Analysis of the role of ERF in prostate cancer: a histological approach

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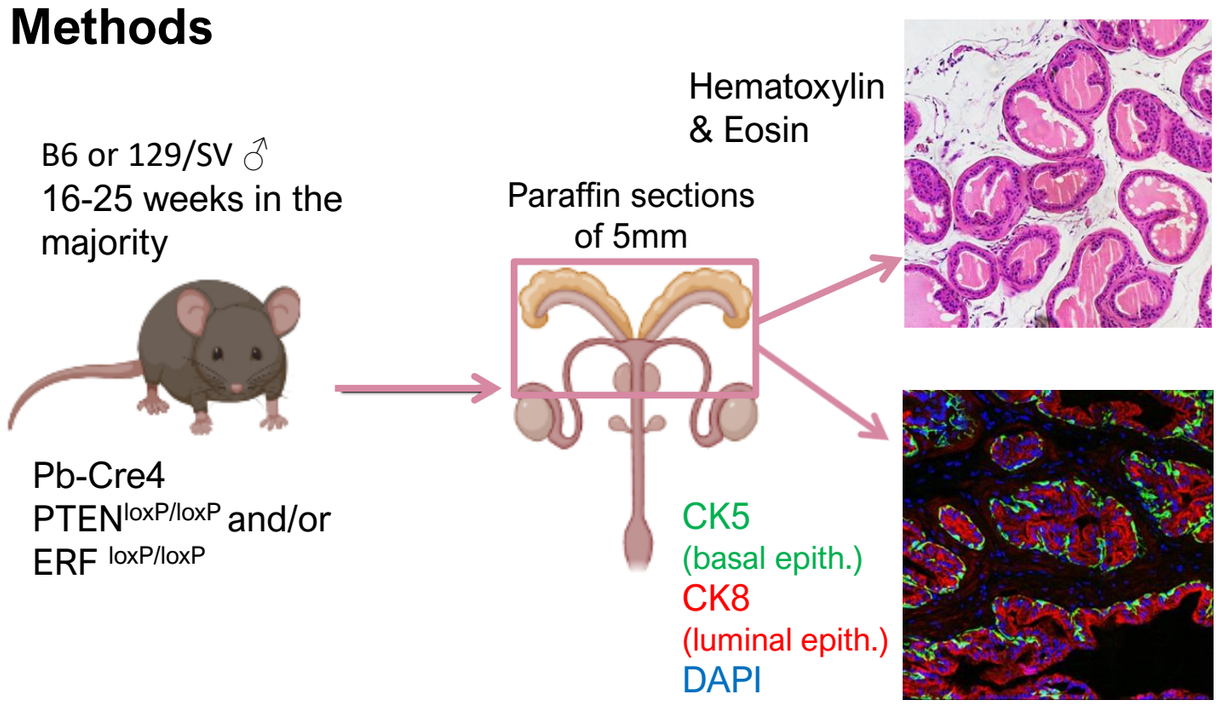
Introduction

Prostate cancer is the second most frequently diagnosed and lethal cancer among men. However, it presents a broad range of heterogeneity among the cases. One consistently affected family of genes is the ETS transcription factors, as for example, the *TMPRSS2:ERG* fusion is considered the most recurrent genetic anomaly of the disease. ERG is a transcriptional activator that antagonizes the repressor ERF, another member of the ETS family. Recent studies observed that ERF is deleted in 1-3% of the prostate cancer cases. In addition, it was highlighted that that *TMPRSS2:ERG* leads to androgen-driven activation of ERG with similar results to ERF deletion. Finally, animal models for the prostate cancer have yet to succeed in representing a realistic progression of the pathology, as there isn't a transgenic mouse model that carries the characteristic metastatic sites, mainly in bones.

In this Bachelor's thesis project, we studied ERF's impact on the initiation and progression of cancer in the murine prostate epithelium through histological observations in combination with the deletion of other commonly affected genes.

Methods



* Control prostates of WT animals

Prostate Samples

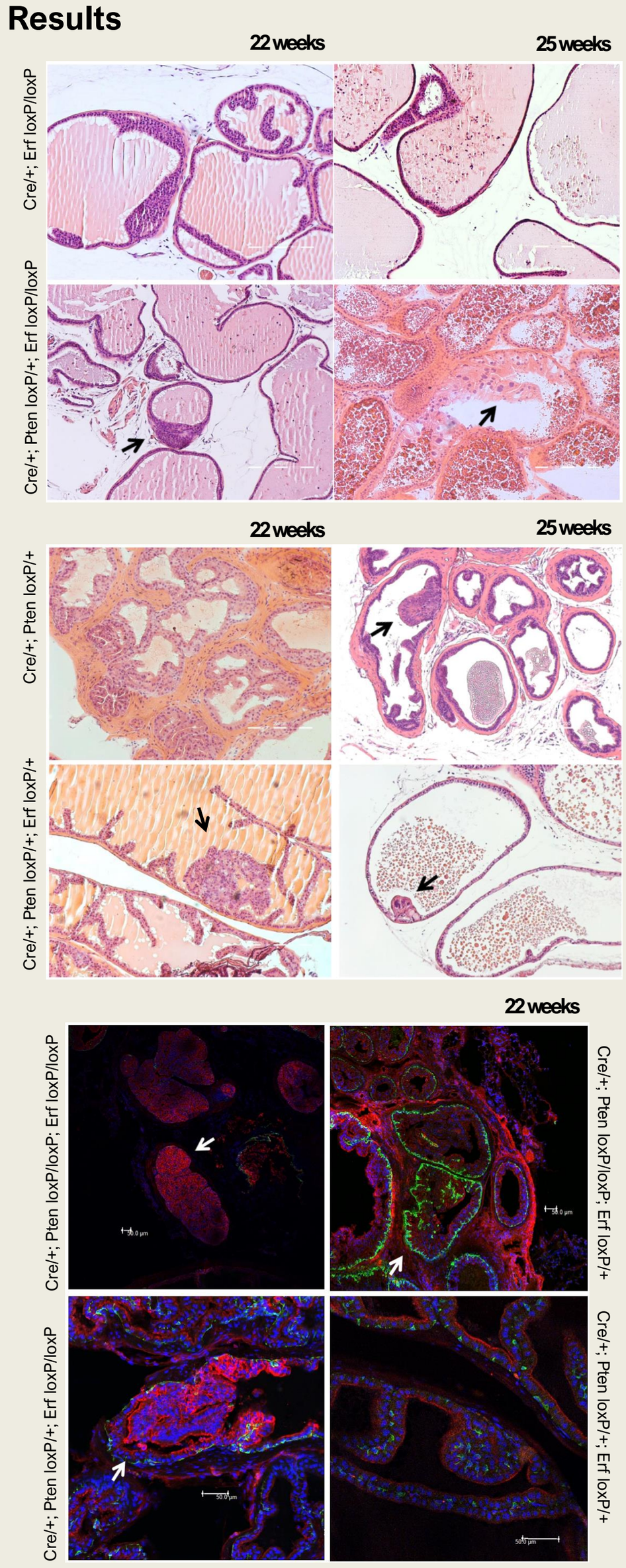
Genotype	13 weeks	16 weeks	19 weeks	22 weeks	25 weeks
Cre/+; Pten loxP/+		H 1/1	H 1/1	H 2/2	PIN 1/2
Cre/+; Erf loxP/loxP		H 2/2		H 2/2	H 1/1
Cre/+; Erf loxP/+; Pten loxP/+		PIN 1/2	H 1/1	PIN 1/2	PIN 1/2
Cre/+; Erf loxP/loxP; Pten loxP/+		PIN 1/1	H 1/1	PIN 1/1	PIN 1/2
Cre/+; Erf loxP/+; Pten loxP/loxP		INV. PCa 1/1	INV. PCa 1/1	INV. PCa 1/1	INV. PCa 1/1
Cre/+; Erf loxP/loxP; Pten loxP/loxP	INV. PCa 1/1		INV. PCa 1/1	INV. PCa 1/1	

PIN=Prostate Intraepithelial Neoplasia
PCa= Prostate Cancer

Conclusions & Future Directions

ERF's role in the prostate cancer seems to affect the progression of the tumor, as it gives rise to earlier signs of neoplasia and a stronger luminal phenotype, when combined with PTEN homologous or heterologous deletion. Whereas, the preliminary data supports the hypothesis that it is a driver mutation in prostate cancer, more mouse samples need to be studied in a broader range of ages, so as we can come to statistically safe conclusions. In the next stage, it is also wise to look into the possible landscape of metastasis and the molecular signatures of the genotypes.

Results



Bose, R., et al. (2017). ERF mutations reveal a balance of ETS factors controlling prostate oncogenesis. Nature, 546(7660), 671–675. https://doi.org/10.1038/nature22820
Valkenburg, K. C., & Williams, B. O. (2011). Mouse Models of Prostate Cancer. Prostate Cancer, 2011, 1–22. https://doi.org/10.1155/2011/895238