

Identification and Characterisation of IRX4 Protein Isoforms in Prostate Cancer

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Introduction

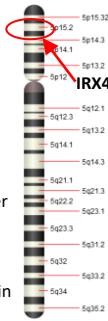
Prostate Cancer (PCa) is the most common cancer in men in Australia¹ and the 3rd most common cause of cancer related deaths in Australia².

IRX4

- A potential candidate gene in PCa³
- Tumour suppressor in PCa³
- Expression associates with PCa risk SNP rs1265394643

IRX4 Isoforms

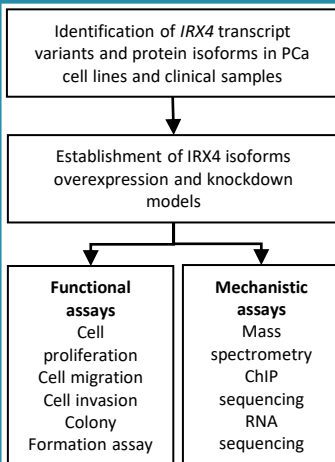
- We found tumour promoter function of IRX4 (Opposite from literature)
- May be due to presence of transcript variants and protein isoforms



Research Objectives

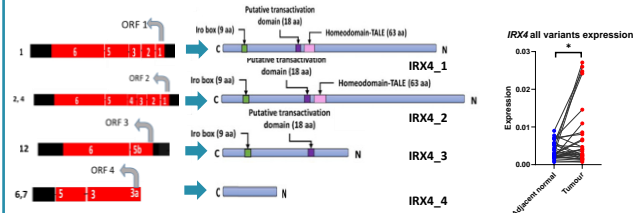
1. To determine the expression of *IRX4* transcript variants and protein isoforms in PCa cell lines
2. To determine the functional role of *IRX4* isoforms in PCa *in vitro*
3. To determine the mechanism of action of *IRX4* isoforms in PCa
4. To validate the diagnostic and prognostic potential of *IRX4* isoforms in PCa patient management

Methods

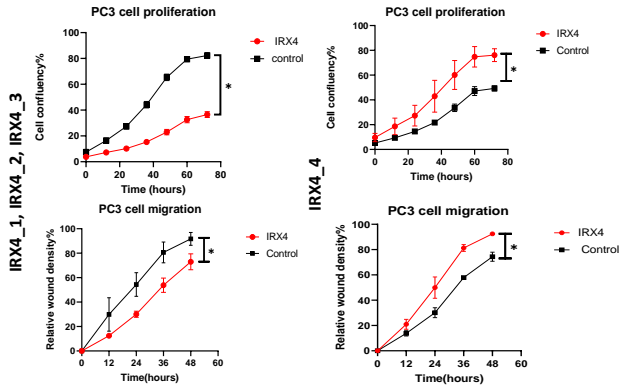


Results

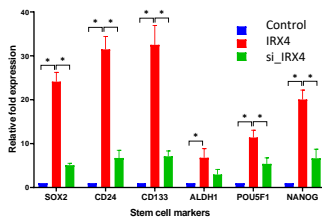
1. *IRX4* gene produces 12 transcript variants and encode 4 protein isoforms in PCa⁴ and are overexpressed in PCa samples compared to their adjacent normal samples.



2. Protein isoforms *IRX4_1*, *IRX4_2*, *IRX4_3*, shows tumour suppressor functions and *IRX4_4* shows tumor promoter functions in PCa.



3. *IRX4* isoforms upregulate prominent PCa stem cell markers *SOX2*, *CD24*, *CD133*, *ALDH1*, *POU5F1*, *NANOG* in PCa.



Discussion

- *IRX4* isoforms 1, 2 and 3 have tumour suppressive properties while isoform 4 has tumour promoting properties in PCa.
- *IRX4* isoforms have a role in stemness regulation in PCa.

Conclusion

The study findings indicate the differential roles of *IRX4* isoforms in PCa, thus provide insights to therapeutically target *IRX4* isoforms individually and their downstream signalling pathways for effective PCa management.

References

1. Australian cancer research foundation
2. Cancer council Australia
3. Ha Nguyen *et al.*, 2012, *IRX4* at 5p15 suppresses prostate cancer growth through the interaction with vitamin D receptor.
4. Fernando *et al.*, 2021. Identification and Characterization of Alternatively Spliced Transcript Isoforms of *IRX4* in PCa.