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Cannabinoid Receptor Profiling Reveals a Low CB1 and High CB2 Signature in Clear Cell Renal Cell Carcinoma

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Background: The endocannabinoid system is a potential regulator of tumour biology; however, the expression and clinical significance of cannabinoid receptors in clear cell RCC (ccRCC) remain poorly understood.

Aim: To characterize **CB1 and CB2 expression** in ccRCC and evaluate their association with clinicopathological features and clinical outcomes.

Study Design

ccRCC patients n=90 → Retrospective cohort n=60, Prospective cohort n=30 → Tumor tissue (n=90) + Adjacent normal tissue (n=13)

Techniques: IHC, qPCR → Western Blotting → Analysis

Key Findings

Distinct cannabinoid receptor signature in ccRCC

CB1 Lower in Tumor ↓

CB2 Higher in Tumor ↑

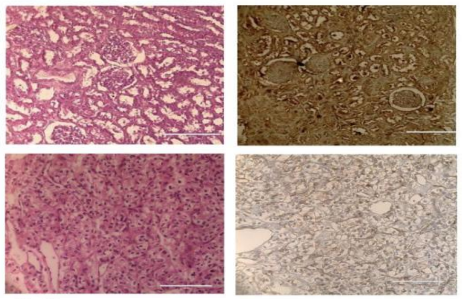
Differential Expression of Cannabinoid receptors in ccRCC

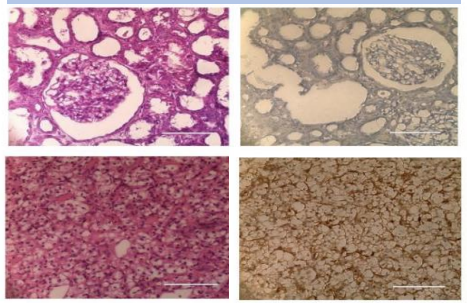
a) CB1 expression

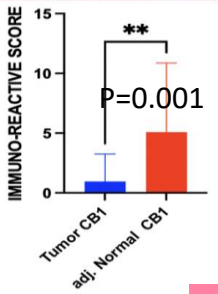
b) CB2 expression

Normal n=13

Tumor n=90

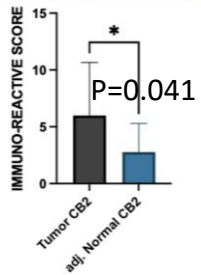






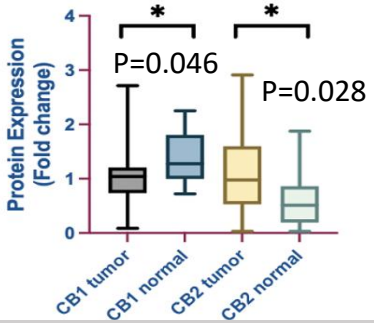
IHC revealed a reciprocal cannabinoid receptor pattern in ccRCC

Reduced CB1 and increased CB2 expression compared with normal kidney.

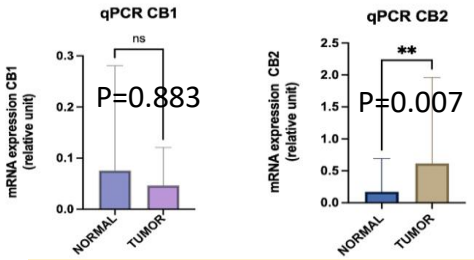


Molecular Validation

Protein level



Transcriptional level



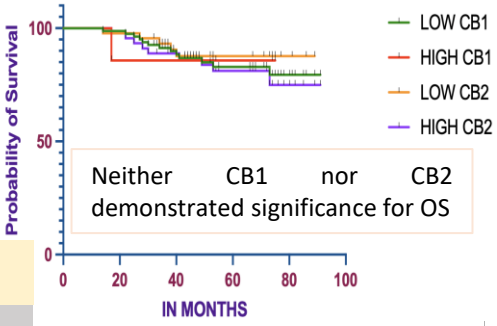
A distinct CB1 regulatory pattern

CB1 Protein	CB1 mRNA
Significant.	Non-significant

Suggesting post-transcriptional regulation of CB1

Overall Survival

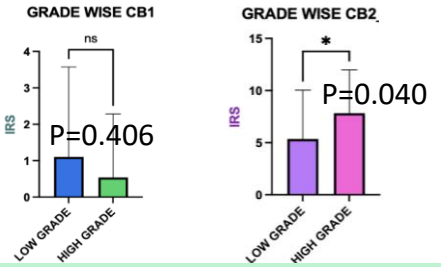
Survival proportions of CB1 and CB2 low vs high expressions



Neither CB1 nor CB2 demonstrated significance for OS

Clinicopathological Association

1. Higher CB2 expression associated with male sex, P=0.010
2. Higher CB2 expression associated with higher tumor grade, P=0.040
3. No significant association was found between CB1 expression and clinicopathological variables



Conclusion

ccRCC exhibits a reproducible low CB1 and high CB2 molecular phenotype

Overexpression of CB2 is associated with higher tumor grade and male sex

CB2 may represent a potential biomarker and candidate therapeutic target in RCC