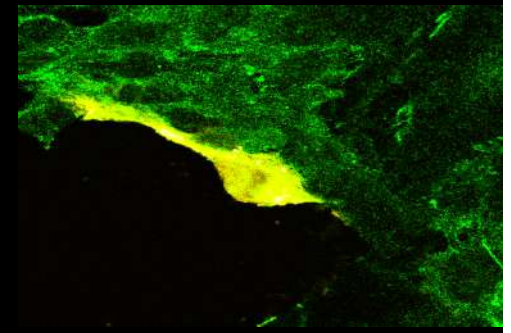
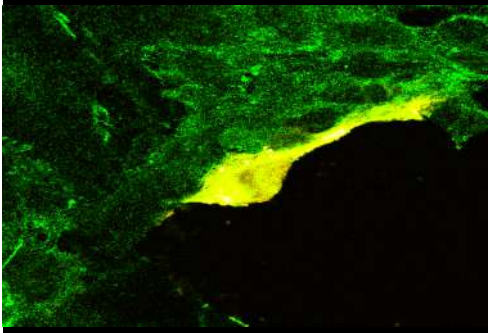


Julie Gavard / Cyrille Mionnet / Philippe Robert

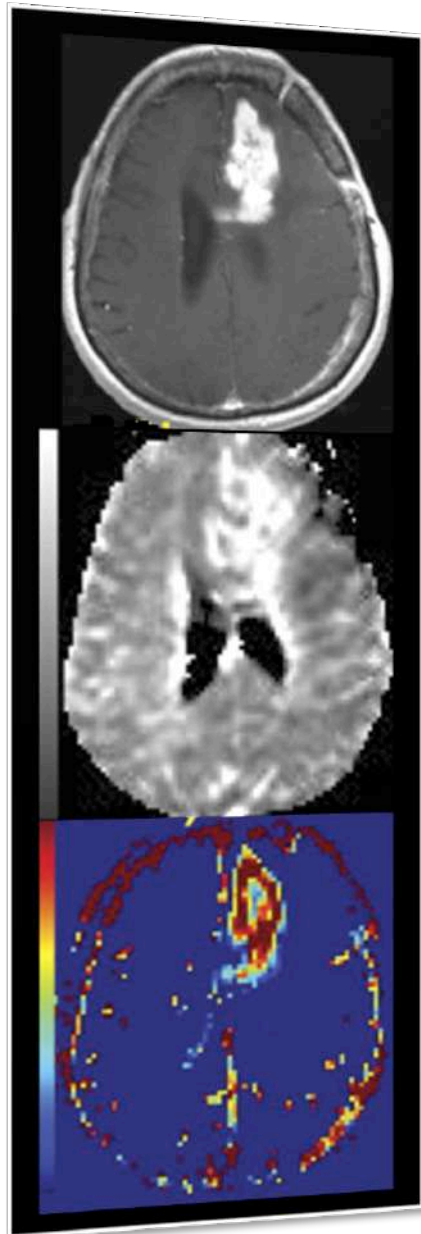
**JAMAICA: comment les JAMs contrôlent
l'Adhérence InterCellulaire et l'Architecture des tumeurs?**

*Signalisation en Oncogenèse, Angiogenèse et Perméabilité
CNRS ERL6001, Nantes*

*Laboratoire Adhésion & Inflammation
CNRS UMR7333, Marseille*



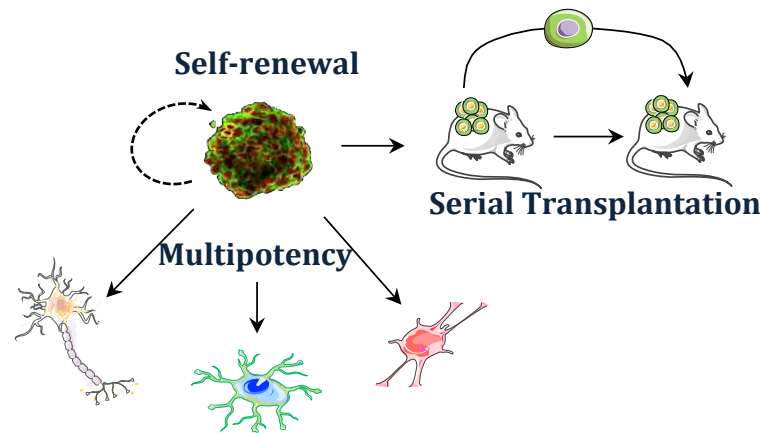
Cancer Stem Cells in Glioblastoma



- Aggressive tumors of CNS with poor prognosis (median survival ranges between 12-15 months)
- Current treatments include surgery, chemotherapy (temolozomide) and radiotherapy
- Growing evidence of cancer stem cells in gliomagenesis



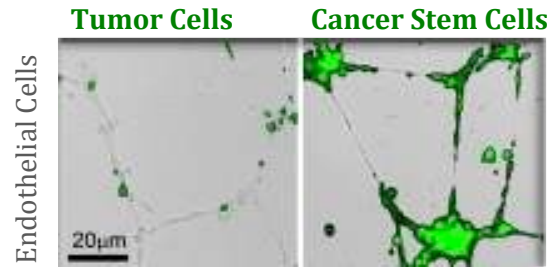
Targeting cancer stem cells:
initiation, progression,
recurrence, resistance



Vascular Niche in Glioblastoma

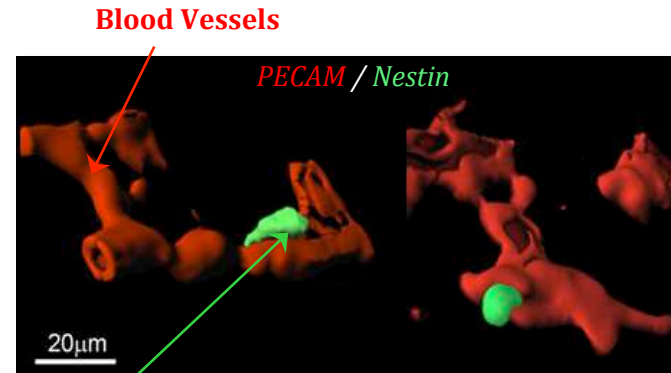
Evidence for Interactions between Endothelial Cells (ECs) and Glioblastoma Stem-like Cells (GSCs)

- *In vitro*



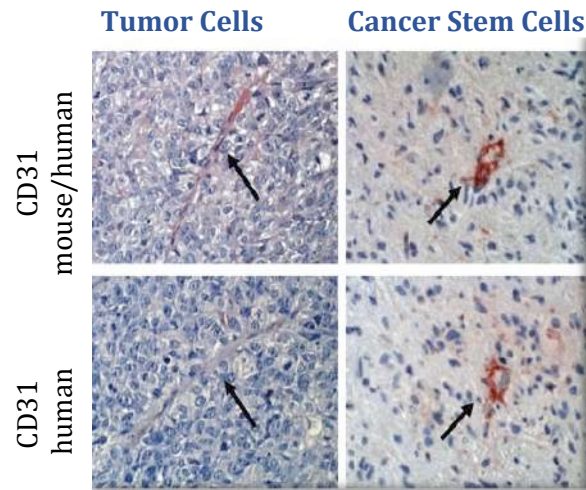
Calabrese et al, Cancer Cell 2007

- *In situ*



Calabrese et al, Cancer Cell 2007

- *In vivo*



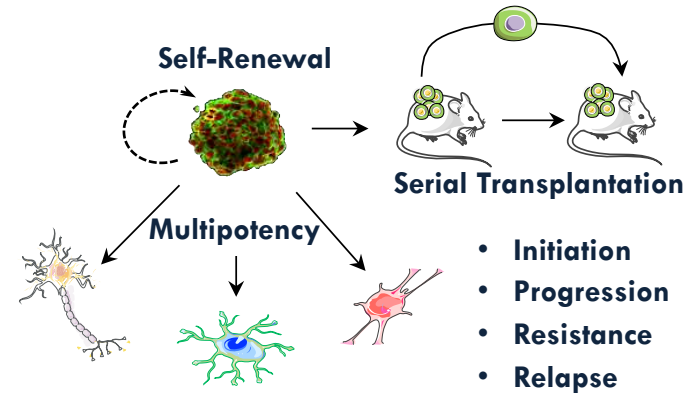
Ricci-Vitiani et al, Nature 2010

➤ **What are the mechanisms involved in GSC/EC interaction?**

Ex vivo Co-Culture Model

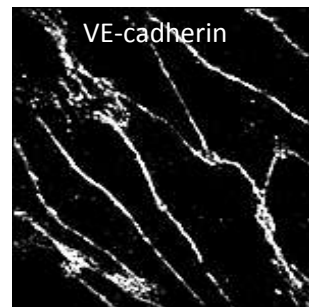
✓ GBM Patient-derived Cells

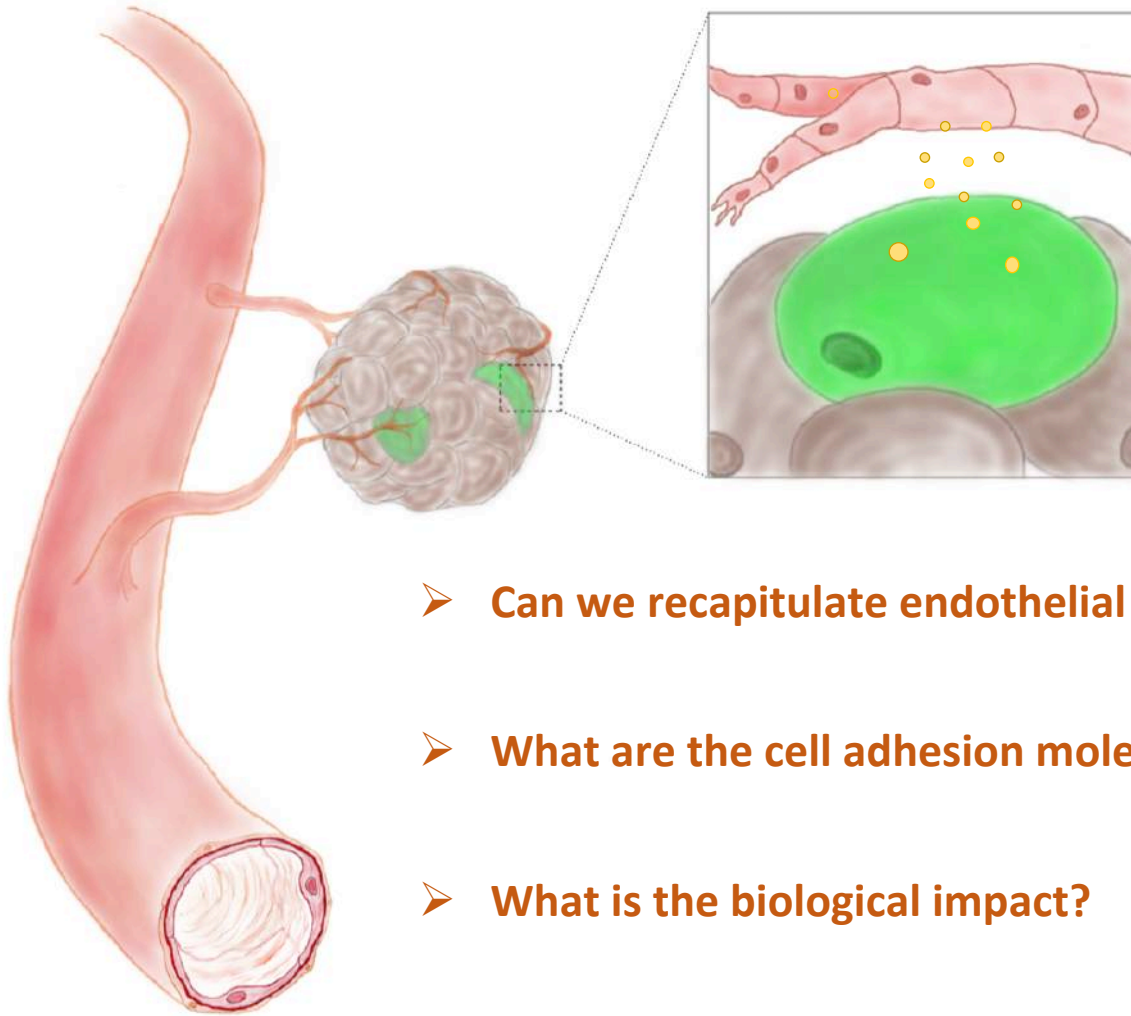
- *stemness markers*
- *3D growth*
- *differentiation*
- *tumor formation*



✓ Human Brain Endothelial Cells

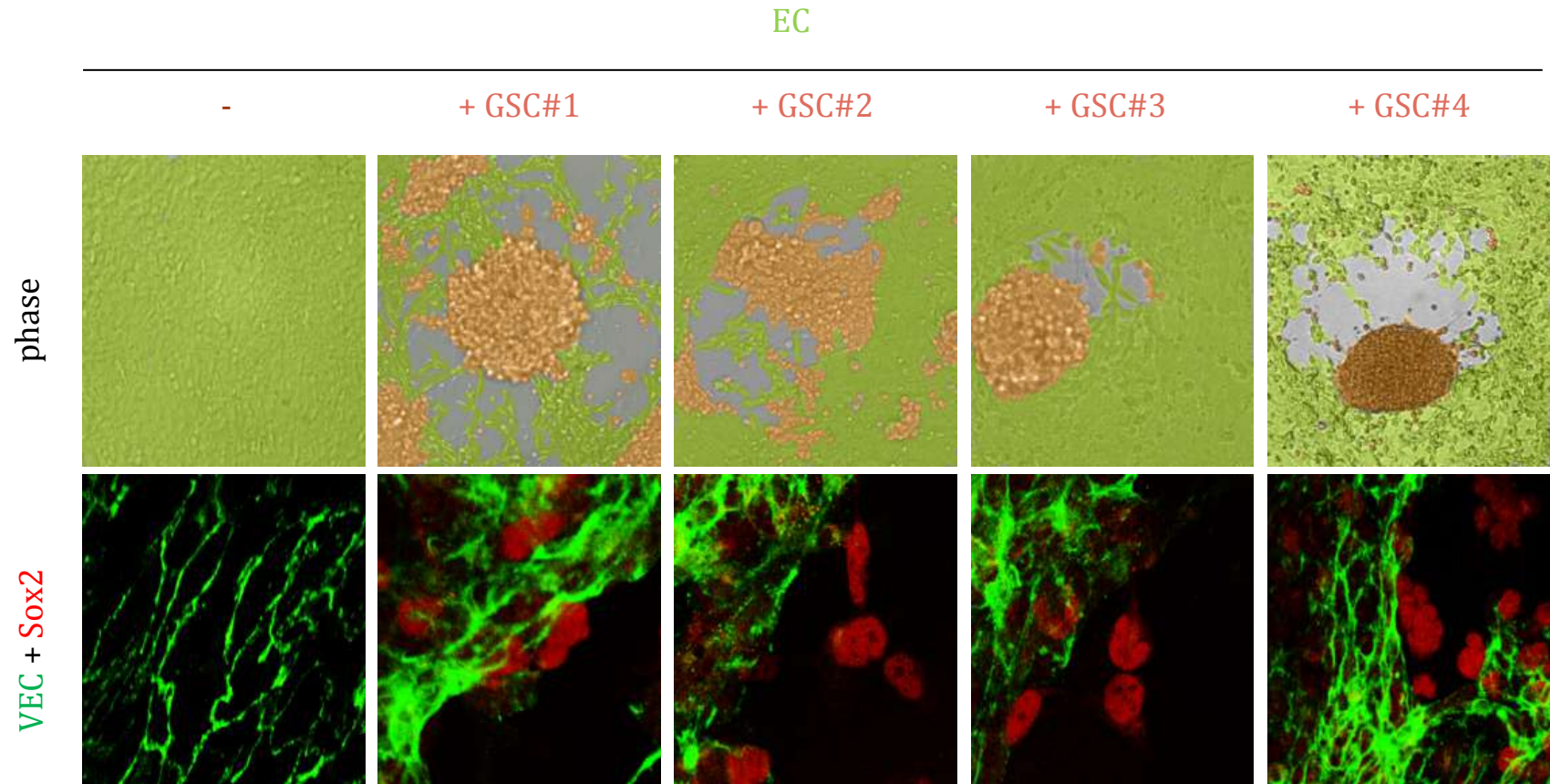
- *junctions*
- *barrier*
- *sprouting*
- *tubulogenesis*





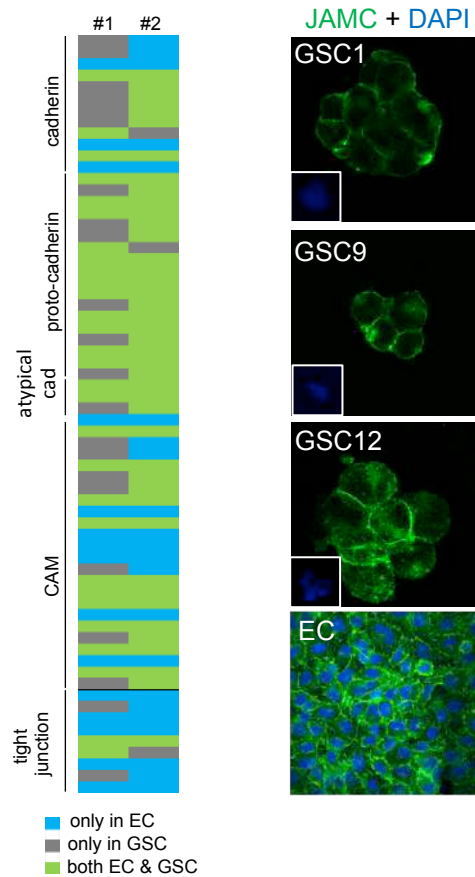
- **Can we recapitulate endothelial cell/cancer cell interaction?**
- **What are the cell adhesion molecules and forces involved?**
- **What is the biological impact?**

GSCs induce a profound remodeling of the endothelial monolayer

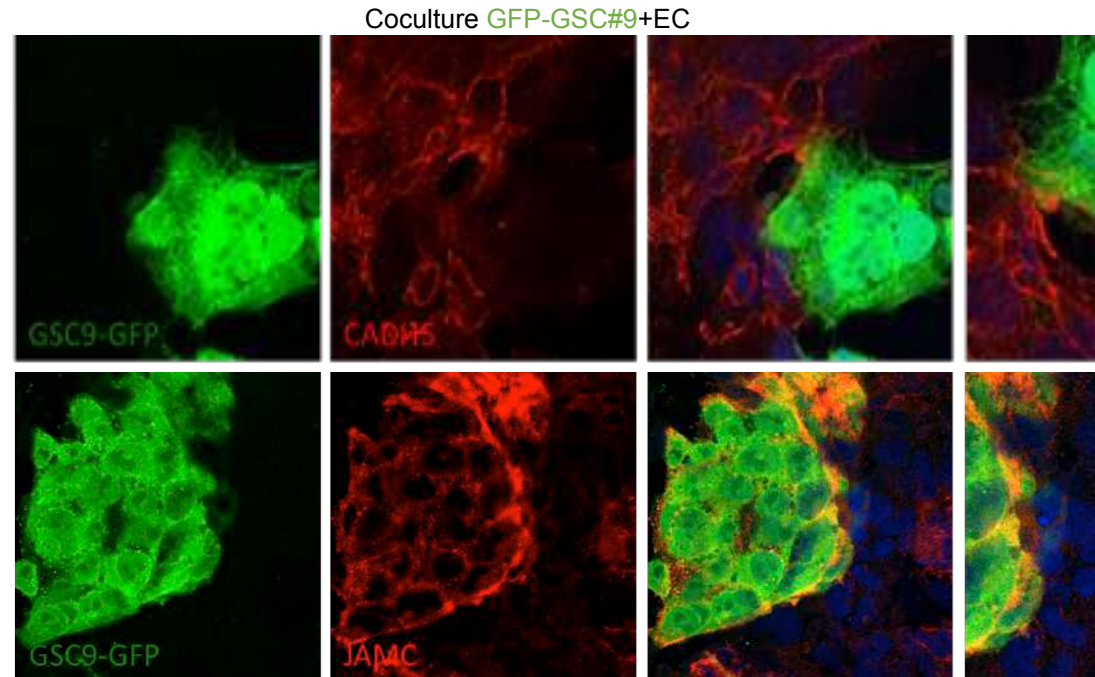


JAM-C accumulated at the Interface between EC & GSCs

- Transcriptomic & Validation



- Confocal Analysis

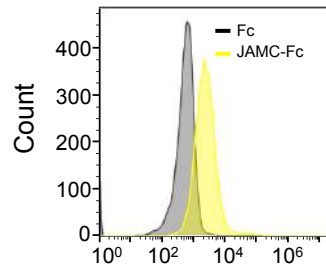


➤ JAM-C can bridge GSCs to EC

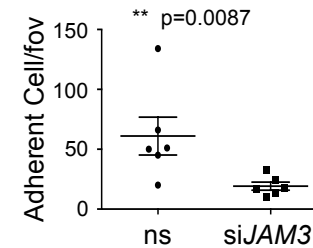
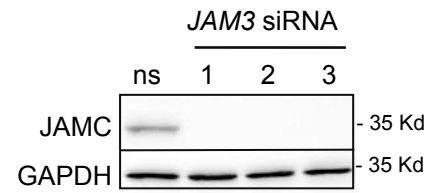
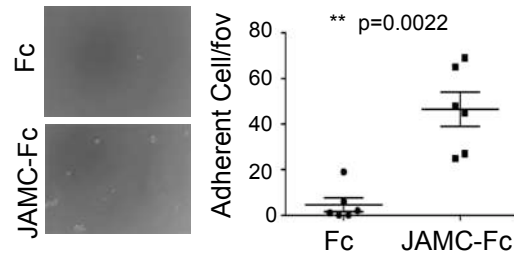
JAM-C is known to mediate cell-to-cell contact in the hematopoietic niche and to recruit polarity complex

GSC-harbored JAM-C mediates Adhesion

- Soluble Binding

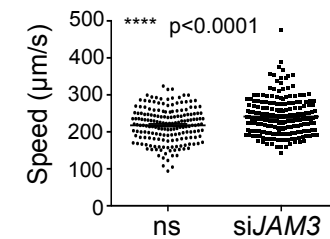
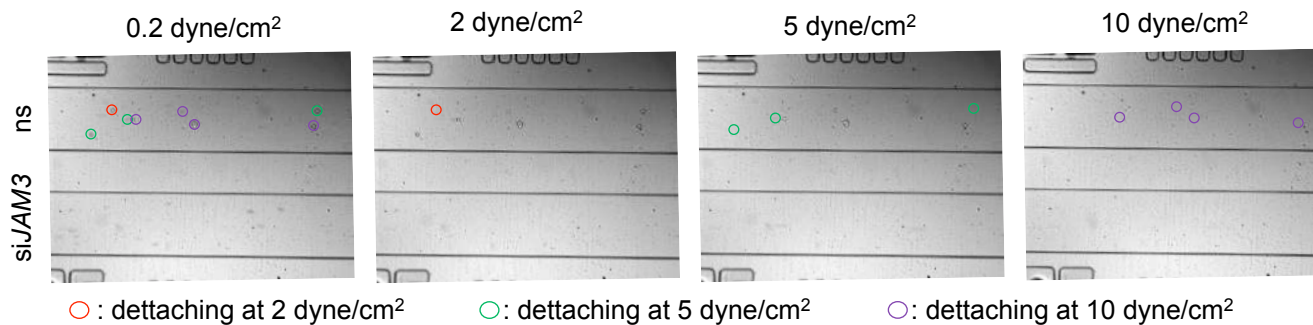


- Immobilized Binding



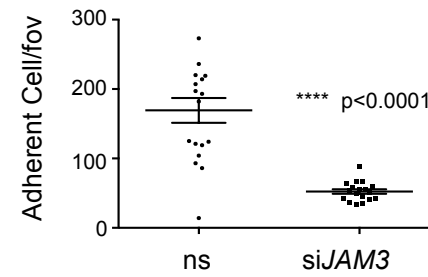
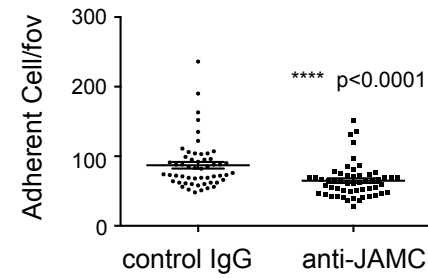
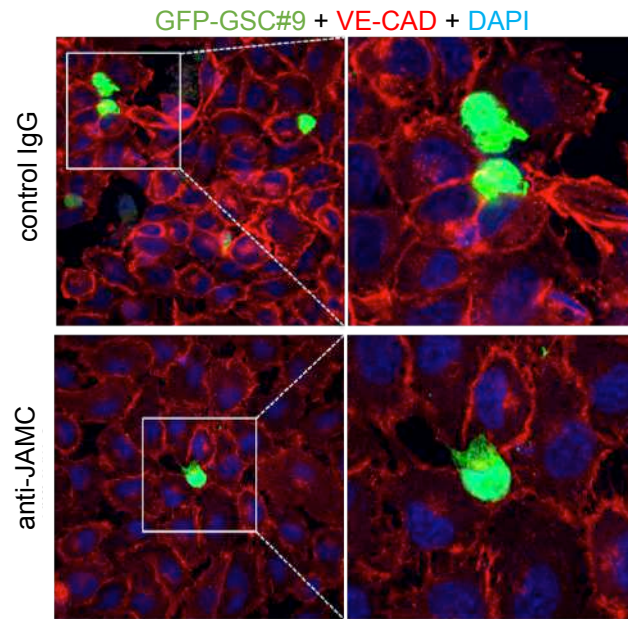
- No interaction with monomeric JAMC
- Weak binding, but specific with GSCs

- Binding under flow

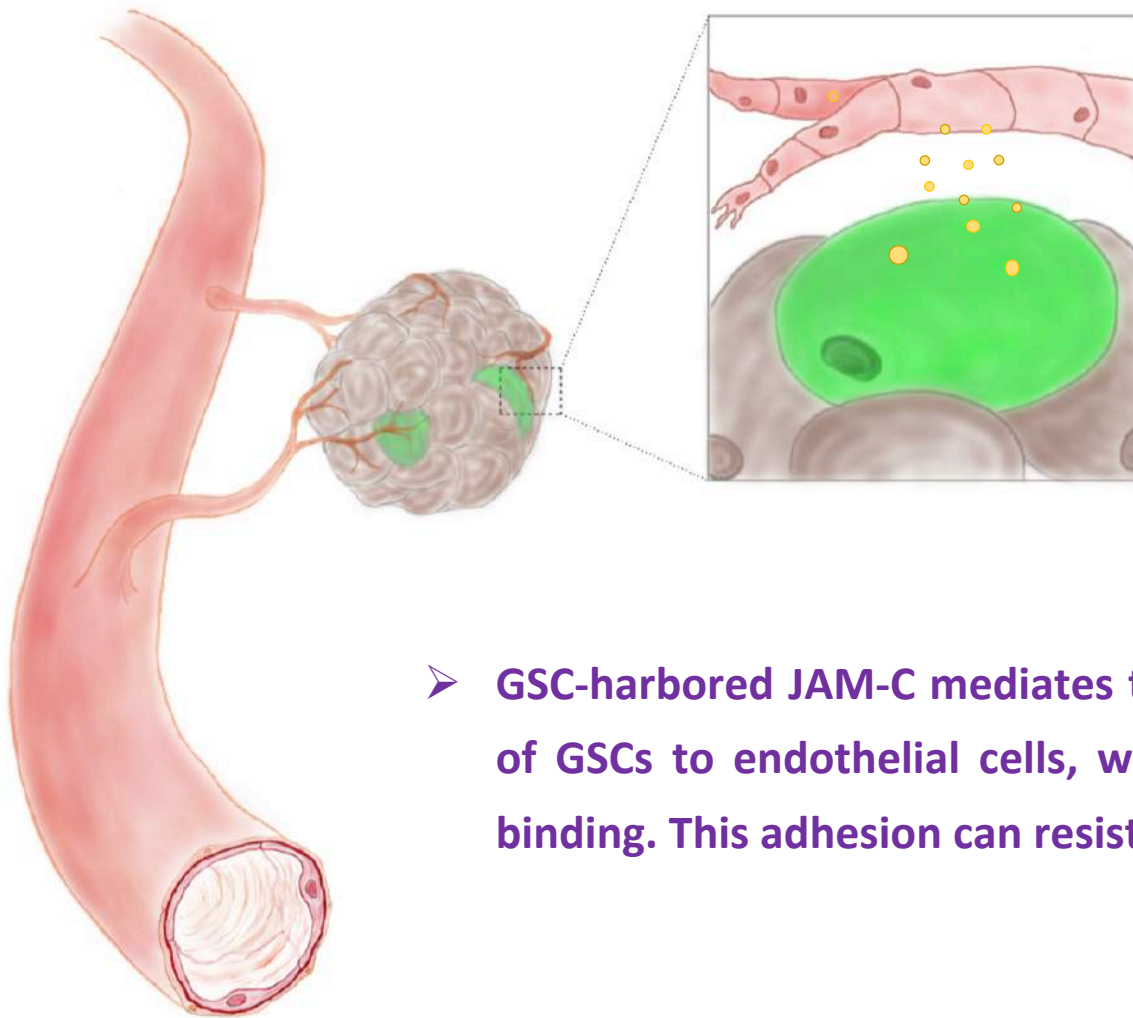


- Specific resistance of JAM-C-attached GSCs

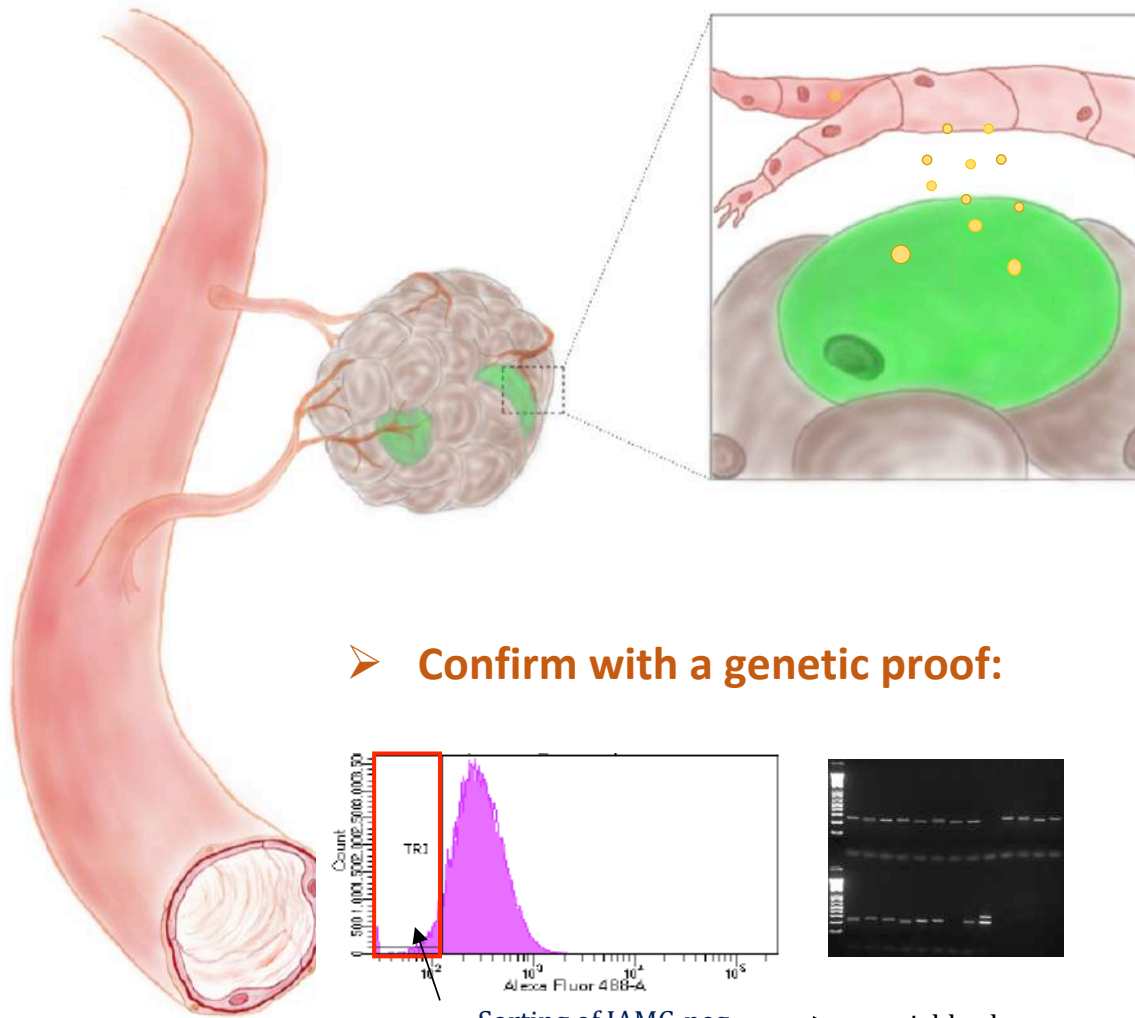
GSC-harbored JAM-C is engaged in Cell-Cell Interaction with Endothelial Cells



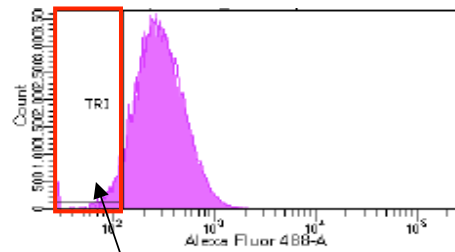
➤ GSC-expressed JAM-C is required for adhesion to EC monolayers



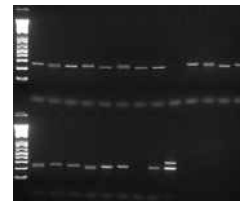
- **GSC-harbored JAM-C mediates the attachment and interaction of GSCs to endothelial cells, with a rather weak, but specific binding. This adhesion can resist to shear stress.**



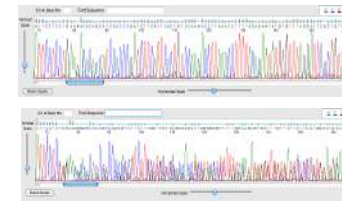
➤ **Confirm with a genetic proof:**



Sorting of JAMC-neg
GSC#1 (96 well plate)

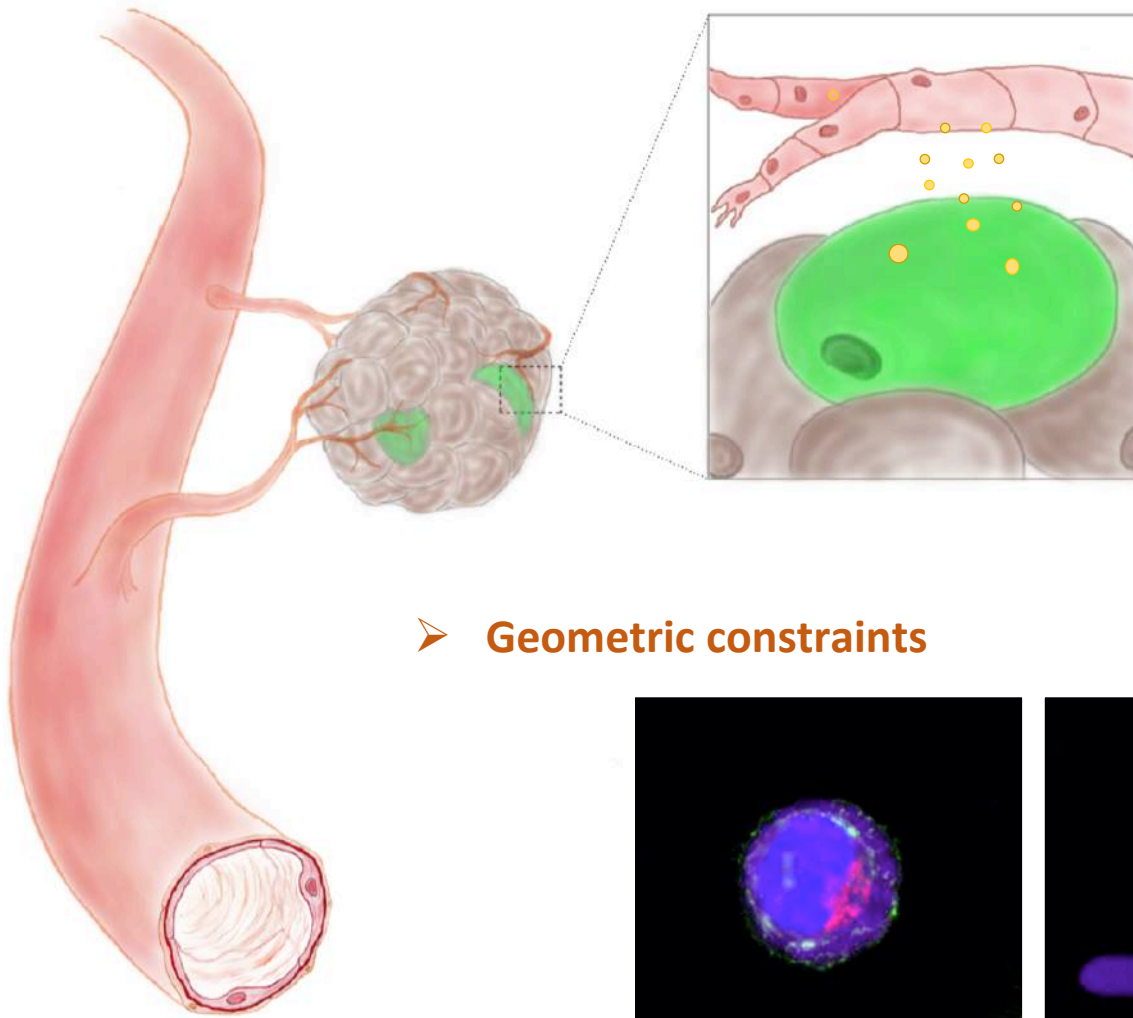


viable clones
PCR screen

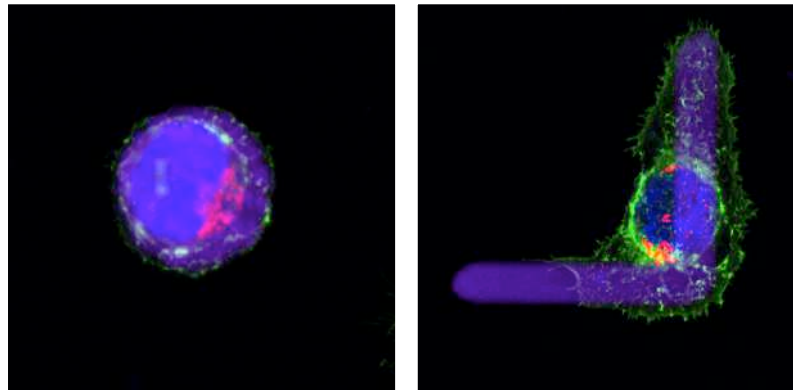


Sequencing
mono, bi-allelic

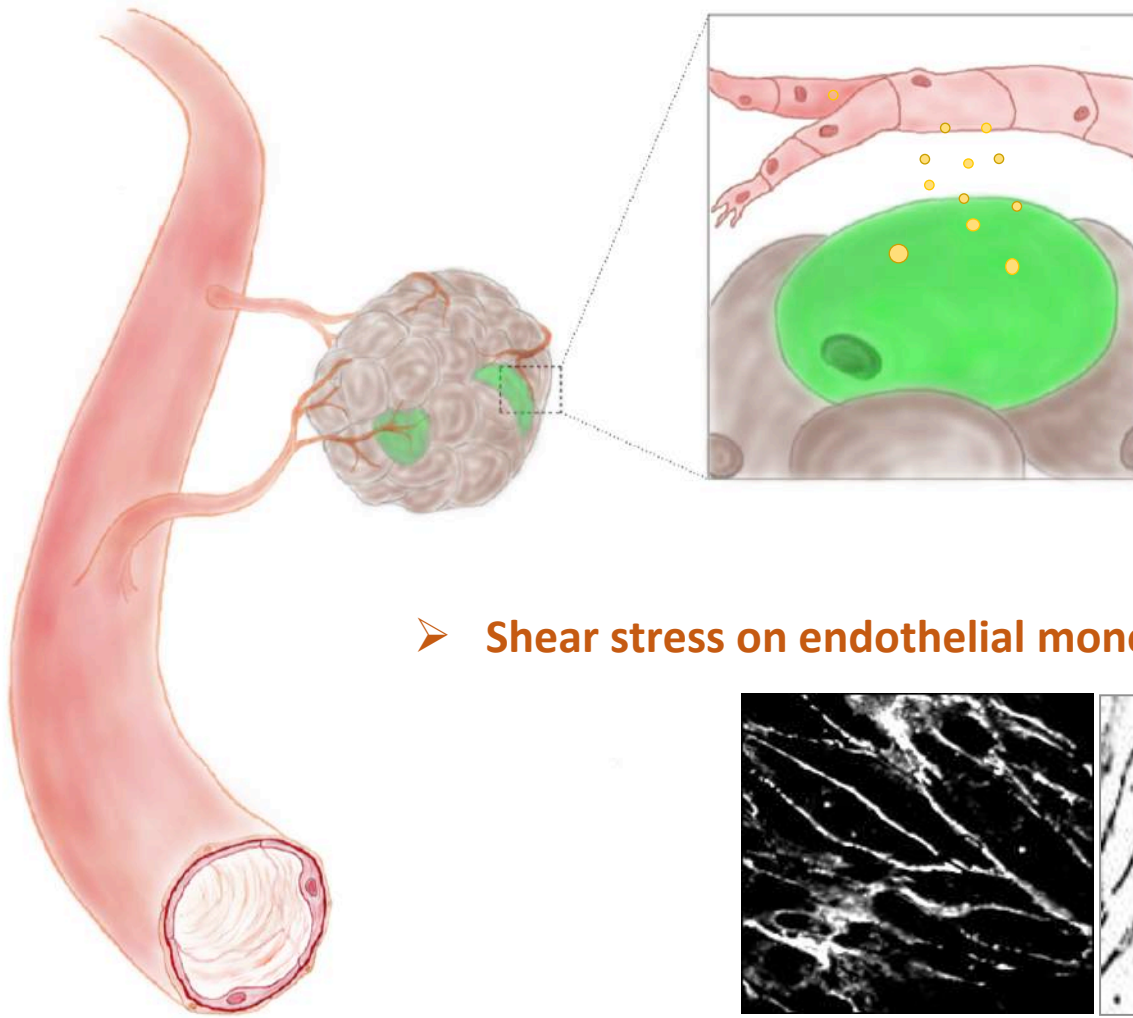
- Adhesion of GSC (WT and KO) on JAMC surface



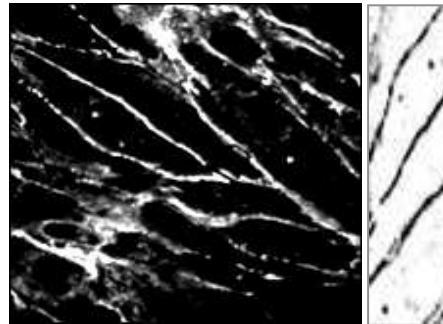
➤ **Geometric constraints**



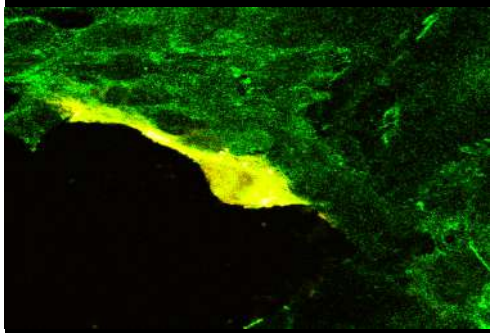
- *Adhesion & Morphology on micropatterns*
- *Functional impact on polarity & cell division*



➤ **Shear stress on endothelial monolayers**



- Adhesion of GSCs (WT and KO) on endothelial surface



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Cyrille Mionnet

