# KRAS$^{G13D}$-Dependent PI3K/AKT Signaling Regulates Fatty Acid Oxidation in Chronic Lymphocytic Leukemia

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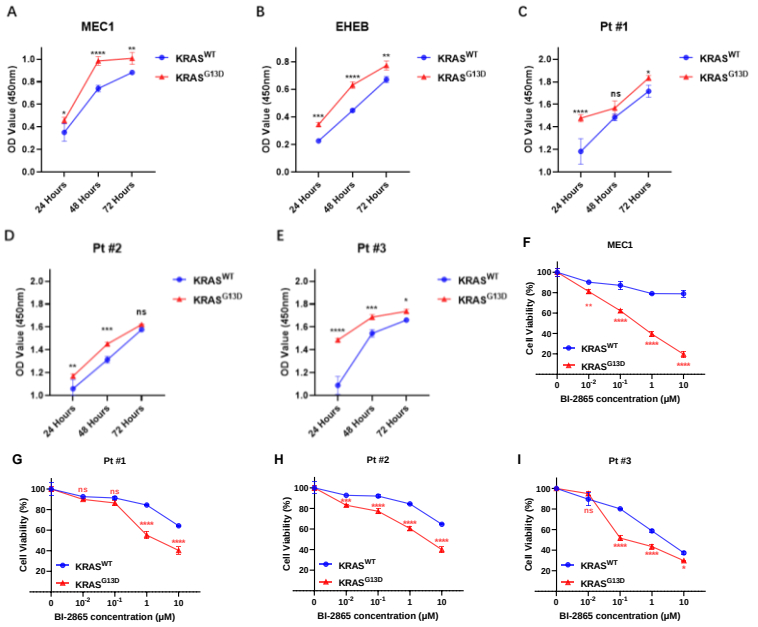
## Background

- Fatty acid metabolism reprogrammed in CLL.
- KRAS mutations indicate adverse prognosis in CLL.
- KRAS mutations regulate tumor metabolic re-programming and activate the PI3K pathway.

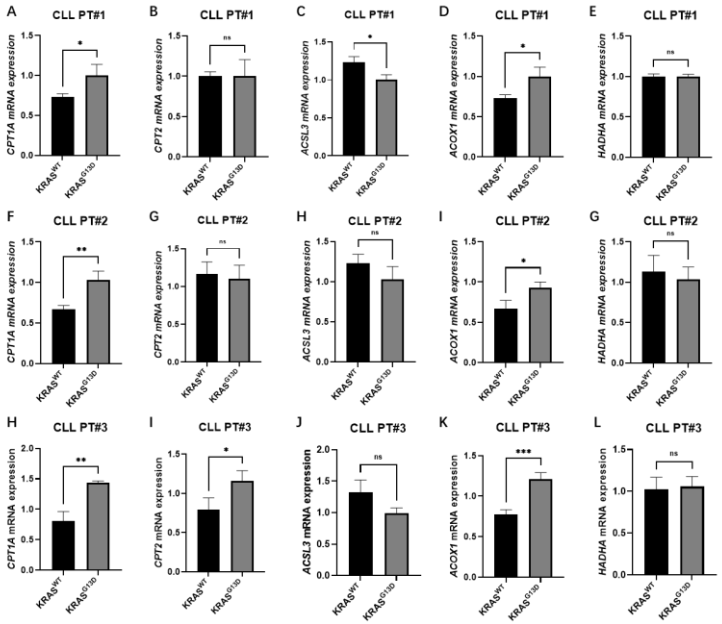
## Results

A total of 8 studies involving 2,440 CLL patients have been included.

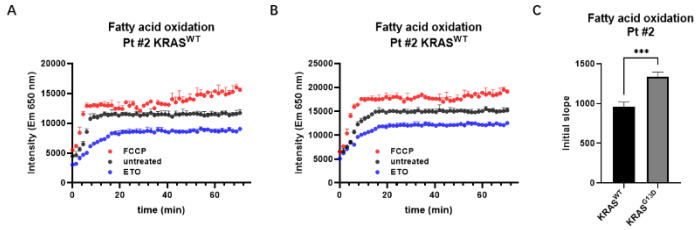
The KRAS mutation frequency was 4.75%, with KRASG13D being the most frequent mutation site (29.84%).

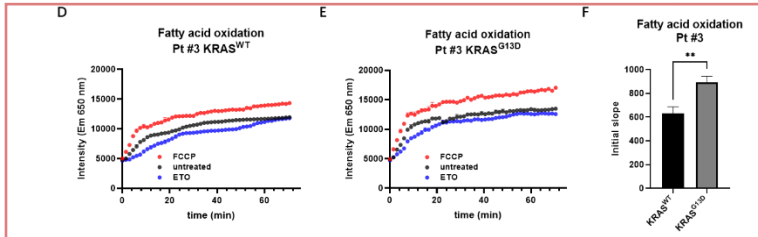



- Compared with KRAS$^{WT}$ CLL cells, KRAS$^{G13D}$ CLL cells exhibited significantly enhanced proliferation activity.

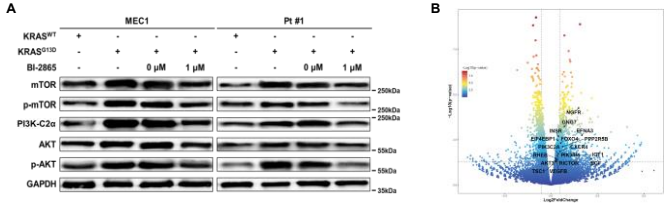



The fatty acid transport and fatty acid β-oxidation were significantly enhanced in KRAS$^{G13D}$ cells compared to KRAS$^{WT}$ cells.

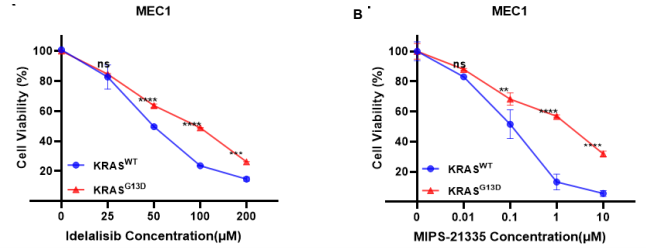



- Genes related to the **PI3K/AKT pathway** were significantly upregulated in KRAS$^{G13D}$ CLL cells.




- KRAS$^{G13D}$-mutated cells reduced sensitivity to MIPS-21335 and idelalisib.




## Conclusion

The KRAS$^{G13D}$ mutation promotes progression via enhanced fatty acid oxidation and activating the PI3K/AKT/mTOR axis.

***All authors declare no relevant conflicts of interest.***