT) signalling pathway, which is often overactivated in prostate cancer.



Credit: P. Morgan/Springer Nature Limited

The investigators created replication-deficient, recombinant adenoviral vectors expressing human *SOCS3* (Ad-hSOCS3) or mouse *Socs3* (Ad-mSOCS3). Human (DU145 and PC3) and mouse (TRAMP-C2) CRPC cells were treated with their corresponding adenoviral vectors. Gene therapy induced SOCS3 overexpression in all three CRPC cell lines. Cell proliferation and expression of phosphorylated STAT3 (pSTAT3) were inhibited in DU145 and TRAMP-C2 cells by gene therapy with Ad-SOCS3. Furthermore, Ad-SOCS3 treatment induced apoptosis in these cell lines. However, Ad-hSOCS3 treatment had no effect on proliferation, pSTAT3 expression or apoptosis in PC3 cells, in which no STAT3 expression was detected.

In DU145 cells specifically, treatment with Ad-hSOCS3 suppressed expression of IL-6. G0–G1 cell cycle arrest was also induced by Ad-hSOCS3, similar to the effect on the cell cycle of suppression of STAT3 expression using small interfering RNA in these cells.

In TRAMP-C2 cells, Ad-mSOCS3 treatment decreased the expression of IFNγ-induced programmed cell death 1 ligand 1 (PD-L1) expression. However, IFNγ treatment did not increase PD-L1 expression in DU145 cells, and Ad-hSOCS3 treatment did not suppress PD-L1 expression in these cells.

Cytotoxicity assays showed that Ad-SOCS treatment considerably increased the cytotoxicity of natural killer (NK) cells in both TRAMP-C2 and DU145 cells; however, the presence of recombinant IL-6 inhibited this effect in DU145 cells.

In vivo, treatment of mice harbouring DU145 xenograft tumours with combined Ad-hSOCS3 and NK cells substantially inhibited tumour growth compared with NK cell treatment alone. Immunohistochemical analysis showed that more $CD56^+$ cells were present in tumours from mice that received combined treatment than those that received NK cells alone.

These results show that treatment of CRPC cell lines with Ad-SOCS3 induces its overexpression in these cells and could increase the sensitivity of CRPC cells to NK cells. Thus, Ad-SOCS3 gene therapy plus NK cell immunotherapy has therapeutic potential in men with CRPC.

Louise Stone

ORIGINAL ARTICLE Yoneda, T. et al. Overexpression of SOCS3 mediated by adenovirus vector in mouse and human castration-resistant prostate cancer cells increases the sensitivity to NK cells in vitro and in vivo. *Cancer Gene Ther.* https://doi.org/10.1038/s41417-018-0075-5 (2018)