# Unraveling the Role of *CASZ1* in T-cell Acute Lymphoblastic Leukemia

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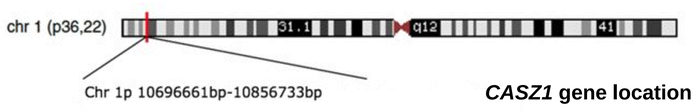
## INTRODUCTION

**T- cell Acute lymphocytic leukaemia (T-ALL)** is a malignant clonal disease that develops when a lymphoid progenitor cell becomes genetically altered through somatic changes and undergoes uncontrolled proliferation (1).

***TAL1*** :

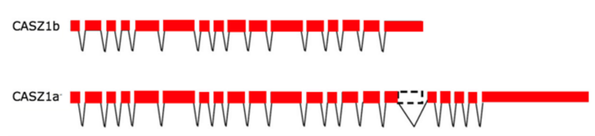
- *Major T-ALL oncogene (2)*
- *Overexpressed in more that 65% of T-ALL patients (2)*
- *Its transcriptional program it is relatively unknown (3)*

***CASZ1*** :

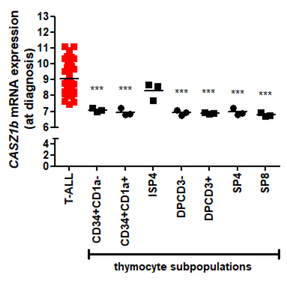


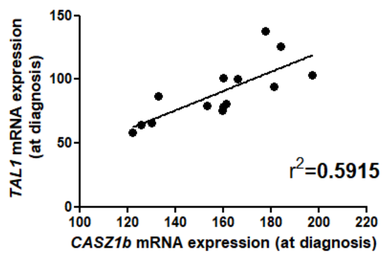

***CASZ1* gene location**

- *Important in Embryonic development (4)*
- *Acts as tumour suppressor or as oncogene depending on the tissue (5-6)*
- *Encodes two different isoforms - CASZ1a and CASZ1b (3)*



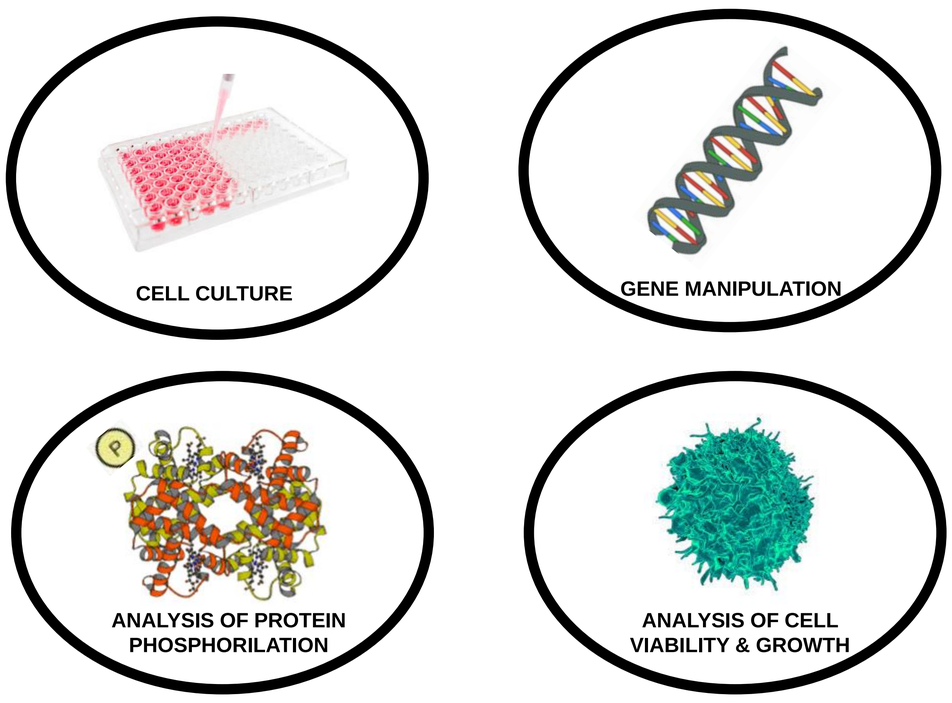

- *The CASZ1b isoform is overexpressed in T-ALL patients with strong association with TAL1 (7)*



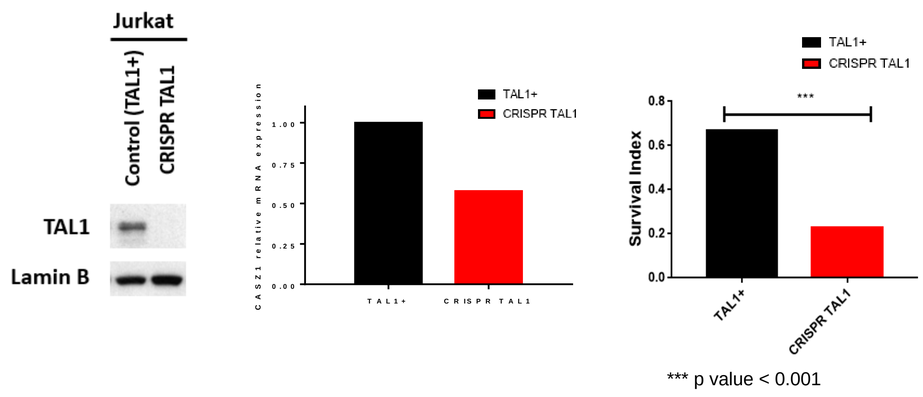

**WHAT IS THE ROLE OF CASZ1 IN T-ALL?**

## MATERIALS & METHODS




## RESULTS & DISCUSSION

### *CASZ1* expression is regulated by *TAL1* in T-ALL cells

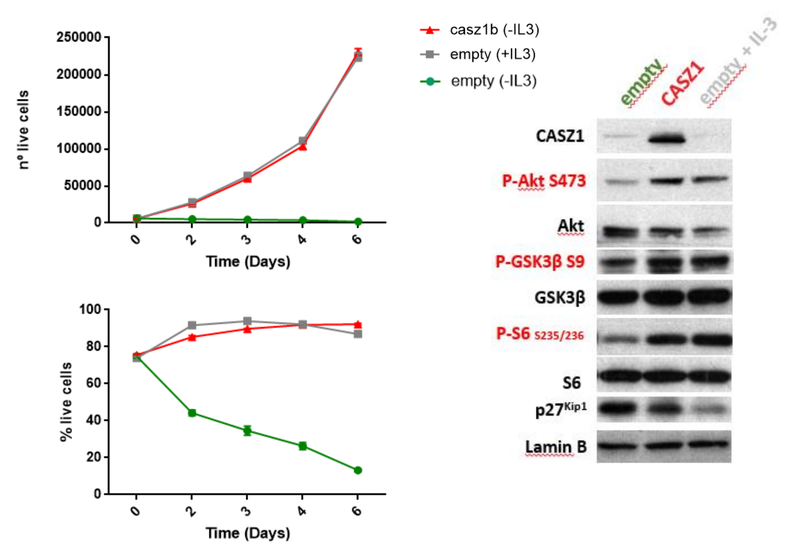



*** p value < 0.001

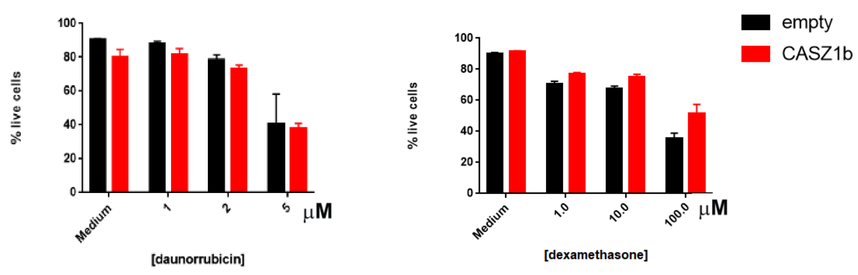
## RESULTS & DISCUSSION

### *CASZ1* promotes BaF3 cell transformation

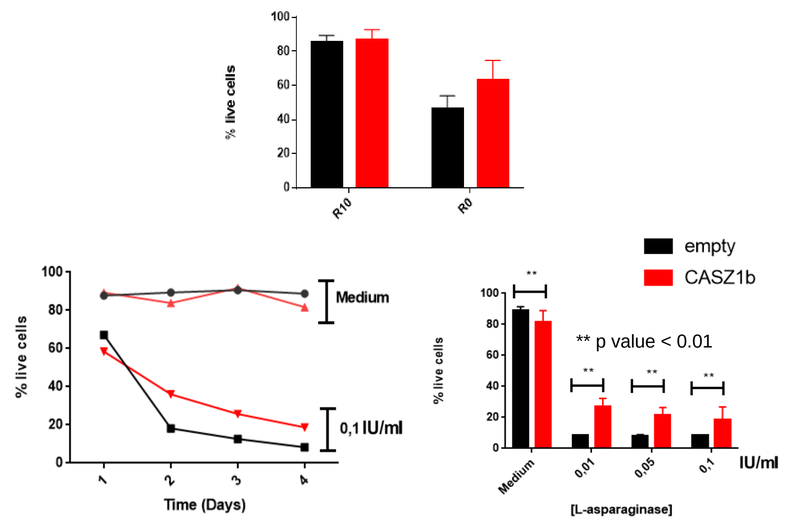
**Increases viability and proliferation upon IL-3 deprivation and activates PI3K-Akt pathway**




### *CASZ1* has no effect against daunorubicin or dexamethasone




### *CASZ1* rescues cell viability under stress conditions (serum starvation and L-asparaginase treatment)




## CONCLUSIONS

- *CASZ1b acts downstream of the TAL1 oncogene*
- *CASZ1b act as an oncogene by activating the PI3K-Akt–mTOR pathway in an IL3-dependent cell line (BaF3 cells).*
- *In the T-ALL context, CASZ1b overexpression is able to rescue viability under stress conditions, such as serum deprivation and Asparaginase treatment.*

Further studies will explore the impact of *CASZ1b* in T-ALL development and response to treatment *in vivo* and assess *CASZ1b* transcriptional program.

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