PROFILE

CTS-963: Advanced Therapies: differentiation, regeneration and cancer" group is focused on the study of the processes of differentiation and the normal and pathological development of the disease, using valid experimental models such as normal and tumour human cell lines, stem cells obtained from patients and experimental models in vivo. In the field of experimental oncology, it has implemented different therapeutic strategies directed against cancer stem cells (CSCs), based on novel natural and synthetic drugs, suicide gene therapy, nanotechnology and combinations of all of them.

SPEAKER

***Houria Boulaid Tassi***, full Professor at University of Granada School of Medicine and member of the Biosanitary Research Institute of Granada (IBS Granada), she is a Corresponding Member of the Royal Academy of Medicine and Surgery of Granada District since 2002. She is author of more than 150 scientific publications and 14 patents. She received 7 research awards, among them the Award of the Social Council of the University of Granada to the "Best Investigating Trajectory of Young Researchers" (2009)

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**PRODUCT**

**HokD and ldrB genes with antitumor activities as novel tool for cancer gene therapy**

**MECHANISM OF ACTION**

Our candidates are *hokD* and *ldrB,* small genes from *Escherichia coli* k12 genome, which encode toxic proteins related with programmed cell death of the prokaryotic cell. When expressed in human tumor eukaryotic cells, under the control of tumor specific promoter our candidates induced a drastic inhibition of proliferation in both *in vitro* and *in vivo* models with a selective manner. Moreover, unlike conventional chemotherapy, *hokD* or *ldrB* genes induced destruction of both cancer differentiated and cancer stem cells (CSCs) *in vivo* without any side effects in our animal models.

The antitumor outcome of *hokD* and *ldrB* is modulated by cell cycle arrest in the G0/G1 phase and different programmed cell death pathways. Scanning electronic microscopy demonstrates that both toxins conserve its pore-forming ability in tumor cells as in E. coli k12.

**TARGET INDICATIONS**

Cancer, mainly solid tumors such as colon, breast and cervical cancers.

**CURRENT STATUS**

The following are last tasks already done and main achieved goals:

- Construction of vectors expressing hokD and ldrB gene under the control of inducible promoter.
- Targeted therapy: Construction of vectors expressing hokD and ldrB genes under the control of tumor specific promoter.

- In vitro study: hokD and ldrB gene expression promotes significant inhibition of proliferation of both cancer differentiated and CSDCs obtained from several tumor cell lines in both 2D

and 3D culture model. Moreover, no expression was detected in normal non-neoplastic cells transfected by genes under the control of tumor specific promoter.

- In vivo study: hokD and ldrB genes under the control of tumor specific promoter induced a severe reduction of tumor growth in vivo without any side effects in our animal models.
- Mechanism of action of hokD and ldrB gene in tumoral cells is known.

## INNOVATIVE ASPECTS

- Reduced size of the hokD and ldrB toxins (51 and 35 amino acids respectively) hence its delivery would be much easier than other toxins that are currently used in clinical trials for different types of cancer such as diphtheria A toxin (535 amino acids) and Botulinum toxin (1249 amino acids).
- Tumor specific promoter that controls its expression increases their tumor targeting and specificity what makes our systems, unlike conventional treatment, more effective with fewer side effects.

## IPR

Constructions expressing hokD and ldrB genes under control inducible promoter are protected by worldwide patent application WO/2020/234498.

A new patent application is being filed to protect constructions expressing hokD and ldrB genes under control of tumor specific promoter.

## PARTNERING OPPORTUNITIES

We are looking for a partner to work in co-development (private-public collaboration) or some company interested in licensing the patent and develop the technology.