Universidad de Navarra

Máster en Investigación Biomédica
Facultad de Ciencias

Research Project Proposal
Academic year 2016-2017

Project Nº 39

Title: HORIZONTAL GENE TRANSFER (HGT) AND CANCER DEVELOPMENT. EXOGENOUS BRCT FROM PATHOGENS MAY INDUCE HUMAN CELL MALIGNANCY.

Department/ Laboratory: Center for Applied Medical Research (CIMA) and Dpt. of Microbiology and Parasitology, University of Navarra.

Director: Dr. Paul Nguewa
Contact: panguewa@unav.es

Codirector: Dra. Esther Larrea Leoz
Contact: elarrea@unav.es

Summary

Eukaryotic BRCT (BRCA C-Terminal) domains come from prokaryotic BRCT domain through horizontal transfer (1). It contains four beta sheets, surrounded by three alpha helices (2). At least 23 proteins of the human genome have BRCT domain. Most are implicated in DNA Damage Response (DDR) (3). BRCT also plays a role in cell cycle checkpoints. It is thought to be implicated in the transmission of DDR signalling from sensors to cycline-dependent protein-kinases. It is usually a 95-amminoacids sequence, and normally located at the C-terminal end of proteins. The number within the protein can vary from a single copy up to six copies. The distance between repetitions is variable.

BRCT also interacts with other BRCT domains as well other protein domains. It also binds to phosphorylated serines and threonines as well as to DNA and PARP (Poly-ADP-Ribose Polymerase). Somatic mutations in BRCT domain are associated with a higher possibility of developing breast and ovary cancer (3). These data show the role of human BRCT in human cancer development. On the other hand, it has been suggested that horizontal gene transfer (HGT) to humans from pathogens may also play a role in cancer. Therefore, in this project, we will study the implication of exogenous BRCT (from pathogens, not human) in human cell and its possible role in the induction of malignancy.

After cloning an exogenous BRCT (not human) into pCDNA vectors, the novel plasmids will be transfected into human cells to obtain clones with heterologous BRCT

expression. Those clones will be then studied (proliferation, cell cycle, formation of colonies, response to treatment…).

References

(1) Sheng et al., 2011. Functional evolution of BRCT Domains from Binding DNA to protein. Evolutionary Bioinformatics, 7, 87.

(2) Zhang et al., 1998. Structure of an XRCC1 BRCT domain: a new protein–protein interaction module. The EMBO journal, 17(21), 6404-6411.

(3) Gerloff et al., 2012. BRCT domains: A little more than kin, and less than kind. FEBS letters, 586(17), 2711-2716.

POSSIBILITY OF PhD

NO