



Rencontre Scientifique FAVA-MULTI  
Paris, 08 mars 2024

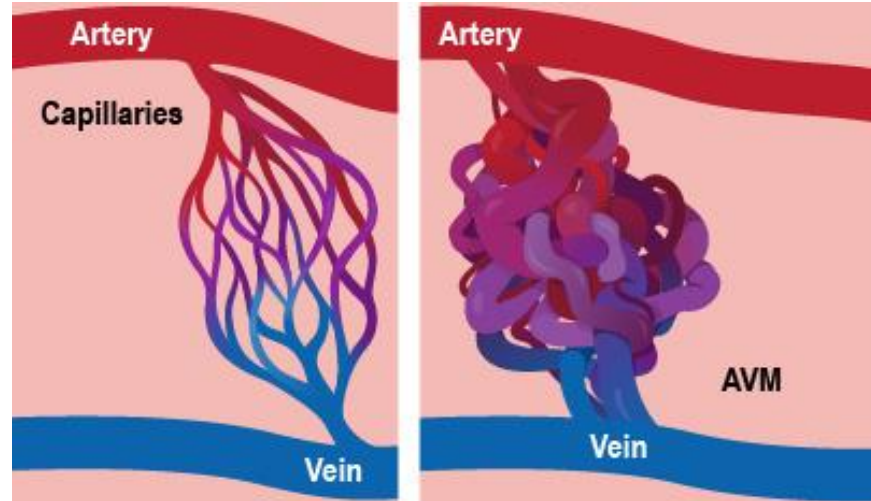
Modèles pré-cliniques de la maladie de Rendu-Osler

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Disclosures:

PM receives financial compensation from Diagonal Therapeutics.  
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# La présentation clinique de la maladie de Rendu-Osler



## Frequency of abnormal HHT vessels :

>95%	Nose ( → nosebleeds)
>90%	Skin (telangiectasia)
50%	Lungs (pulmonary AVMs)
50%	Liver (hepatic AVMs)
20%	Gastrointestinal tract
10%	Brain (cerebral AVMs)
<2%	Spine (spinal AVMs)
	<i>...and other sites</i>

## Compared to general population, more frequent:

- Iron deficiency anemia
- Strokes (ischaemic and haemorrhagic)
- Brain (and other deep-seated) abscesses
- Migraines
- Venous thromboemboli (VTE)
- Pulmonary hypertension
- Maternal death in pregnancy

## but less frequent

- Cancer
- *Myocardial infarction*

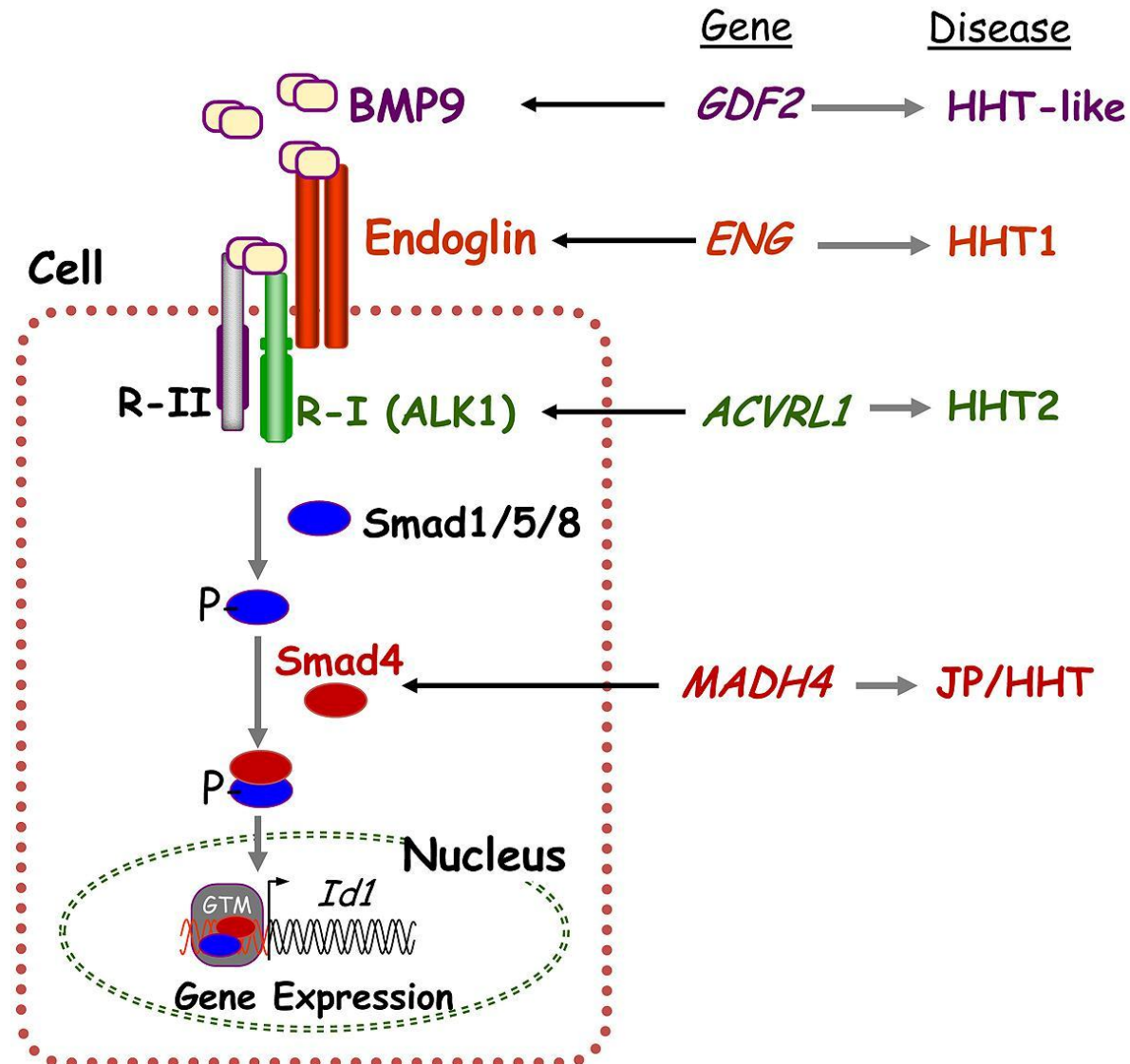


European  
Reference  
Networks

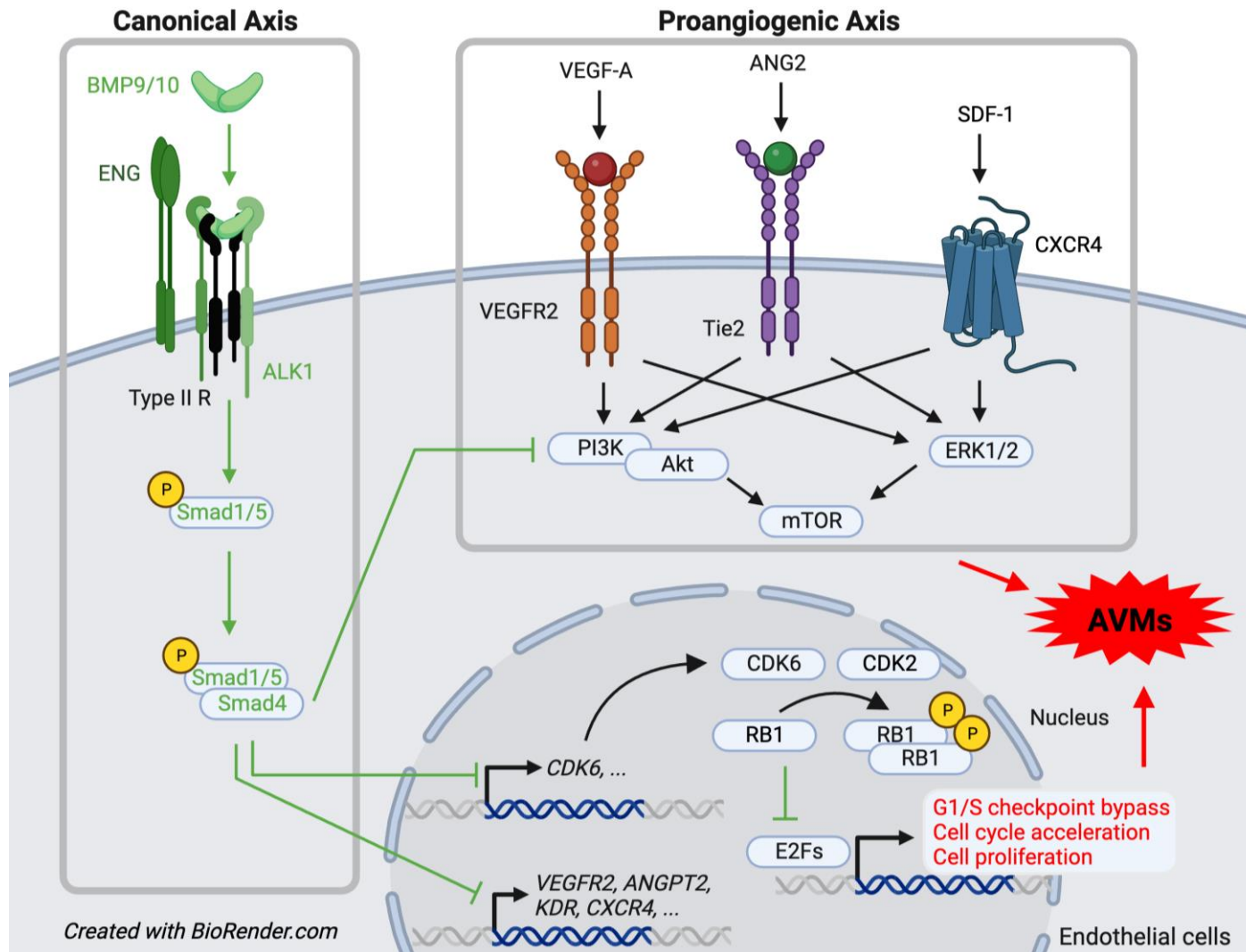
Vascular Diseases  
(VASCERN)



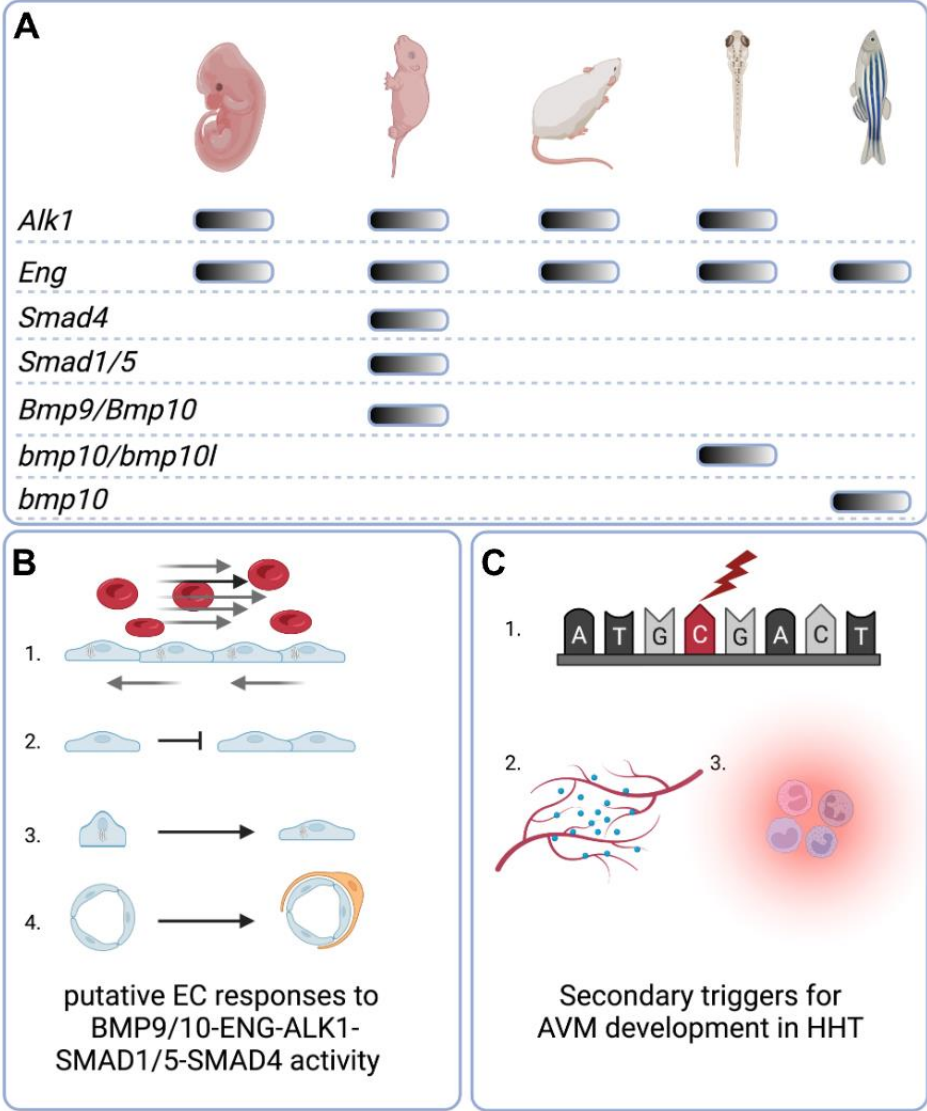
# La génétique de la maladie de Rendu-Osler



# La pathogénèse de la maladie de Rendu-Osler

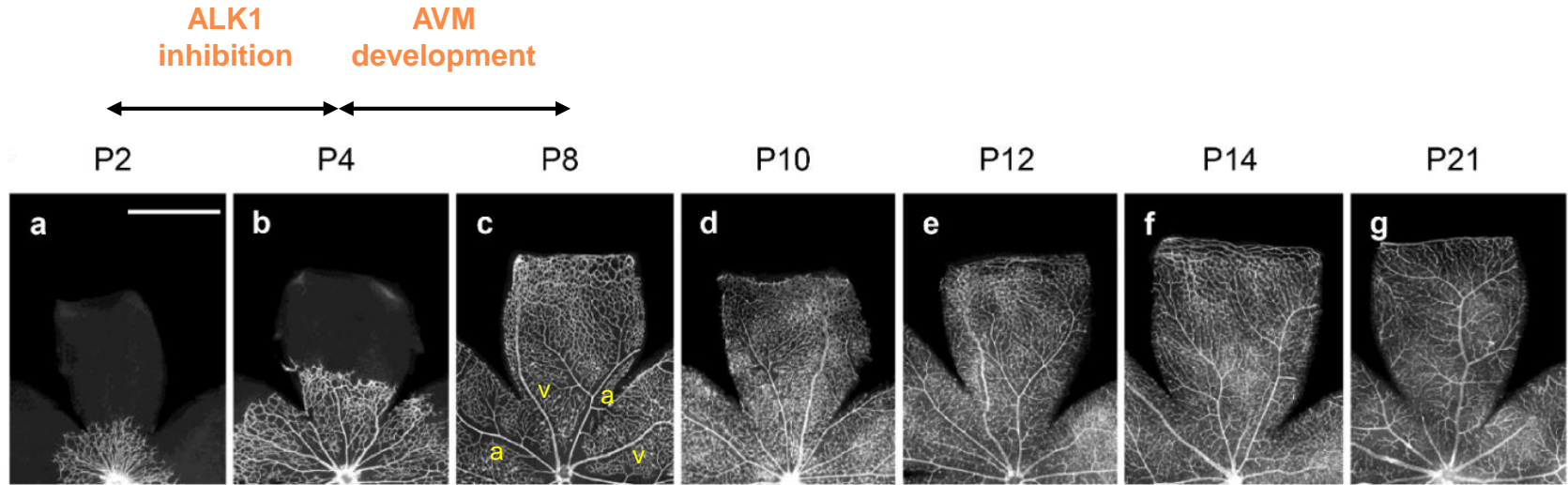


# Les modèles pré-cliniques de la maladie de Rendu-Osler





# La rétine de souris comme modèle d'angiogenèse postnatale

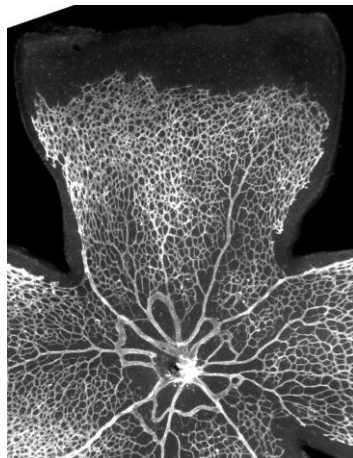


Morita et al., *J Pharmacol Sci* (2018)



P6/7

AVMs

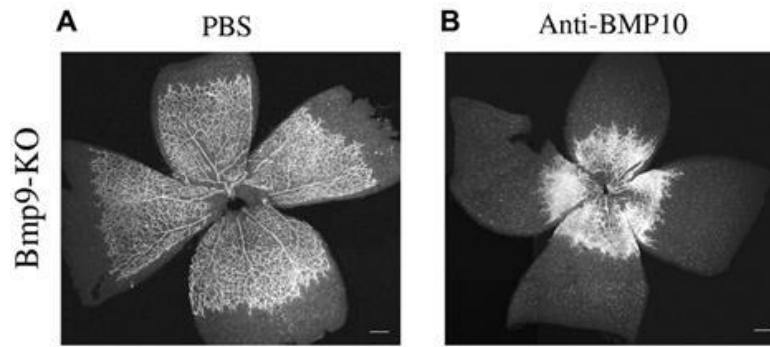


## BMP9 and BMP10 dual neutralization

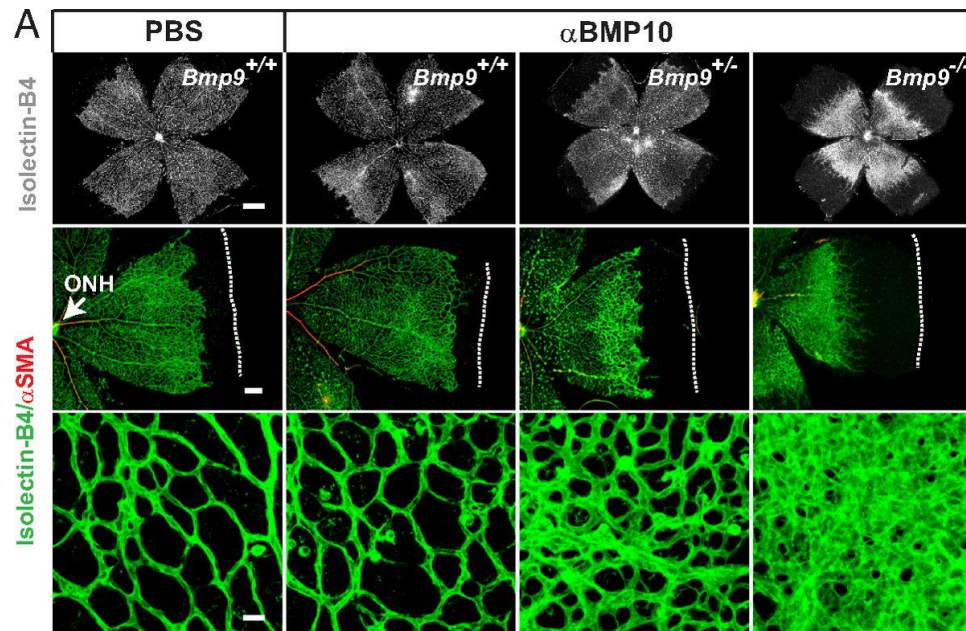
Ruiz et al., *Sci Rep* (2016)



# Modèles de souris déficientes en BMP9 et BMP10

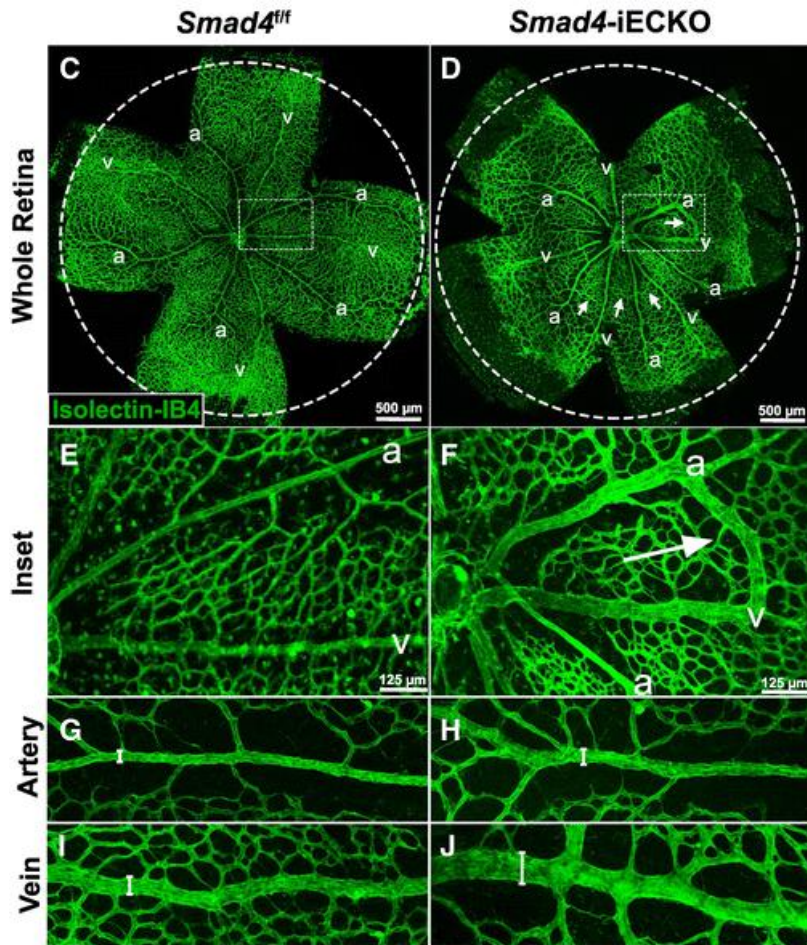


Ricard et al., Blood (2012)



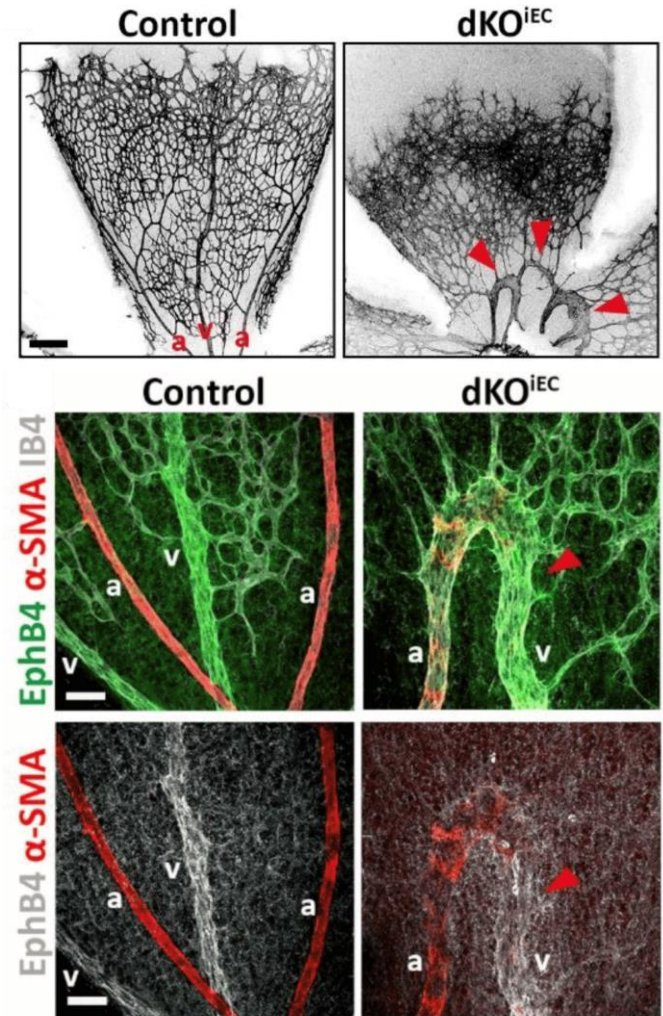
Chen et al., PNAS (2013)

# Smad4 iECKO mice



Crist et al., Angiogenesis (2018)  
 Kim et al., J Am Heart Assoc (2018)  
 Ola et al., Circulation (2018)

# Smad1/5 iECKO mice



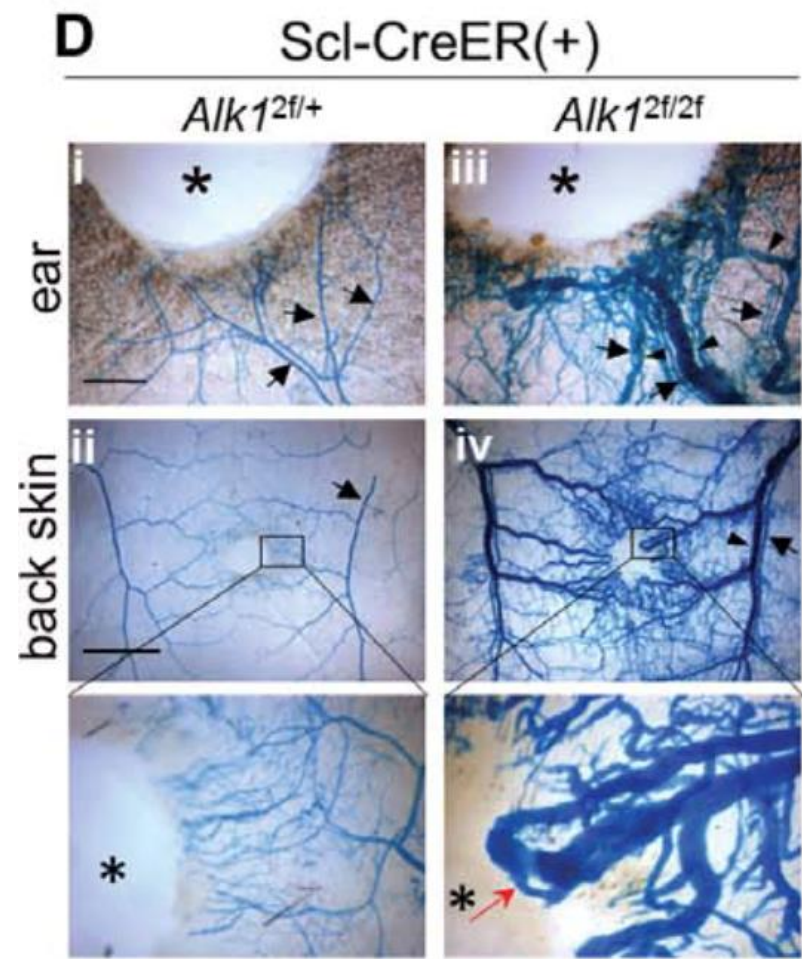
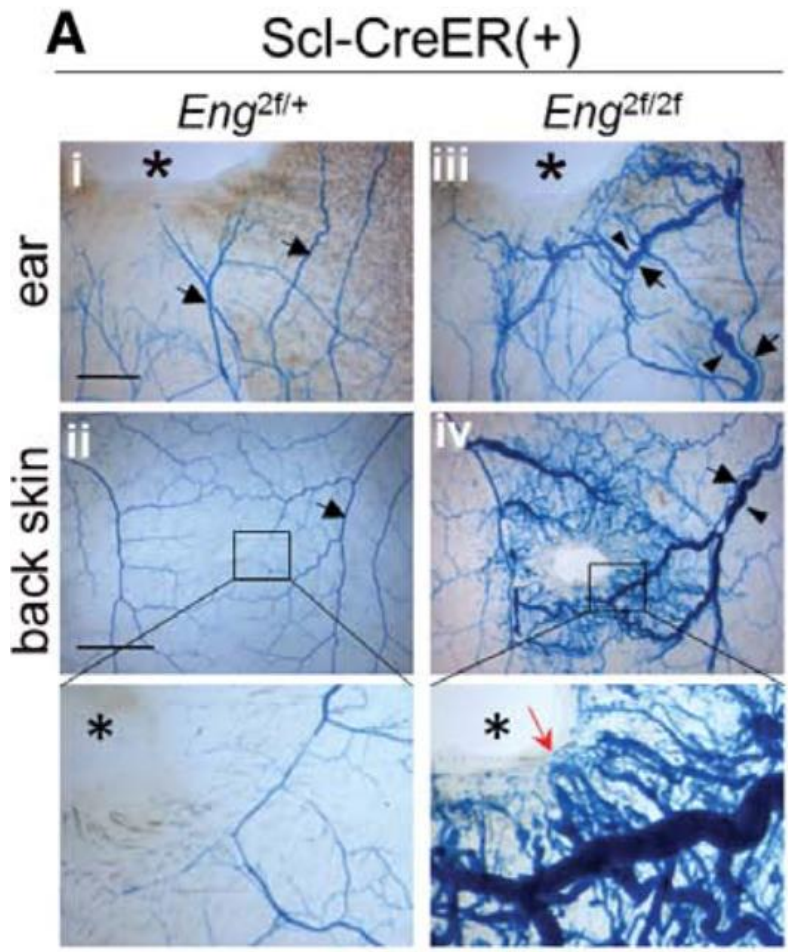
Benn et al., Biomolecules (2020)





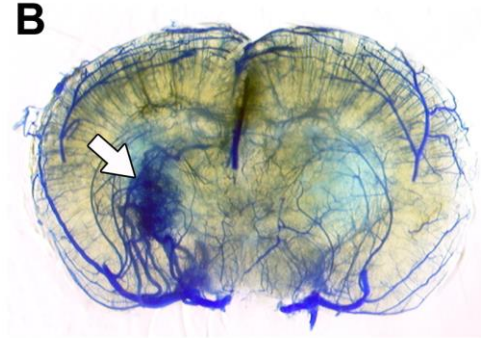
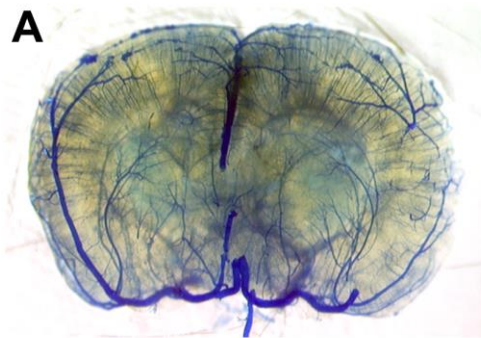
Adult ENG iECKO mice

Adult ALK1 iECKO mice

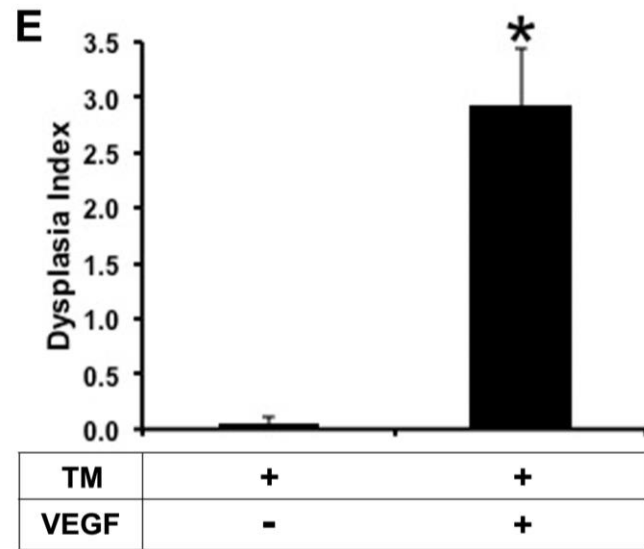
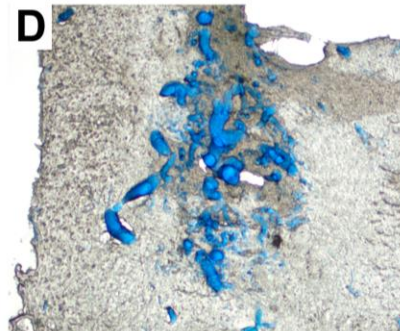
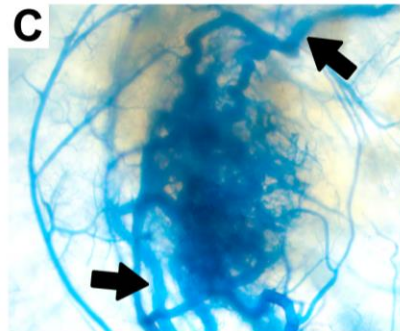




# Adult ENG iECKO mice

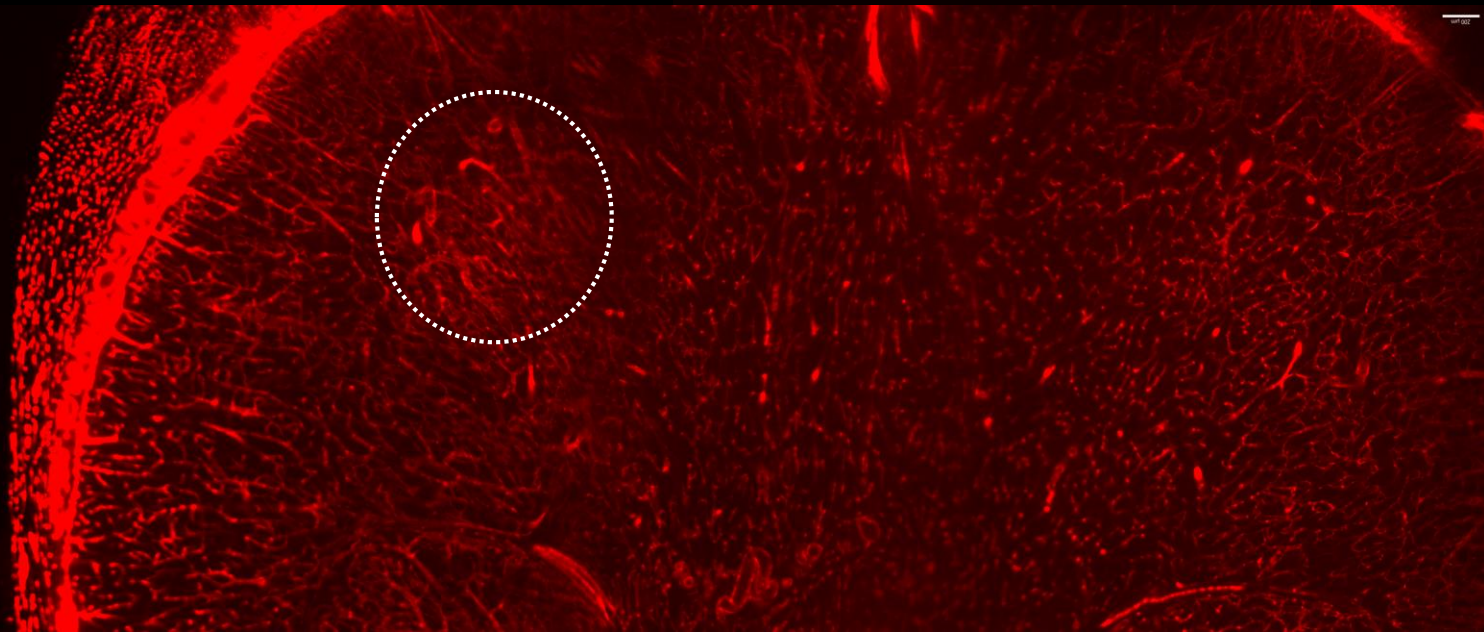
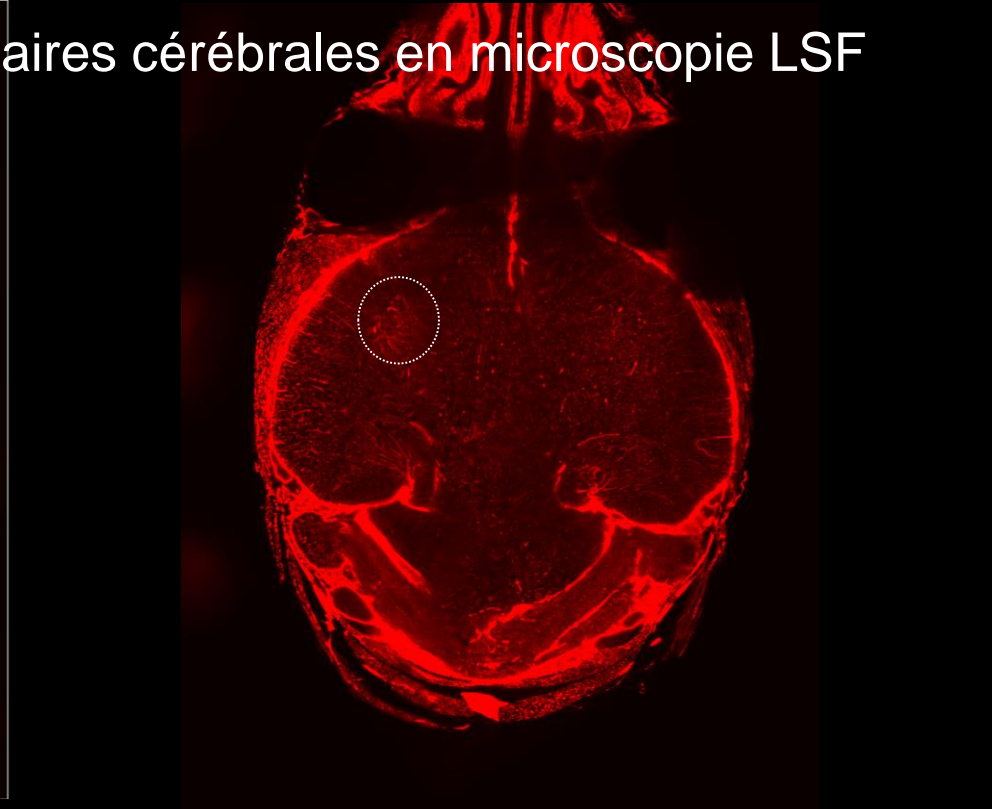
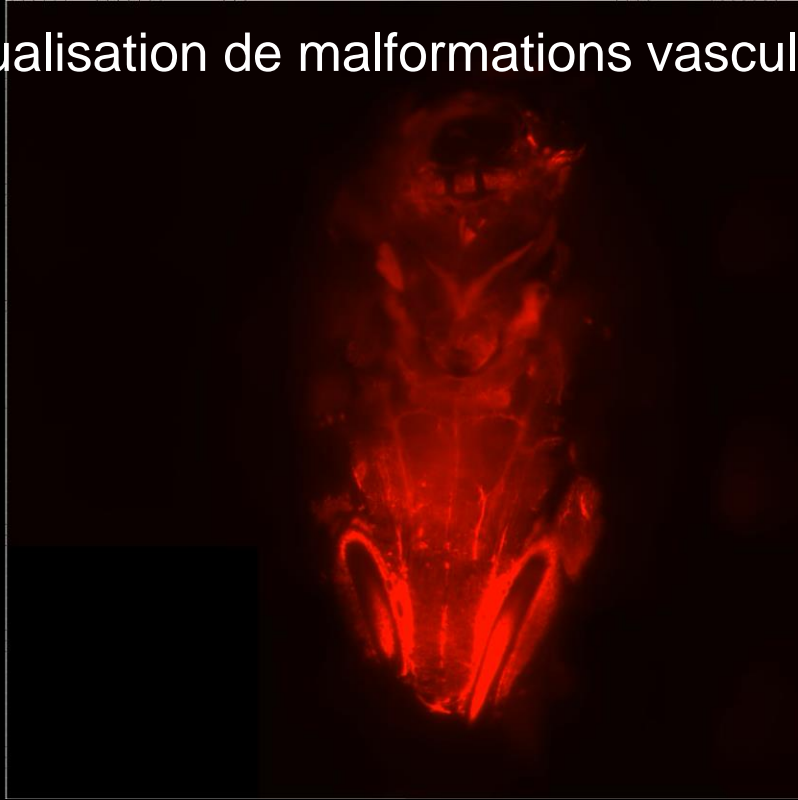


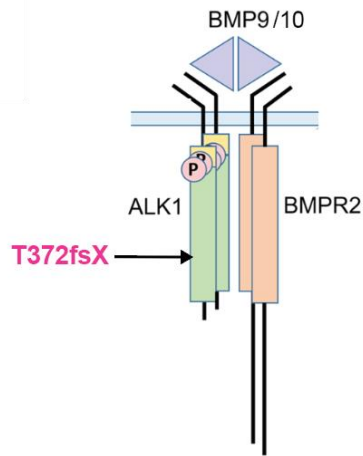
+VEGF



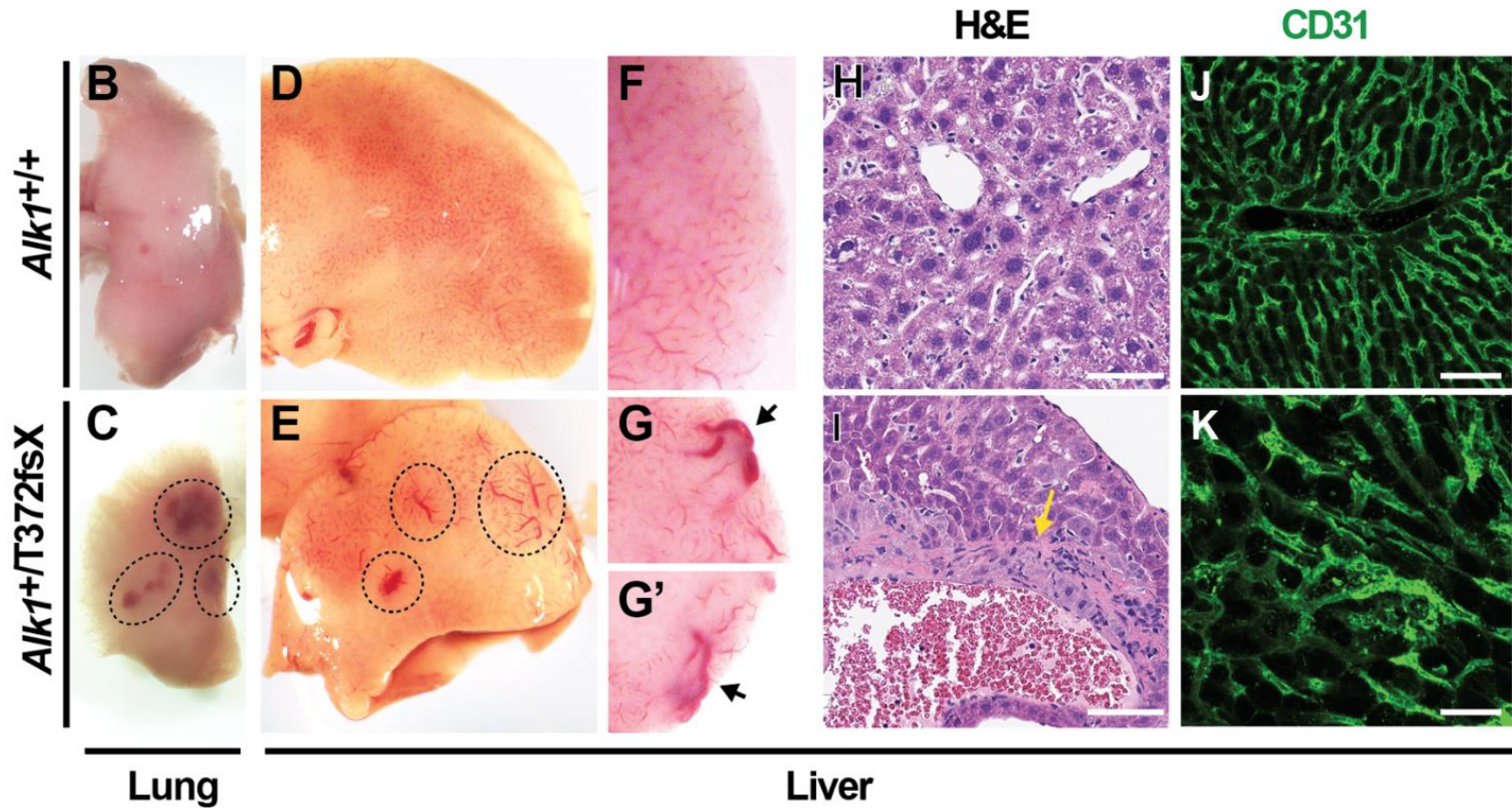
Choi et al., PLoS One (2014)

# Visualisation de malformations vasculaires cérébrales en microscopie LSF

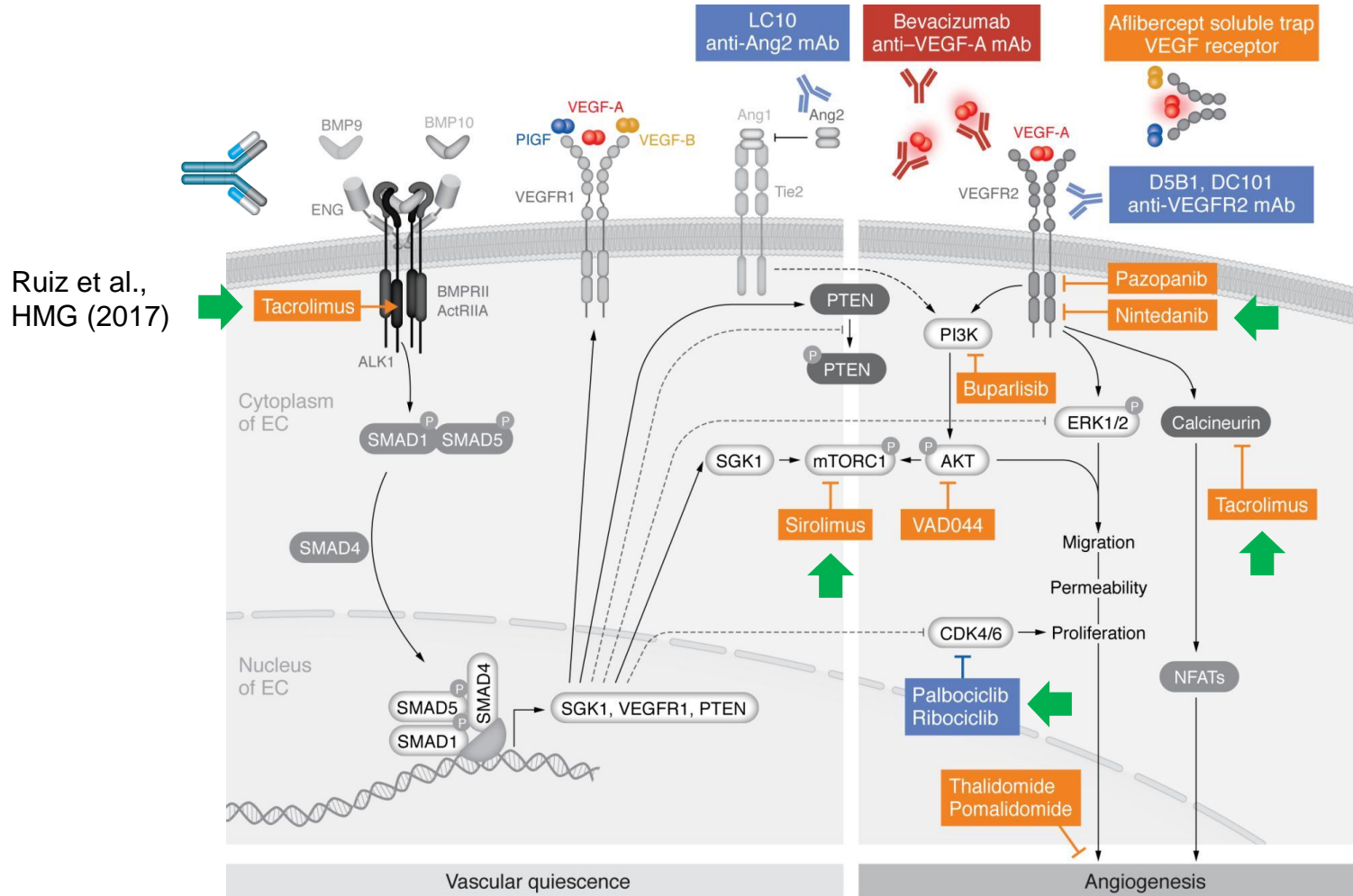




Un modèle de souris adulte exprimant une mutation pathologique de l'ALK1



# Approaches cliniques et précliniques dans la maladie de Rendu-Osler



■ Drugs tested in completed clinical trial    
 ■ Drugs currently under testing or with a case report    
 ■ Drugs tested only in preclinical models

## Lab members:

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**Zhiming Wang, MD**

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**Aya Kitabayashi, PhD**

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Research Assistant

**Sajeth Dinakaran**

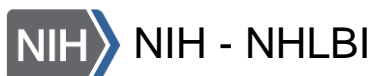
Ph.D. Student, Zucker School of Medicine at Hofstra/Northwell

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Marie E. Faughnan, MD (St. Michael's Hospital Toronto, Canada)



DoD - CDMRP

