MATWIN
MATURATION & ACCELERATING TRANSLATION **WITH INDUSTRY**

TECHNOLOGY OFFER

SUPPORTING INNOVATION AND TECHNOLOGY TRANSFER IN ONCOLOGY

FASTY

UNIQUE PHOSPHORYLATED FAS (CD95/TNFSFR6) ANTIBODIES: DETECTION OF FAS PHOSPHORYLATION FOR CANCER DIAGNOSIS AND PATENT STRATIFICATION

CONTEXT & BACKGROUND

It is becoming clear that many cancer therapeutics provide only marginal benefits to the majority of the patients to whom they are administered. The inability to identify, among overall patient population, the individuals who will indeed benefit from therapies along with the almost inevitable development of drug resistance are main reasons that current therapies often do not satisfactorily improve overall survival. Patient stratification and using multi-target therapies are strategies to overcome this challenge.
Fas, a well-known transmembrane protein of the tumor necrosis factor receptor (TNFR) superfamily, that can, depending of the cellular context, activate either cell death (apoptosis) or survival pathways, is a potential therapeutic target.The resistance to Fas-mediated apoptosis and the emergence of Fas-mediated proliferation and invasiveness have been demonstrated in oncogenesis and progression of several types of cancers. Current designs of Fas-based therapies are either to exploit apoptotic or inhibit survival function of Fas. However, without means to predict the mode of Fas signaling the risk of failure for such therapies is high.
We have discovered that Fas tyrosine phosphorylation (pY) turns off apoptosis and turn on survival signal. This discovery and the possibility to detect phospho-Fas by antibodies that we created provide us with the first means to predict responses (cell death or proliferation/ invasion) to Fas-related interventions but also to others chemotherapeutics drugs.

INNOVATIVE COMPONENT & TECHNOLOGY

- Differential detection of phospho-Fas is achievable using two new monoclonal antibodies (working at least in immunohistochemistry, ELISA, and immunoblotting) that specifically detect phosphorylation levels of Fas in biological samples of patients (blood samples, biopsies...).
- Phospho Fas biomarkers assays: Sensitive & Specific; Quick & easy to perform; Not invasive

OBJECTIVES

Our main objective is to translate this discovery to clinic by establishing pY-Fas as predictive/ prognostic biomarker in cancers to aid the decision in several chemotherapies (Fas-based therapies but also others chemotherapeutic drugs) in order to increase the chance for therapeutic success. More specifically we wish to:
- Develop phospho-Fas (p-Fas) biomarker assays for clinical settings: robust and reliable enough for biological sample (biopsies) handling.
- POC as a diagnostic and predictive tool: more samples have to be tested for colorectal cancer (CRC) and chronic myeloid leukemia (CML); extend tests for other cancer types (such as brain, breast, and ovarian cancer).
- Identify cancer types that p-Fas can be used as predictive/prognostic marker and to identify patient subgroups who may benefit from the prediction of Fas signalling outcome
- Demonstrate that the predictive value of pY-Fas status can help provide better targeted therapies by guiding the use of anti-cancer agents that target Fas pathway in combination with other current targeted therapies that often fail due to recurrent.

SCOPE

Differential tyrosine phosphorylation of Fas (CD95, APO-1 or TNFRSF6) can be used as a unique biomarker for patient stratification and treatment monitoring, guiding the choice between activation and inhibition of Fas signaling and predicting resistance to currently used drugs, relapse, and therapeutic response.

KEYWORDS

Targeted anti-cancer Therapy, biomarker, tyrosine phosphorylation, antibodies, tumor stratification, apoptosis

DEVELOPMENT & MATURATION STAGE

The application domain of this tool is targeted cancer therapies. We wish to use our method based on the measurement of Fas tyrosine phosphorylation status for more accurate biological characterization of patients in order to achieve maximum benefits of targeted therapies
Our tools can be used as biomarker accompanying Fas-targeted therapies as well as therapies targeting other pathways that cross-talk with Fas signaling which occupy a large percentage of current targeted anti-cancer therapeutics market. Given that this will be the first biomarker that can predict the outcome of Fas signaling, one of the most important cellular life/death regulators, that also influences other major 'cancer-drivers', it is expected that the successful development of the proposed biomarker based on phospho-Fas (p-Fas) will lead to its widespread clinical applications.

INTELLECTUAL PROPERTY & PATIENT CO-OWNER(S)

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Co owners: Hueber, AO; Chakrabandhu, K.

TARGET PROFILE

The products obtained will be the first predictive biomarker assays for Fas signaling outcome (apoptotic/proliferative) in several types of cancer. The prediction of Fas signaling outcome based on Fas tyrosine phosphorylation status will find widespread applications in Fas-targeted therapies as well as in other targeted therapies in which the cross-talk with Fas occurs. This will cover a large percentage of targeted cancer therapies. The targeted patient population includes, but not limited to patients suffering from malignant haematological and solid tumours which often exhibit drug resistance and recurrence.

STRENGHTS & COMPETITIVE ADVANTAGES

Clinical trials are in progress on therapeutic compounds targeting Fas but no biomarkers and companion tests that predict the mode of Fas signaling are available.
No existing tool allows direct and quantitative measure of Fas phosphorylation: These are first antibodies enabling specific detection of Fas tyrosine phosphorylation levels
Direct, quick and reliable methods
Unique predictive marker for :
- patient stratification
- Influence of cancer promoting activities of Fas.
- resistance to some anti-cancer drugs.

INDUSTRIAL APPLICATIONS & OPPORTUNITIES

APPLICATIONS
- Early diagnosis of cancer
- Help stratify patients and adapt the treatments
- Monitoring the efficacy of treatments

CONTACT MATWIN : Lucia Robert: Lucia.Robert@matwin.fr