SELECTED OPPORTUNITIES IN ONCOLOGY

Method for the treatment of disease associated with angiogenesis (BIO13165)

METHOD FOR THE TREATMENT OF DISEASE ASSOCIATED WITH ANGIOGENESIS (BIO13165)

Product factsheet

- **Target:**
  - N-Methyl-D-aspartate receptor (NMDAR)
- **Product:**
  - NMDAR antagonist
- **Application:**
  - Angiogenic pathologies (tumor angiogenesis or ocular neovascular disease)
- **Technology:**
  - Small molecule, antibody, polypeptide
- **Rational / POC:**
  - NMDAR activation promotes pulmonary arterial remodeling in pulmonary arterial hypertension.
  - Blocking the NMDAR constitutes an alternative therapeutic axis in a disease associated with vascular cell proliferation and misguided and uncontrolled angiogenesis
  - POC in vitro, in vivo POC (cancer models and ocular neovascular disease models) are ongoing
- **Patent and publication:**
  - WO2017093354: Nmdar antagonists for the treatment of diseases associated with angiogenesis

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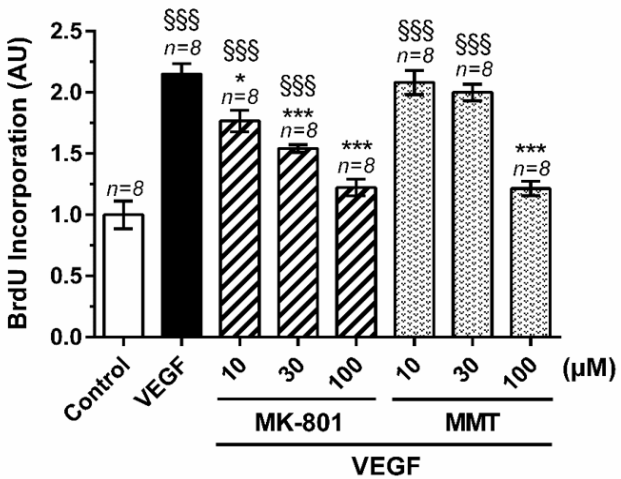
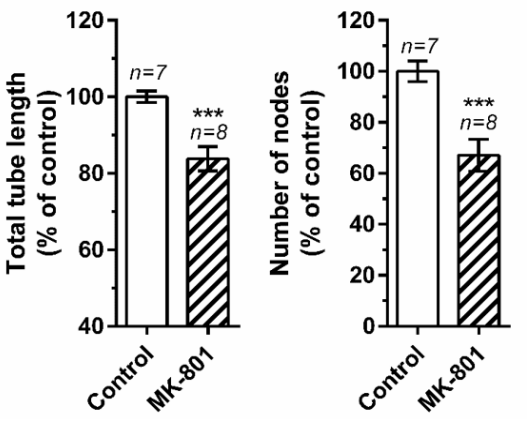
METHOD FOR THE TREATMENT OF DISEASE ASSOCIATED WITH ANGIOGENESIS

Proof of concept

NMDAR antagonists MK-801 and MMT reduces proliferation induced by VEGF or FSB (not shown) and angiogenesis in vitro

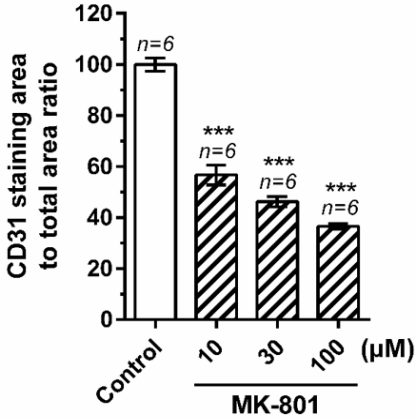


Measurement of control hPMVEC proliferation (BrdU incorporation), after exposure to VEGF-A (10ng.ml-1) in absence or presence of incremental concentrations of NMDAR antagonists MK-801 or memantine (MMT) (both from 10µM to 100µM). Values are normalized to those of non-stimulated cultures.



In vitro angiogenesis experiments using control hPMVEC in the MatrigelTM assay

with or without 100 µM NMDAR antagonist (+)-MK-801 maleate. On the left automatic quantification of total tube length and total number of nodes using the "Angiogenesis analyzer" plugin from ImageJ software on a total of 7-8 images (1 image/replicate, each image covering nearly all the well area). Values are expressed as percent of control.



In vitro angiogenesis experiments in a coculture assay using control hPASMC and hPMVEC. hPMVEC were seeded on the top of the confluent hPASMC layer with or without incremental concentrations of NMDAR antagonist (+)-MK-801 maleate ranging from 10 to 100 µM, in six replicate cultures for each concentration. CD31 labelling was used to visualize the tube network after 15 days of co-culture.

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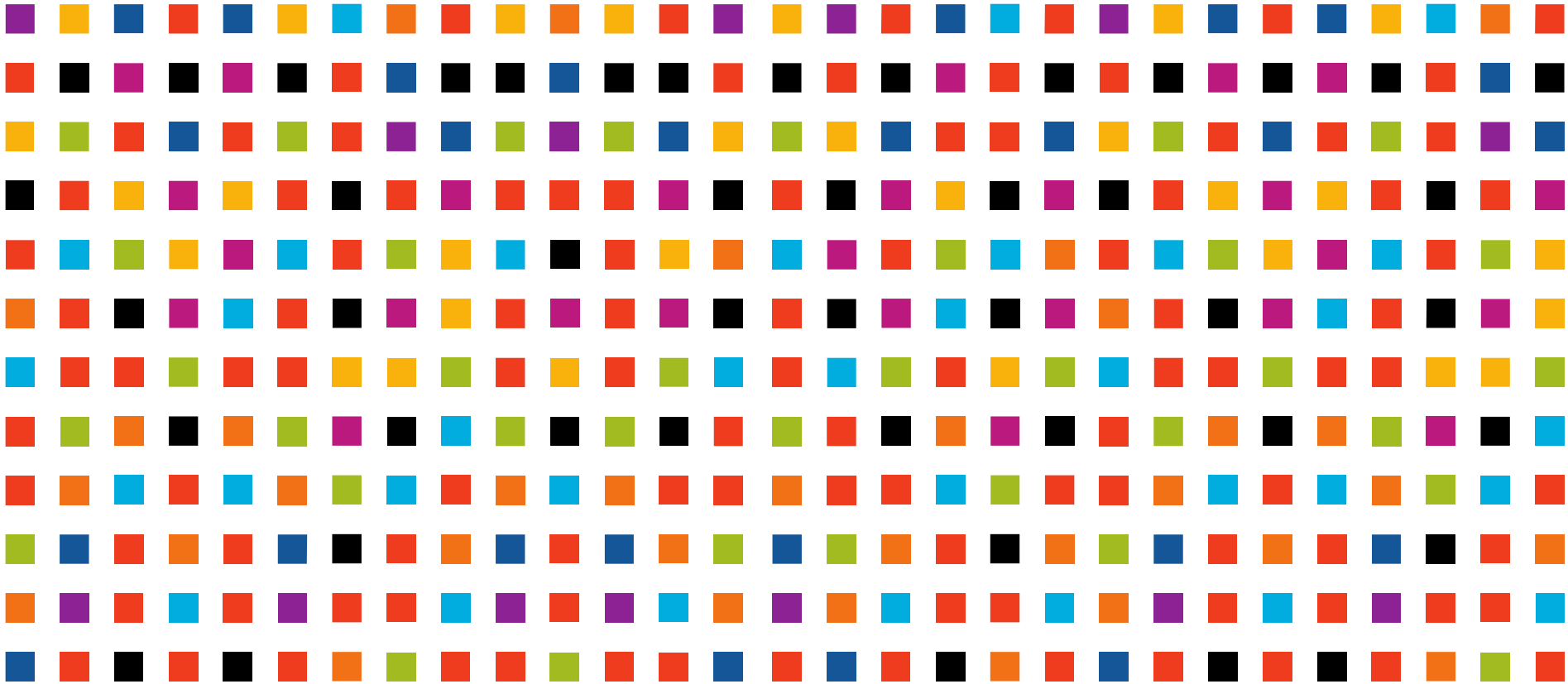

ANNE.COCHI@INSERM-TRANSFERT.FR

Inserm Transfert - Paris Biopark
7 Rue Watt - 75013 Paris
Tel: +33 1 55 03 01 00 / Fax: +33 55 03 01 60
www.inserm-transfert.fr