EG-VEGF Receptor, the PROKR2, is a target for the treatment of gestational choriocarcinoma: in vitro and in vivo studies

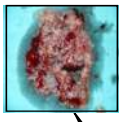
Traboulsi.W, Brouillet. S, Slim. R, Aboussaouira.T, Feige.JJ, Benharouga.M, Alfaidy.N.

INSERM U1036, CEA Grenoble, Université Grenoble Alpes

Paper recently published in
Clin Cancer Res. 2017

Gestational trophoblastic diseases

Partial Hydatidiform Moles (PHM)



Complete Hydatidiform Moles (CHM)

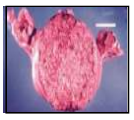
Benign forms

0,5-1% (Noal et al. 2010).

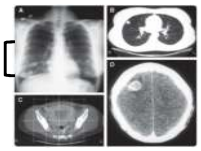
2-6% (Noal et al. 2010).

Choriocarcinoma

(Ozalp & Oge, 2013)



Lungs

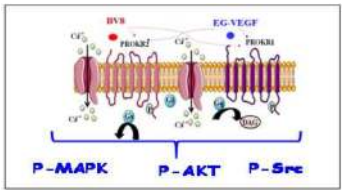


Brain

Neither the mechanism of Choriocarcinoma development, nor the factors that contribute to its rapid progression are known ?

EG-VEGF:
Endocrine Gland -derived Vascular Endothelial Growth Factor

- Expressed in endocrine glands (ovaries, testis, adrenals & placenta)
- Associated to multiple reproductive cancers



EG-VEGF acts via two GPCR receptors: PROKR1 et PROKR2

Clinical Study

INSERM/CNRST
Casablanca hospital and Hospices de Lyon

n=38 Complete hydatiform mole (CHM)

n=9 Choriocarcinoma (CC)

Serum

- Measurement of circulating EG-VEGF

- Comparison of EG-VEGF Expression in placental tissue

Placental tissue

In vitro Study

Characterization of the role of EG-VEGF in choriocarcinoma cell line, JEG3

JEG-3 cells

Using 2D and 3D culture systems

EG-VEGF effect On JEG-3:

- proliferation,
- migration
- invasion
- spreading

In vivo study

Development of a new animal model of choriocarcinoma

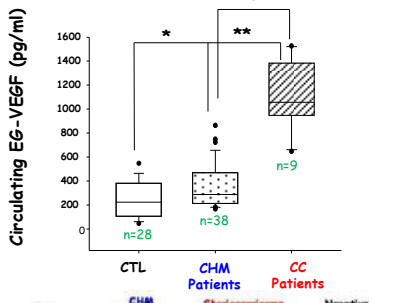
CHO-SCID Mice

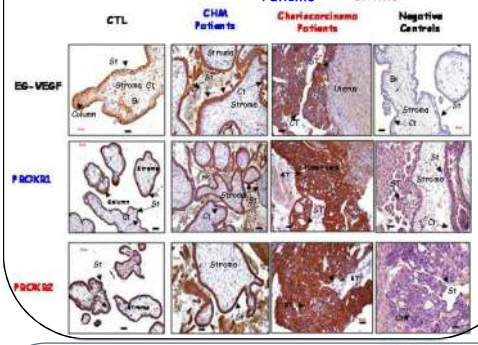
Test of the therapeutical potential of PROKR1 and PROKR2 antagonists

PC - 7

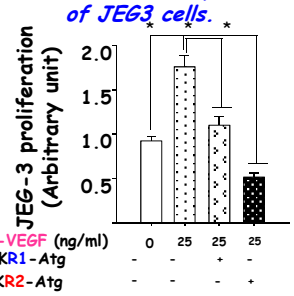
PKRA-505

EG-VEGF levels in CHM and CC

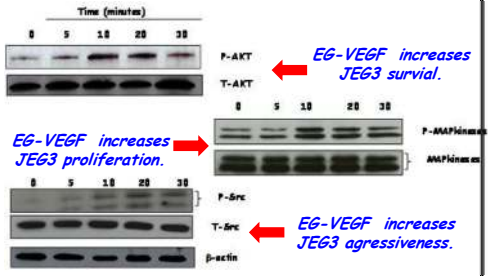


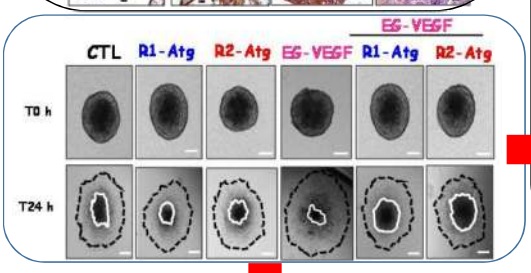


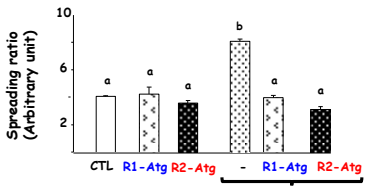
EG-VEGF effect on the proliferation of JEG3 cells.



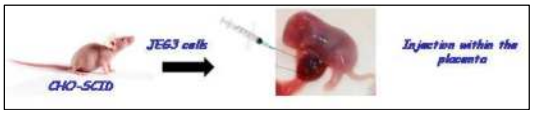
EG-VEGF effect on tumor signaling pathways in JEG3 cells.



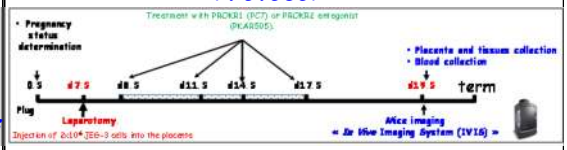


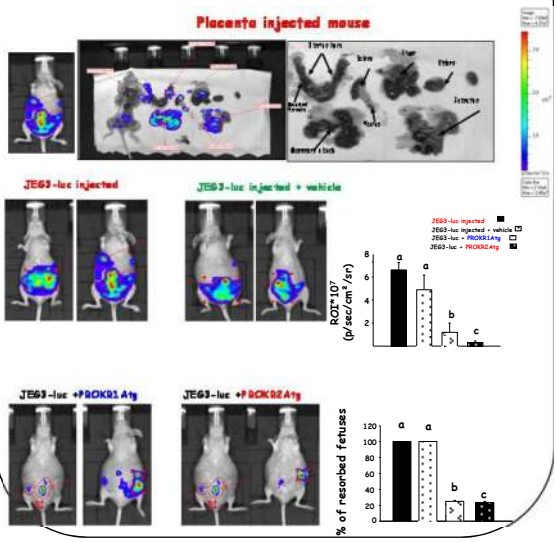


Development of an orthotopic choriocarcinoma model !



Protocol





EG-VEGF:
informative value in the detection and follow up of choriocarcinoma.

EG-VEGF
Involved in the development of choriocarcinoma

New model to study the mechanisms of placental tumor development (Patent 1)

Validation of the therapeutical potential of EG-VEGF receptors antagonists to treat choriocarcinoma PKRA50, PC-7, 5 (Patent 2)

Contact information
nadia.alfaidy-benharouga@cea.fr