

## NEW STRATEGY TO DISCRIMINATE PRO-TUMORIGENIC PATHWAYS

A research group from CIBER and Institut Hospital del Mar d'Investigacions Mèdiques (IMIM) has patented new I $\kappa$ B $\alpha$  mutants capable to predict the specific pathway altered in I $\kappa$ B $\alpha$ -deficient tumors.

### The Need

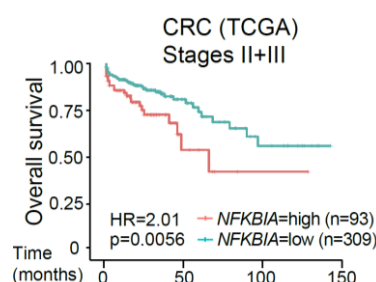
I $\kappa$ B $\alpha$  (nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor A) is a cellular protein which inhibits the NF- $\kappa$ B (nuclear factor-kappa B) transcription factor. Besides, it has been shown that I $\kappa$ B $\alpha$  can exert an alternatively function as a regulator of polycomb repression complex 2 (PRC2) activity. There is an unmet medical need of finding reliable strategies for assessing whether a cancer type characterized by the inactivation of I $\kappa$ B $\alpha$  protein, which is a marker of poor prognosis, has been originated via activation of NF- $\kappa$ B or, alternatively, via PRC2 dysregulation.

### The Solution

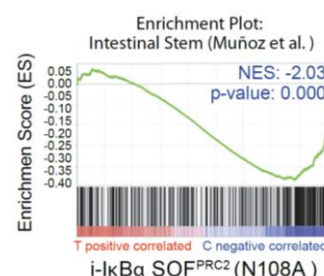
We have generated new separation-of-function I $\kappa$ B $\alpha$  mutants, which represent an innovative and unique tool for assessing whether a cancer type characterized by the inactivation of I $\kappa$ B $\alpha$  protein is originated by and depends on aberrant NF- $\kappa$ B activation or PRC2 miss-regulation. Identification of the driving force in specific I $\kappa$ B $\alpha$ -deficient cancer subtypes or individuals will have a clear impact in patient treatment management and will allow the design of specific inhibitors directed towards NF- $\kappa$ B or PRC2 pathways. Moreover, these mutants will allow setting-up medium or high-throughput platforms for the screen of clinically approved anti-cancer drugs.

### Innovative Aspects

- Separation-of-function mutants has a clear impact in the treatment of patients carrying I $\kappa$ B $\alpha$ -deficient tumors (i.e., Hodgkin's lymphoma, squamous cell carcinoma, liver cancer or glioblastoma).
- They could also be used to better stratify patients either for diagnosis, therapy prescription and as inclusion criteria in clinical trials (A).
- The identification of the specific residues involved in the activation of the NF- $\kappa$ B pathway could be essential to develop specific inhibitors of NF- $\kappa$ B signaling in tumors, since all the existing compounds are very toxic in patients.



**A.** Representation of overall survival over time for CRC patients from the TCGA Portal, with high or low expression of *NFKBIA*.



**B.** GSEA of an intestinal stem cell (ISC) gene set associated to poor prognosis, from genes significantly repressed upon ectopic expression (16 hours) of i-I $\kappa$ B $\alpha$  SOF<sup>PRC2</sup> (unchanged when expressing i-I $\kappa$ B $\alpha$  SOF<sup>NF- $\kappa$ B</sup>).

### Stage of Development:

Validated in "in vitro" experiments on transformed cells derived from colorectal cancer patients and with ongoing experiments in adult and pediatric glioblastoma.

### Intellectual Property:

- Priority European patent application filed (March, 2<sup>nd</sup> 2022) suitable for international extension (PCT application)

### Aims

Looking for a partner interested in a license and/or a collaboration agreement to develop and exploit this asset.

### Contact details

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