NEW STRATEGY TO DISCRIMINATE PRO-TUMORIGENIC PATHWAYS

A research group from CIBER and Institut Hospital del Mar d’Investigacions Mèdiques (IMIM) has patented new IκBα mutants capable to predict the specific pathway altered in IκBα-deficient tumors.

The Need

IκBα (nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor A) is a cellular protein which inhibits the NF-κB (nuclear factor-kappa B) transcription factor. Besides, it has been shown that IκBα 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 IκBα protein, which is a marker of poor prognosis, has been originated via activation of NF-κB or, alternatively, via PRC2 dysregulation.

Innovative Aspects

• Separation-of-function mutants has a clear impact in the treatment of patients carrying IκBα-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-κB pathway could be essential to develop specific inhibitors of NF-κB signaling in tumors, since all the existing compounds are very toxic in patients.

Intellectual Property:

• Priority European patent application filed (March, 2nd 2022) suitable for international extension (PCT application)

The Solution

We have generated new separation-of-function IκBα mutants, which represent an innovative and unique tool for assessing whether a cancer type characterized by the inactivation of IκBα protein is originated by and depends on aberrant NF-κB activation or PRC2 miss-regulation. Identification of the driving force in specific IκBα-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-κB or PRC2 pathways. Moreover, these mutants will allow setting-up medium or high-throughput platforms for the screen of clinically approved anti-cancer drugs.

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.

Aims

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

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