

## Prostate cancer

# GHR expression and prostate cancer proliferation

A new study in *The Prostate* provides insights into the role of growth hormone receptor (GHR) in the proliferation of prostate cancer.

Mutations in *GHR* have been observed to confer protections against certain cancers, including prostate cancer, through disruption of the growth hormone (GH)–insulin-like growth factor 1 (IGF1) axis. Congenital GH–IGF1 axis disruption in a mouse model of prostate cancer (C3(1)/TAG) has also been shown to prevent development of prostatic intraepithelial neoplasia (PIN).

Using this mouse model, Unterberger et al. investigated the role of *Ghr* in prostate cancer through loss-of-function and gain-of-function models. C3(1)/TAG transgenic mice were bred to mice with a conditionally null *Ghr* allele, Rosa-Cre-ER<sup>T2</sup> mice, PB-Cre4 transgenic mice and/or transgenic GH-antagonist expressing mice. The resulting mice comprised the C3(1)/TAG prostate cancer model with inducible global loss of *Ghr* function; inducible prostate-specific loss of *Ghr* function; or expression of a GH antagonist.

Overall, all three models of disruption displayed decreased GH–IGF1 axis activity. At 6 months, histopathological assessment showed that PIN lesions had developed less extensively in these mice than previously recorded in C3(1)/TAG mice. Additionally, prostate epithelial cell stratification and epithelial proliferation were reduced in all three models.

Subsequently, the authors analysed data on GHR expression from The Cancer Genome Atlas using UALCAN; GHR was overexpressed in prostate

cancers with ERG-fusion genes or ETV1-fusion genes (~50% of prostate cancer cases) compared with normal prostate. Furthermore, GHR and ERG expression were positively correlated in prostate cancer.

To replicate this overexpression the authors then created PTEN-P2 and TRAMP-C2 mouse prostate cancer cells that expressed *Ghr* 2.9-fold and 2.5-fold more than control cell lines, respectively. These overexpressing cell lines grew at increased rates and demonstrated higher proliferation rates in vivo compared with the controls.

The results from this study illustrate a link between GHR activity and proliferation in prostate cancer cells and raise the possibility of GH signalling disruption as a treatment for prostate cancer.

**Tim Thomas**

**Original article:** Unterberger, C. J. et al. Conditional gene regulation models demonstrate a pro-proliferative role for growth hormone receptor in prostate cancer. *Prostate* <https://doi.org/10.1002/pros.24474> (2022)

## In brief

### Testicular cancer

#### Semen parameters across testicular cancer stages

Testicular cancer stage does not affect semen parameters, according to data from a retrospective study of 38 patients with testicular cancer. Semen parameters, cancer stage and tumour histology were collected from patients, who also underwent cryopreservation before orchiectomy. Abnormal semen parameters recorded in patients included azoospermia (11%), abnormally low semen volume (18%), abnormal total sperm count (47%) and abnormal motility percentage (24%). Semen parameters did not vary significantly between patients with stage I cancer and patients with stage II/III cancer, or between patients with seminoma and patients with non-seminomatous germ cell tumours. Additionally, no significant association was found between abnormal semen parameters and tumour histology or cancer stage.

**Original article:** Badia, R. R. et al. Impact of testicular cancer stage on semen parameters in patients before orchiectomy. *Urol. Oncol.* <https://doi.org/10.1016/j.urolonc.2022.11.004> (2023)

### Infection

#### Semen quality recovery following COVID-19

Semen quality in patients with COVID-19 improves between the infection and recovery stages of the disease, according to data published in *Basic and Clinical Andrology*. Mohammed et al. collected and analysed semen samples from 100 patients with confirmed mild or moderate COVID-19 (defined by symptom severity and chest CT). Two samples were taken from each patient, timed to represent the infection and recovery stages of disease. Abnormal semen quality (defined as at least one abnormal semen parameter) was present in 33% of patients during the infection stage versus 11% of patients in the recovery stage ( $P < 0.001$ ). Additionally, sperm progressive motility ( $P = 0.043$ ) and normal morphology ( $P < 0.001$ ) significantly increased between infection and recovery samples.

**Original article:** Mohammed, N. et al. Semen quality changes during infection and recovery phases of mild-to-moderate COVID-19 in reproductive-aged patients: a prospective case series. *Basic Clin. Androl.* **33**, 2 (2023)

### Kidney cancer

#### Pembrolizumab + axitinib beyond first-line therapy for mRCC

Pembrolizumab and axitinib combination therapy is a potential treatment for patients with metastatic renal cell carcinoma (mRCC) who have received previous lines of therapy, according to new data. In a cohort of 38 patients, pembrolizumab + axitinib was administered as a second-line therapy (in 55.5% of patients), third-line therapy (13.2%) or beyond third-line therapy (30.2%). Median progression-free survival was 9.7 months (95% CI 4.1–15.3) at a median follow-up of 17.1 months. Overall response rate was 25% and disease control rate was 66.6% in the 36 response-evaluable patients. Grade 3 (in 18.4% of patients) and grade 4 (6.4%) adverse events attributable to pembrolizumab and axitinib were observed, and 86.8% of patients overall experienced adverse events.

**Original article:** Dizman, N. et al. Outcomes with combination pembrolizumab and axitinib in second and further line treatment of metastatic renal cell carcinoma. *Clin. Genitourin. Cancer* <https://doi.org/10.1016/j.clgc.2023.01.002> (2023)