Exploring the activity of deiodinase 2 in the human prostate stem cell niche & the implications for prostate carcinogenesis

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Aims

- To optimise primary antibodies to stain different markers in human prostate & ureter tissue using immunohistochemistry (IHC) techniques
- To stain deiodinase 2 (DIO2) in the human prostate stem cell niche to assess its distribution using the Opal Immunofluorescence Kit
- To use the staining data to form a hypothesis about how DIO2 may be affecting prostate carcinogenesis

Background

- Prostate cancer is the most common cancer among men and is often not detected until late stages
- The prostate stem cell niche is located in the junction between the ureter and the prostate and is partly responsible for the development of prostate cancer
- DIO2 catalyses the production of triiodothyronine (T3), a thyroid hormone (1)
- T3 has been linked with cancer cell proliferation in human prostate tissue (2)
- Increased DIO2 levels in colo-rectal tissue have been shown to contribute to stem cell differentiation (3)
- Increased DIO2 levels are also correlated with increased PSA, a protein associated with prostate carcinogenesis at high levels (4)

Methods

- *Immunohistochemistry*
- In this method a cell marker chosen to signify a structural area or process is stained through antibodies binding to antigens in the tissue
- Optimisation involves changing the concentration of the antibody solution to attain the best stained image of the cell marker
- *Opal Immunofluorescence*
- This method is similar but allows for multiple markers to be stained & viewed in different colours with an immunofluorescence microscope

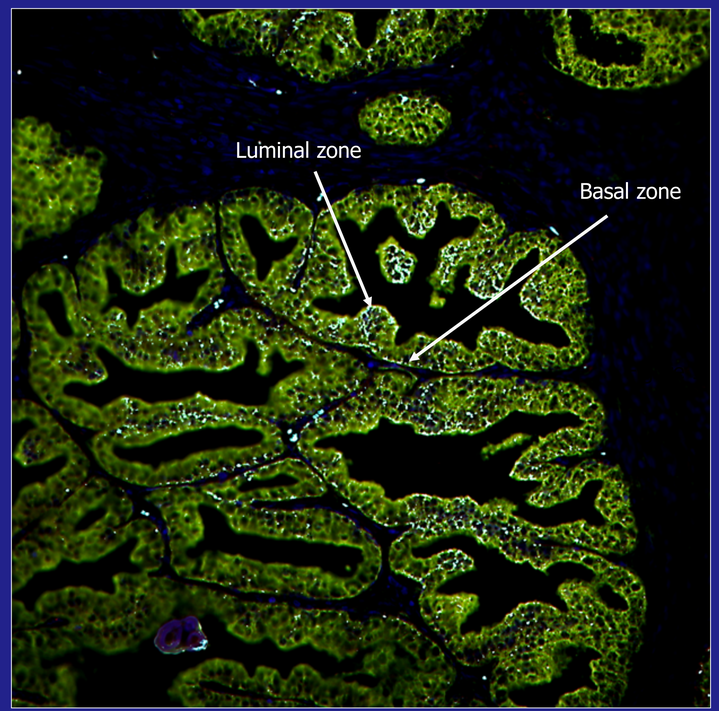

Figure 1

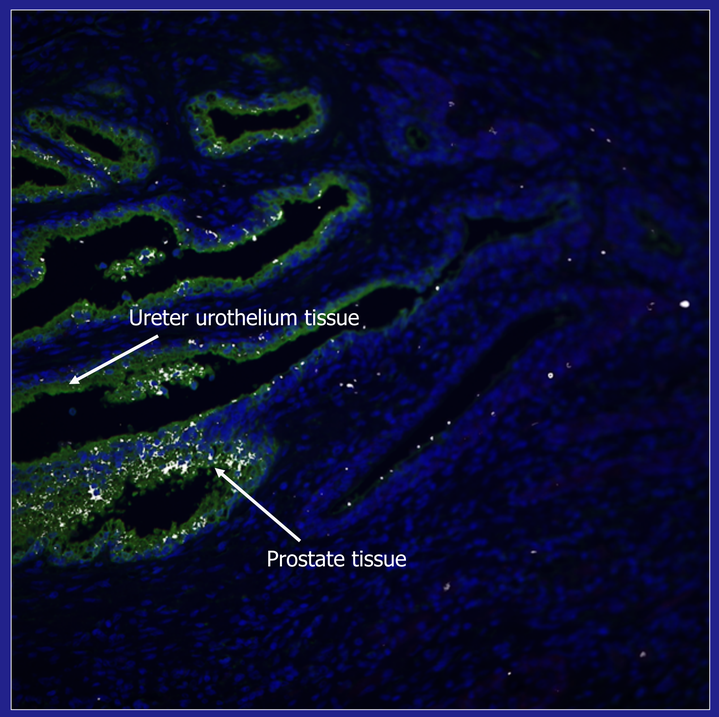

Figure 2

Results

- **Figures 1 & 2** were attained using the Opal Immunofluorescence technique
- **Figure 1** displays human prostate tissue glands in light green, with marked luminal & basal zones The DIO2 is marked in white & appears to mainly have a basal distribution with some areas of increased luminal presence
- **Figure 2** displays human prostate tissue in light green & urothelial tissue in thin bands of dark green
- The urothelium doesn't contain any white DIO2 whilst the prostate tissue near the stem cell niche contains areas of luminal DIO2
- Therefore, in areas of metastatic potential, such as the prostatic stem cell niche, DIO2 tends to be present in luminal zones
- In quiescent areas, such as the normal prostate tissue seen in **Figure 1**, DIO2 tends to be present in more basal areas

Conclusions

- A series of antibodies were optimised successfully to mark different areas of prostate & ureter tissue
- The presence of DIO2 in more luminal zones in the human prostate stem cell niche may suggest a luminal shift for differentiation in areas of metastatic potential
- These results suggest that the targeting of DIO2 may present a new approach to overcoming castration-resistant disease & may provide a foundation for the use of antithyroid drugs in men with prostate cancer

References

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