How can stem cells help us understand stroke and CADASIL?

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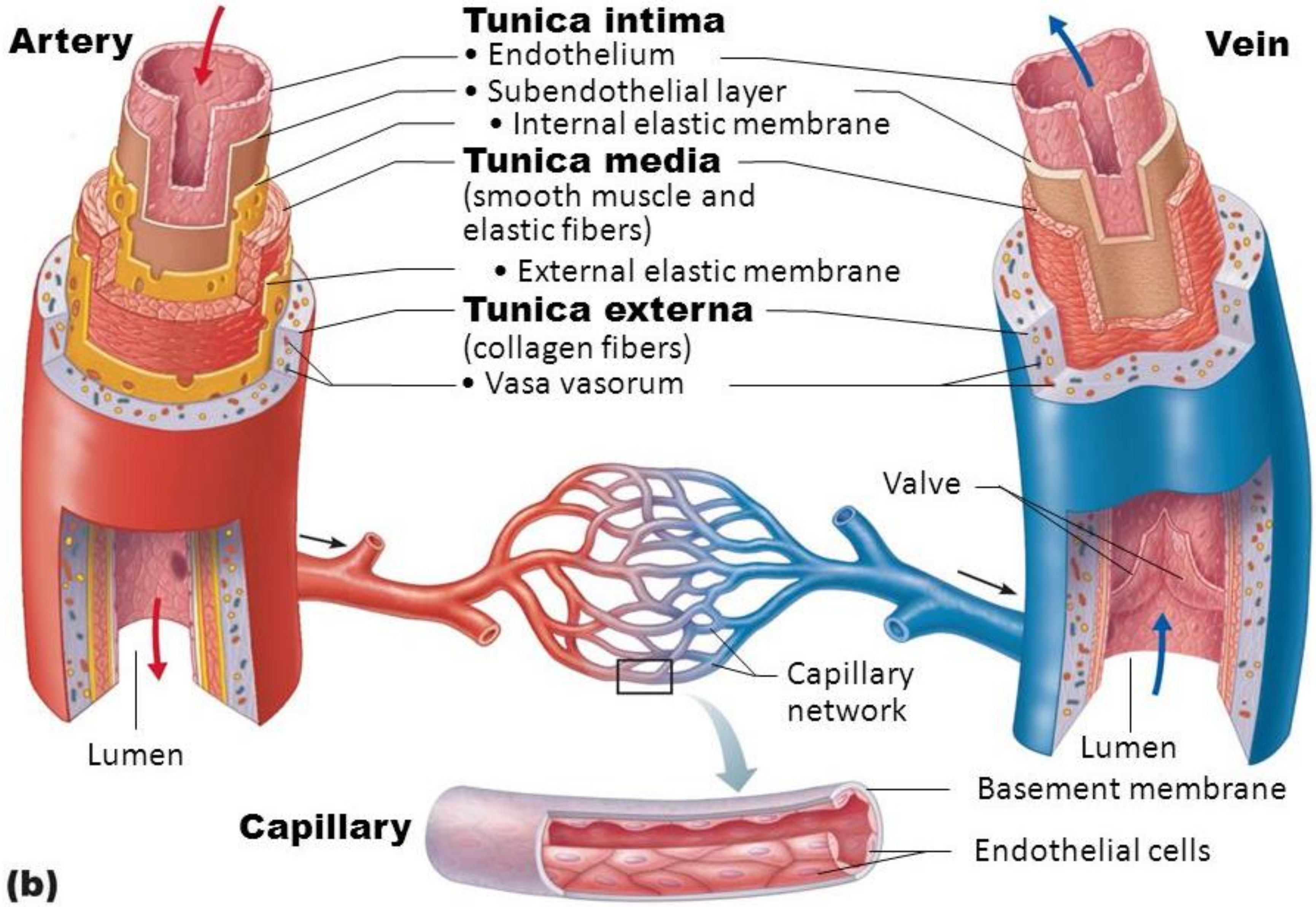
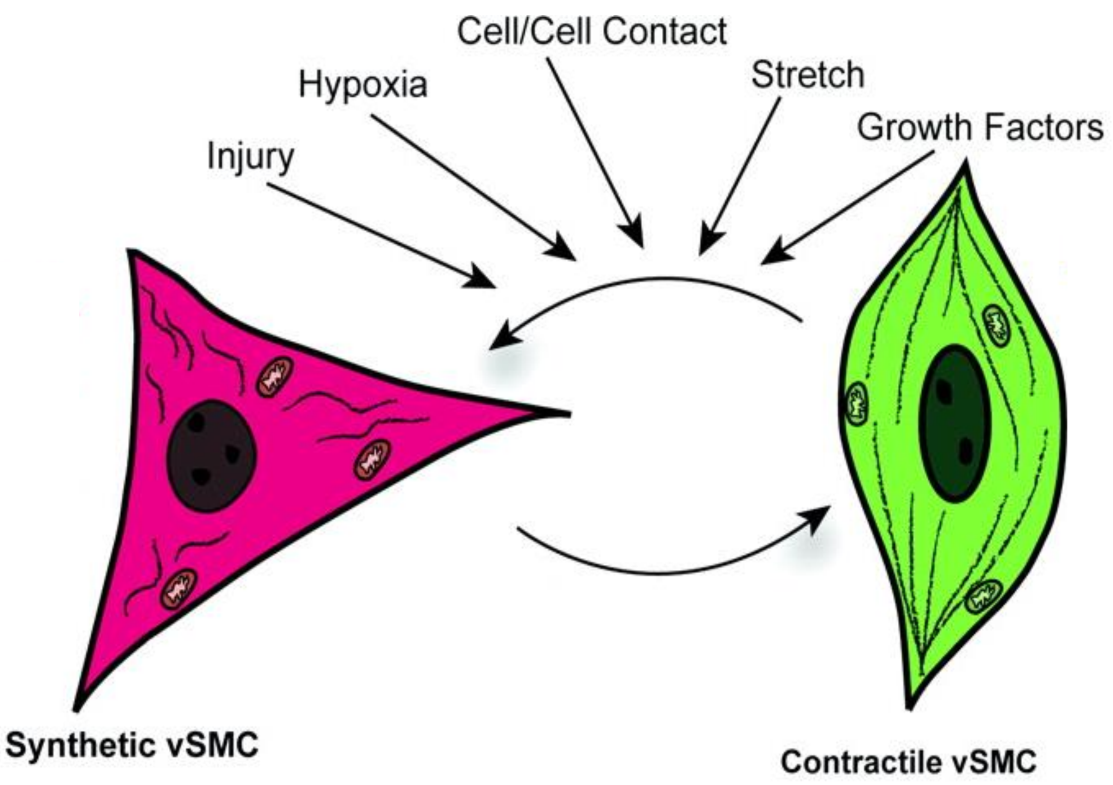
Cells of the Vasculature



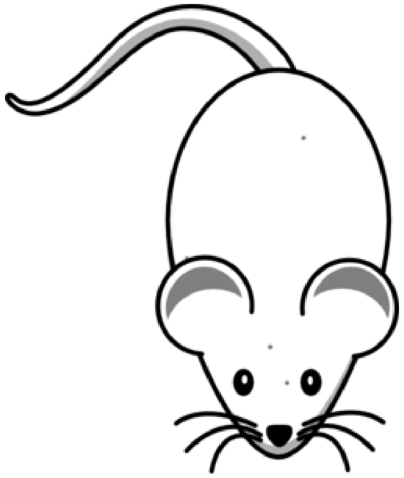
Vascular Smooth Muscle Cells



- Vascular smooth muscle cells (and pericytes) regulate blood flow through the vessels.
- Vascular smooth muscle cells (and pericytes) are the main cell types involved in disease progression in CADASIL.

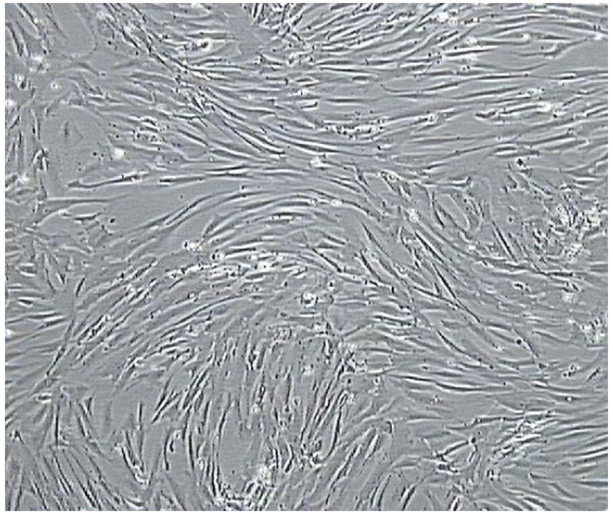
How Can We Study Vascular Smooth Muscle Cells in the Lab?

Animal Models

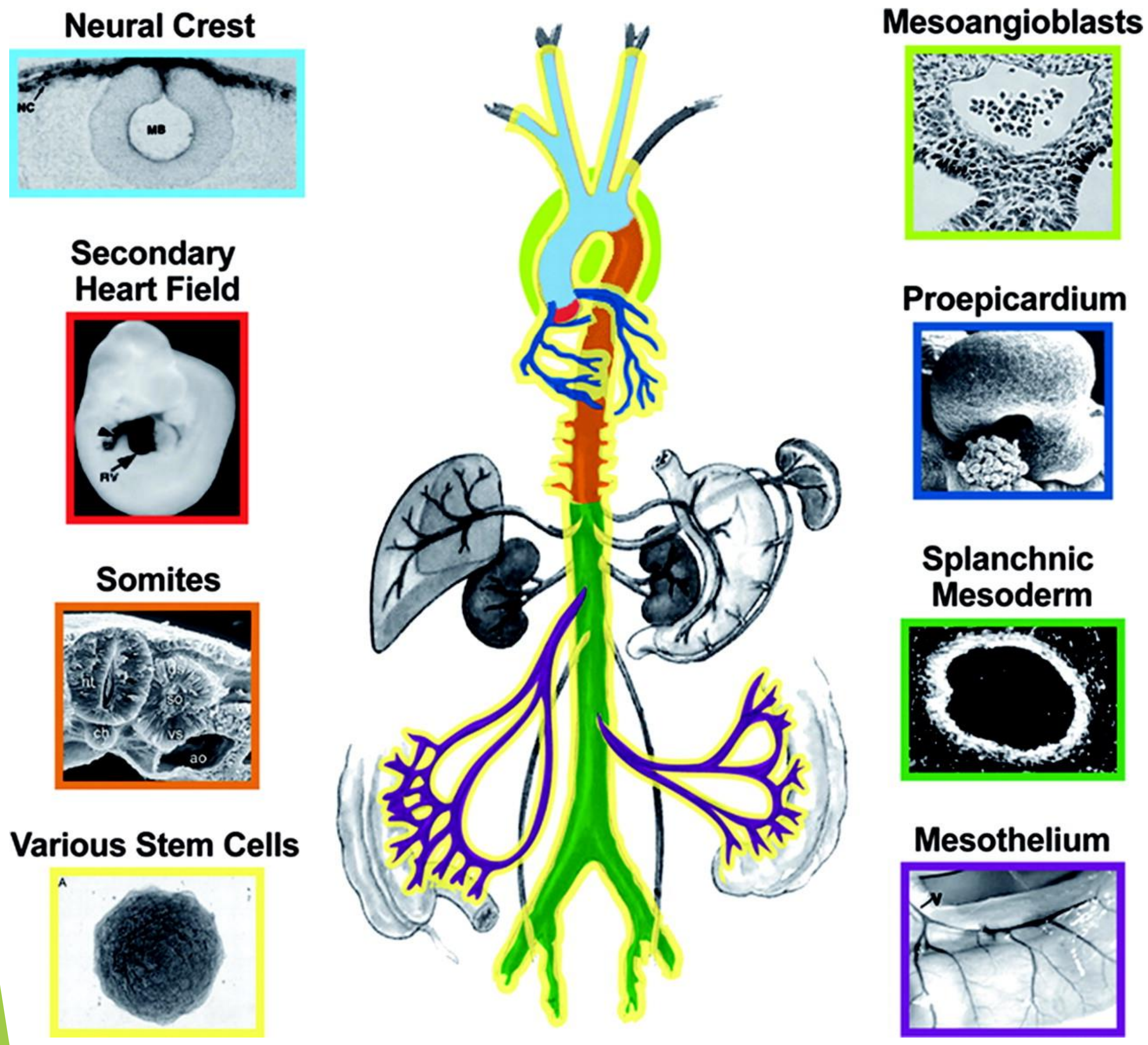


Human Tissue

Commercial Cells



Diversity of Vascular Smooth Muscle Cells

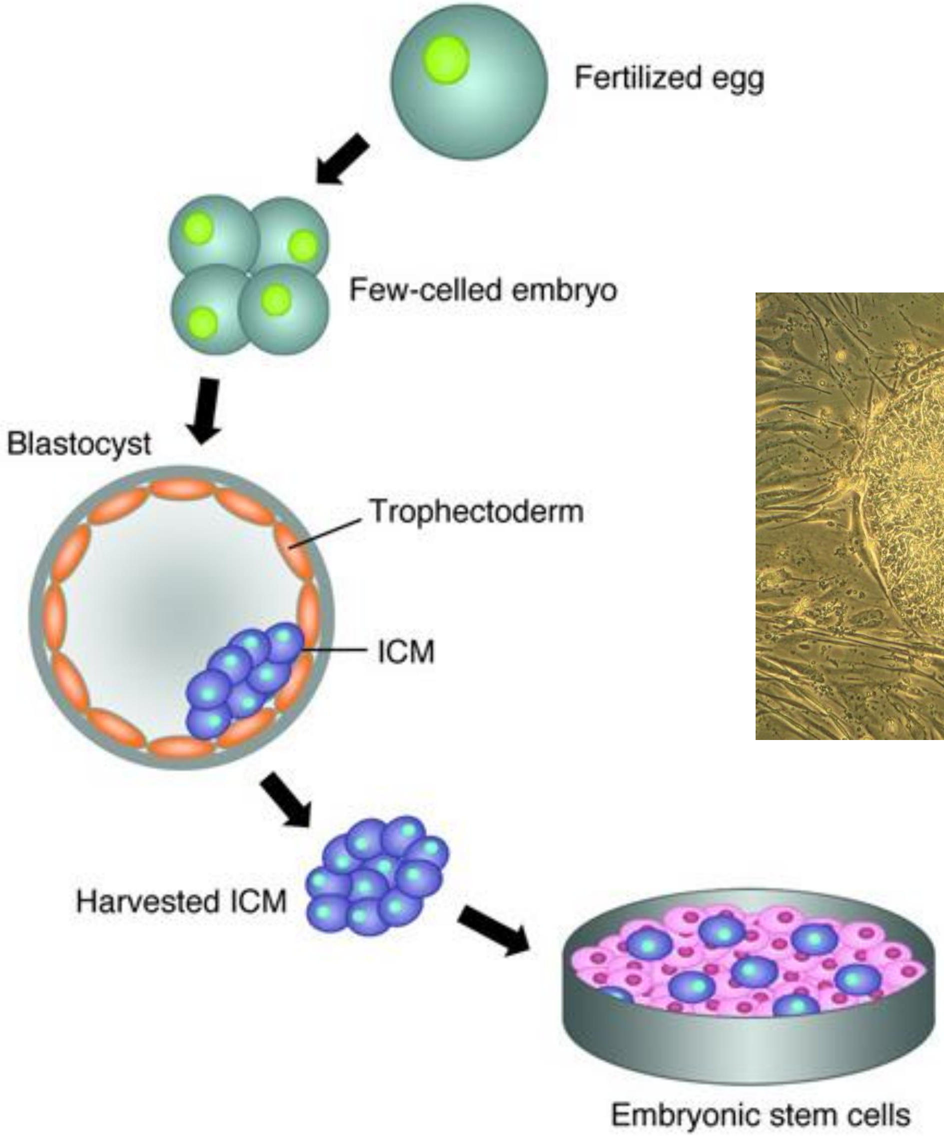


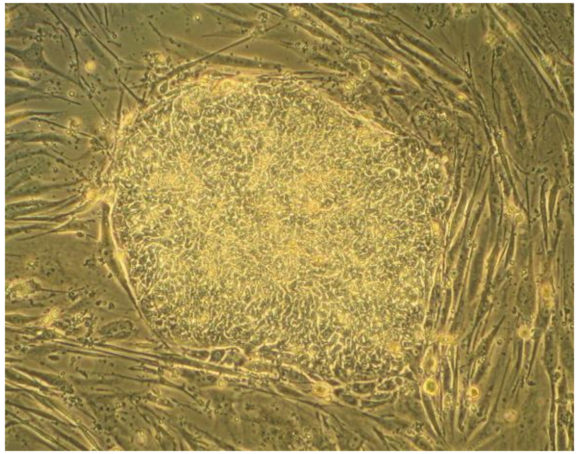
- Vascular smooth muscle cells arise from different parts of the embryo during development.
- We believe that this origin may have an impact on the susceptibility of specific vascular smooth muscle cells types in disease

Can we develop a new, human, model of CADASIL?

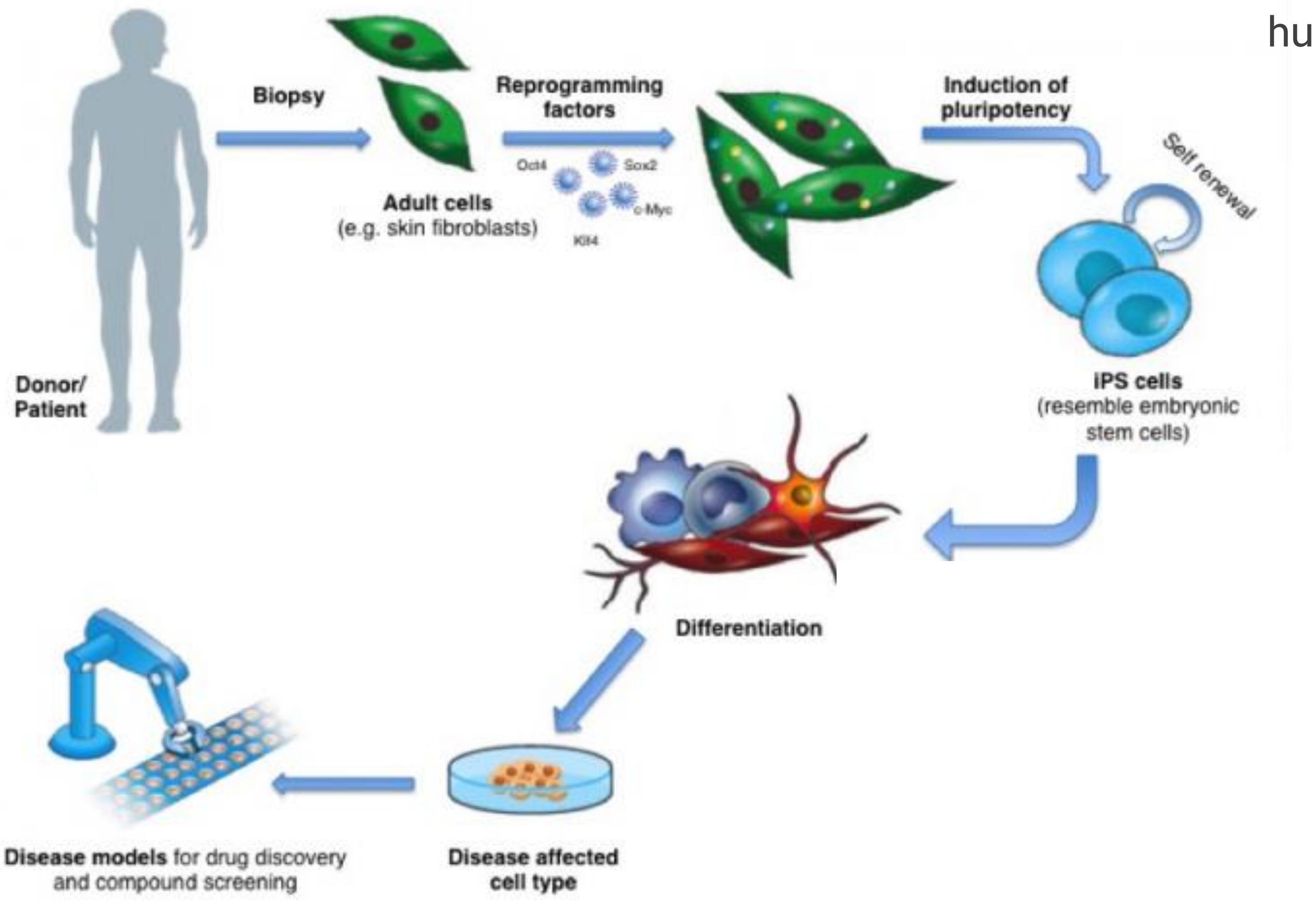
What are stem cells? Embryonic Stem Cells

- First isolated in 1981 from the mouse
- Isolated from humans in 1998





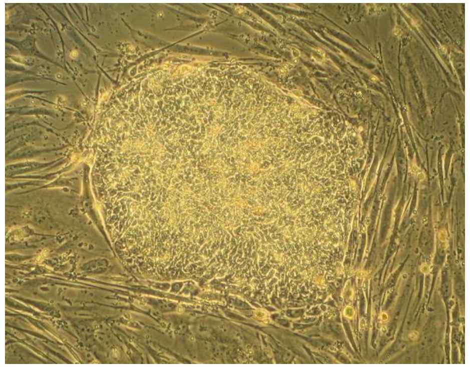
What are stem cells?
Induced Pluripotent Stem Cells



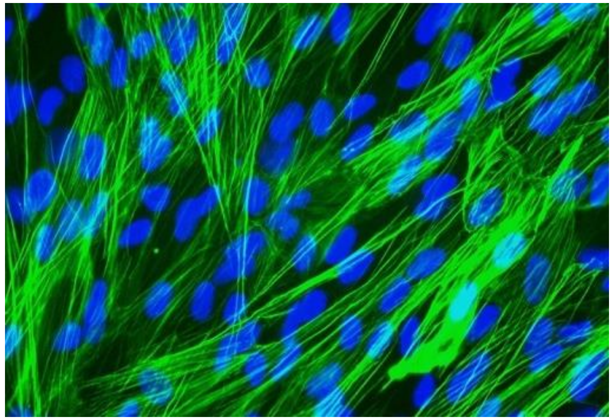
- First generated from humans in 2007

Stem Cells for CADASIL Research

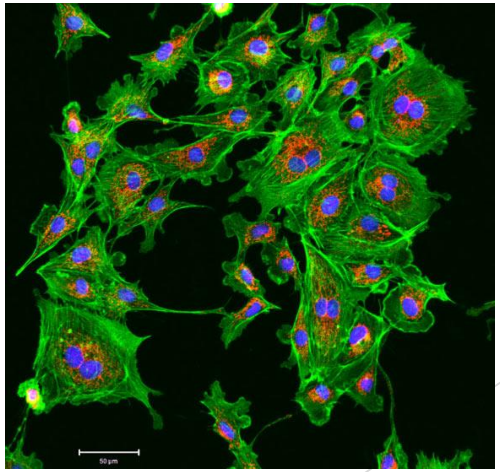
- Aimed to generate a "bank" of patient skin biopsies, to subsequently generate induced pluripotent stem cells.
- Obtained five biopsies from collaborators in Paris (Dr Anne Joutel), and successfully reprogrammed to induced pluripotent stem cells.



CADASIL iPSC



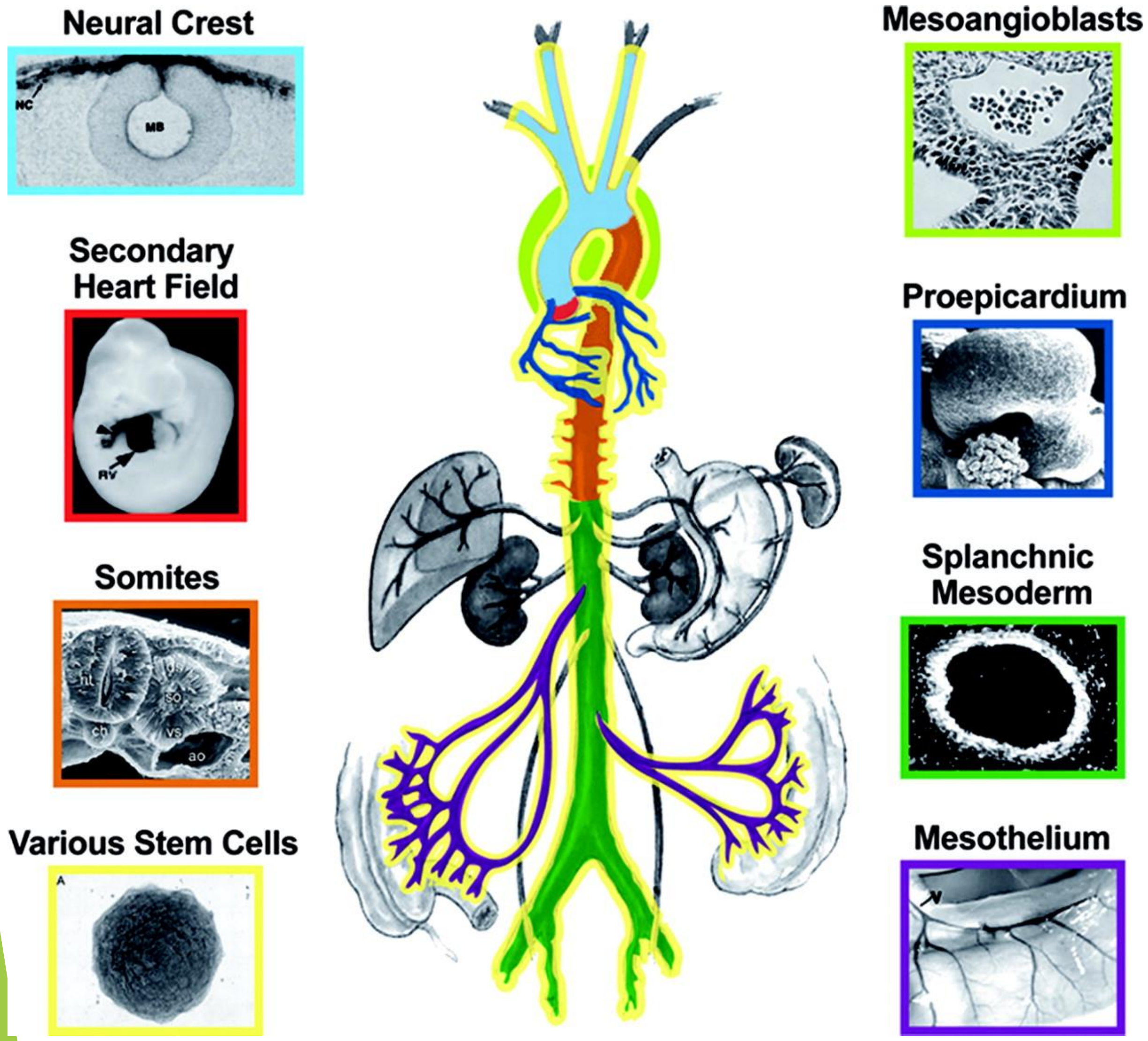
Smooth Muscle Cells



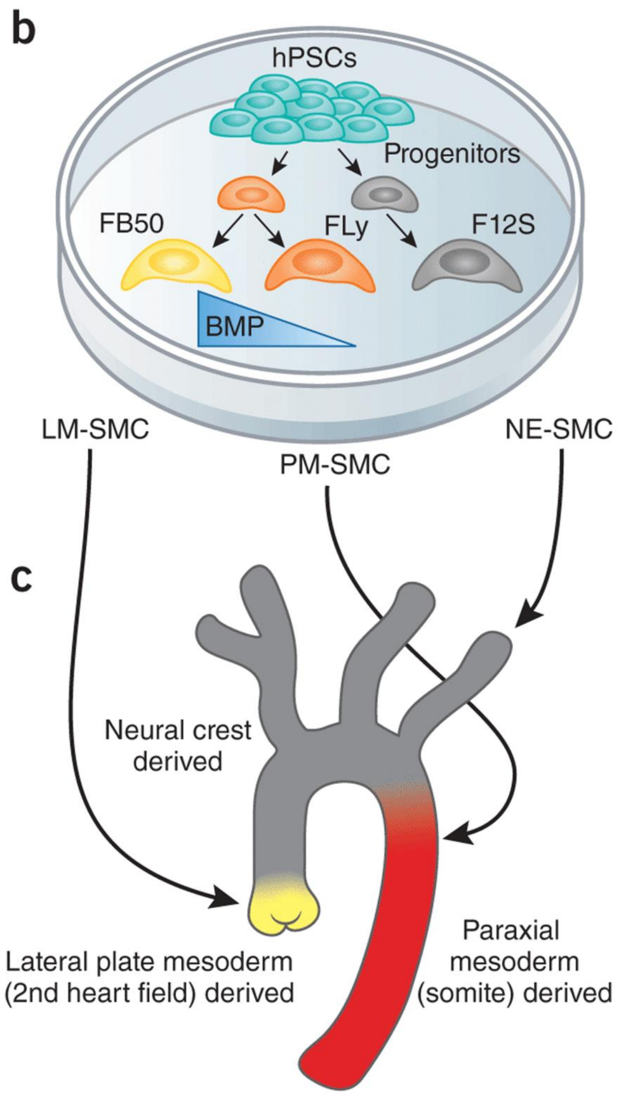
Endothelial Cells

Stem Cells for CADASIL Research

Developmental Diversity of Vascular Smooth Muscle Cells

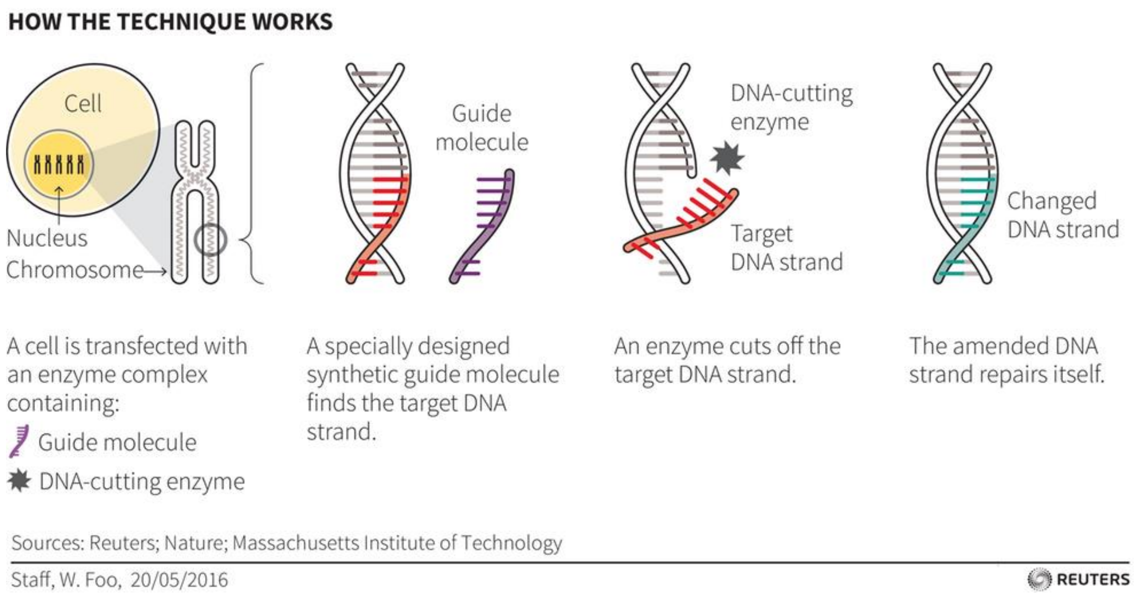


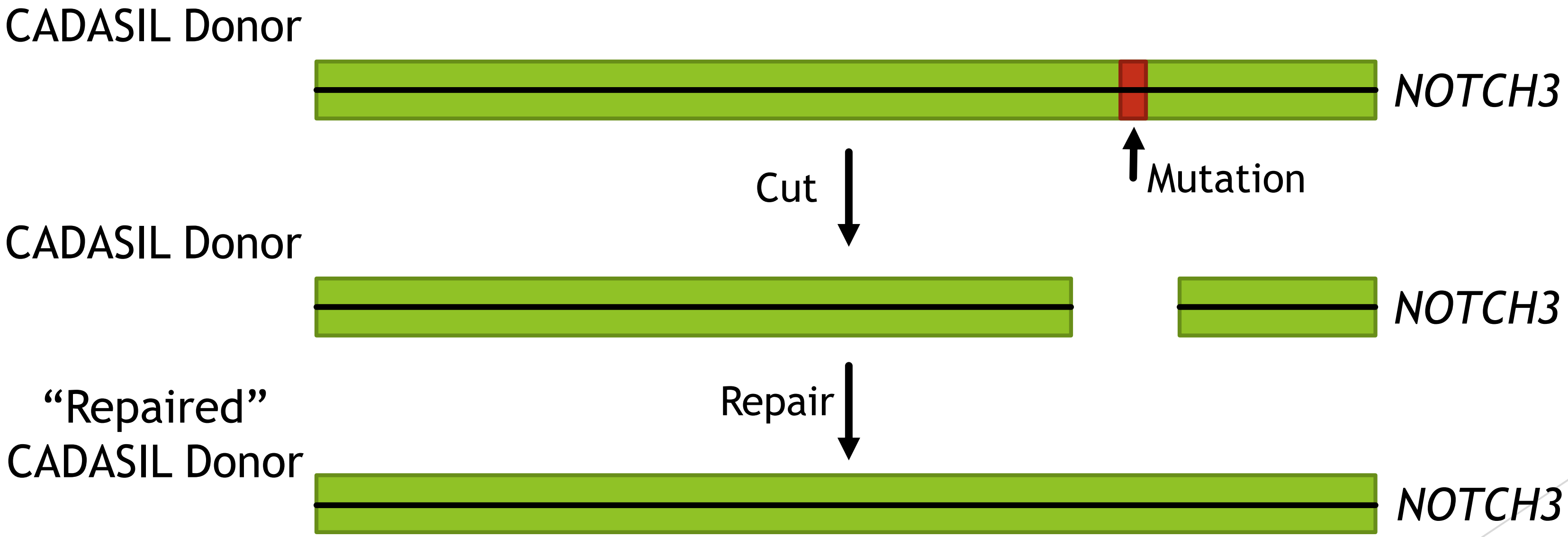
Development from Stem Cells



How do you Control for Diversity?

Genome Editing for CADASIL Research





Stem Cells for CADASIL Research

- We have generated Induced Pluripotent Stem Cells (iPSC) from CADASIL patients with different disease causing mutations.
- We can use these iPSCs to generate patient, and disease, specific vascular smooth muscle cells.
- We aim to use the generated cells to understand what happens to vascular smooth muscle cells during the development and progression of CADASIL.
- Ultimately, we aim to use this technology to identify and develop new therapeutic strategies to treat CADASIL.

Acknowledgements and Contact Details

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