Becas colaboración curso 2018/2019

Fecha: 28 Junio 2018

Vicerrectorado de Investigación, Innovación y Transferencia

Subcomisión de I+D+i

Propuesta del departamento *BIOTECNOLOGIA*

Núm Proyecto: *2018/02/00016*

Responsable
Jantus Lewintre, Eloisa

E-mail
ejantus@btc.upv.es

Ext.

Responsable
Sirera Pérez, Rafael

E-mail
rsirera@btc.upv.es

Ext
79556

Título proyecto
Análisis de la secuencialidad en terapias dirigidas anti EGFR en CPNM

Valoración proyecto
4

Descripción proyecto
Lung cancer is the most important tumour diseases in terms of its worldwide incidence and mortality. Specifically, lung cancer is the leading cause of cancer-related mortality in men and women worldwide, with more than 1.8 million estimated new cases each year (Jemal et al., 2011). Non-small cell lung cancer (NSCLC) is the most common type of lung cancer representing around 85% of all new diagnosed cases. In 10-15% of samples taken from lung adenocarcinonas (which are around 50% of all NSCLC), the tyrosine kinase activity of the EGFR has been found to be dysregulated by the EGFR gene mutation (Lynch et al., 2004; Paez et al., 2004) and targeted therapies has been developed to treat EGFR-mutant NSCLC. Even though, resistances are developed and clonal heterogeneity and a small population of cancer stem cells (CSC) has been related with them.
CSCs are considered responsible for cancer maintenance, dissemination, drug resistance (as pointed before) and recurrence. Once has been clearly demonstrated that EMT participates in the induction and maintenance of CSCs stemness. In order to produce a model that closely mimic the in vivo tumor microenvironment and simultaneously shown clearly stem-like properties (CSCs) has been development 3-dimensional model (3D), that compared to adherent counterparts (2D), these floating-spheroids cells shown typical EMT phenotype and higher migratory and invasive capacity in vitro, as well as higher tumorigenic and metastatic potential in vivo. This 3D model allows study the complex interactions with extra-cellular matrix and others cell types as well as the hypoxia effect, and permeabilization gradients of soluble factors that have been associated with both drug resistance. This outstanding 3D model will be used in this project due to enormous experimental advantages that represent and due to extensive experience that our group hold in this particular 3D culture model in rutine practice lab-duties and in new generation drug development program. Preliminaries results generated by our group have allow us develop a hightrough put screen platform for various chemist libryries with more than 10.000 compounds.

Therefore, understand the molecular bases of tumour resistance are critical to enhance patient´s benefits. In consequence, in the “sequential treatment” using multiple anti-EGFR drugs still needs to be defined molecular determinants in acquired resistance and tumour evolution terms.
There is still an open question regarding the best sequencing treatment approach of EGFR TKIs to achieve highest patient´s benefit. Thus, in this project we aim to develop a resistance model to evaluate the treatments effects targeted against EGFR, applying an in vitro 3D models, to achieve resistance cell lines (derived from NSCLC patients) in order to explain mechanisms of tumour resistance to first-, second- and third-generation EGFR tyrosine kinase inhibitors, and to develop appropriately customized sequential treatment approaches.

Actividades a realizar por el alumno

1. To develop in vitro models (2D and 3D) of acquired resistance to EGFR TKIs (first, second and third generation).
2. Based on the previously generated models of acquired resistance, it will necessary to analyse exhaustively the phenotypic and genotypic changes associated to acquired resistance
3. To perform a comparative analysis between 2D and 3D cultures after resistance development.

Horario

A convenir entre alumno y responsable