

# Apport des organoïdes rétiniens pour l'étude des dystrophies rétiniennes héréditaires

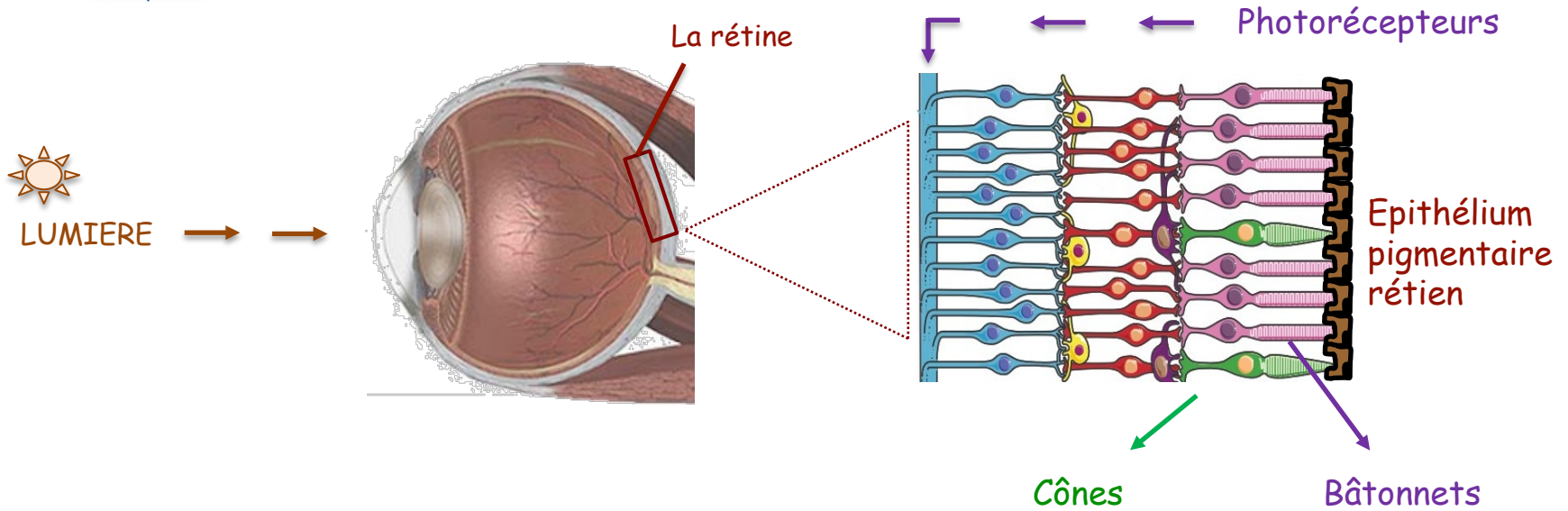
Viki Kalatzis

Lauréate

Prix de Biologie Alfred Kastler 2021

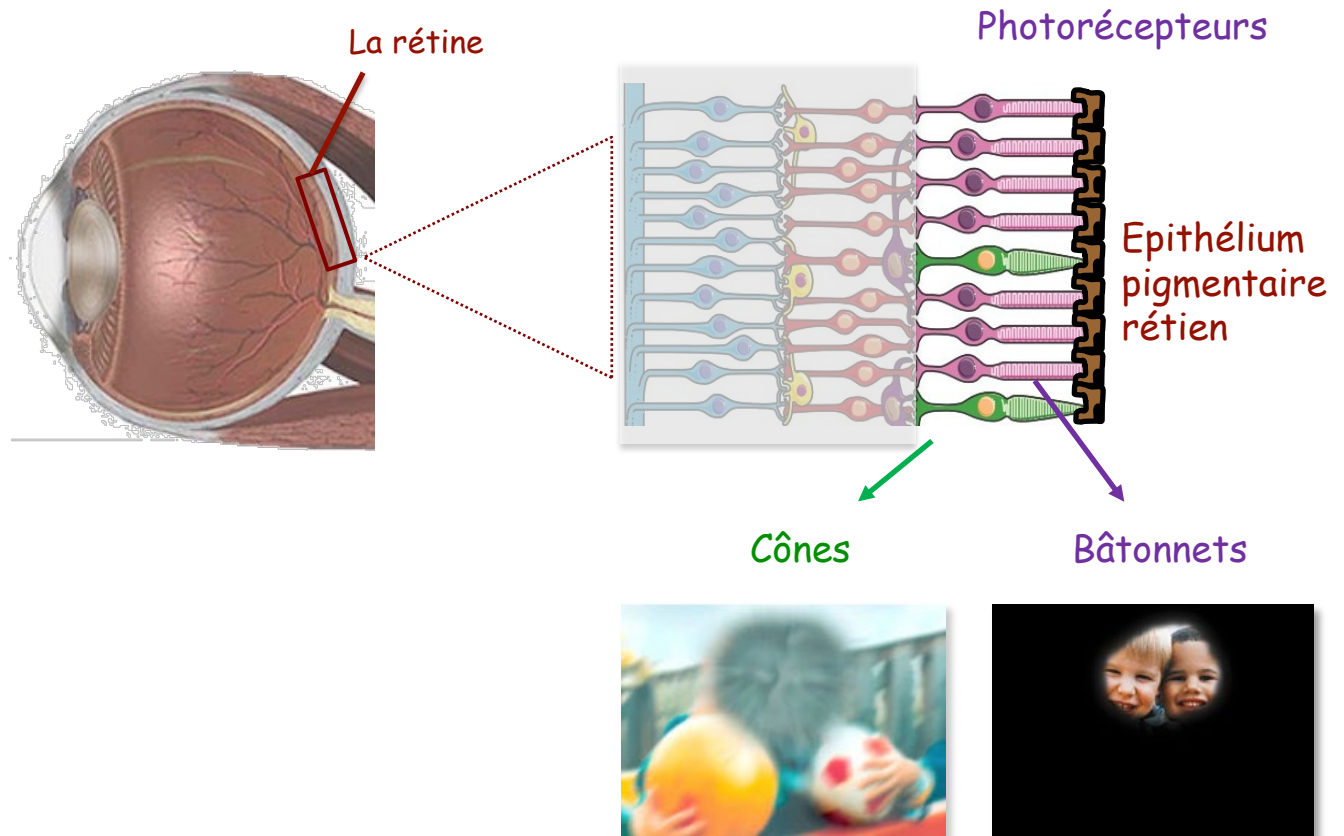


# La rétine



- Vision central
- Vision diurne
- Vision périphérique
- Vision nocturne

# Les maladies rétiniennes héréditaires



- Hétérogénéité clinique

=> Perte progressive de la vision, évolution et sévérité variable

- Cône-bâtonnet

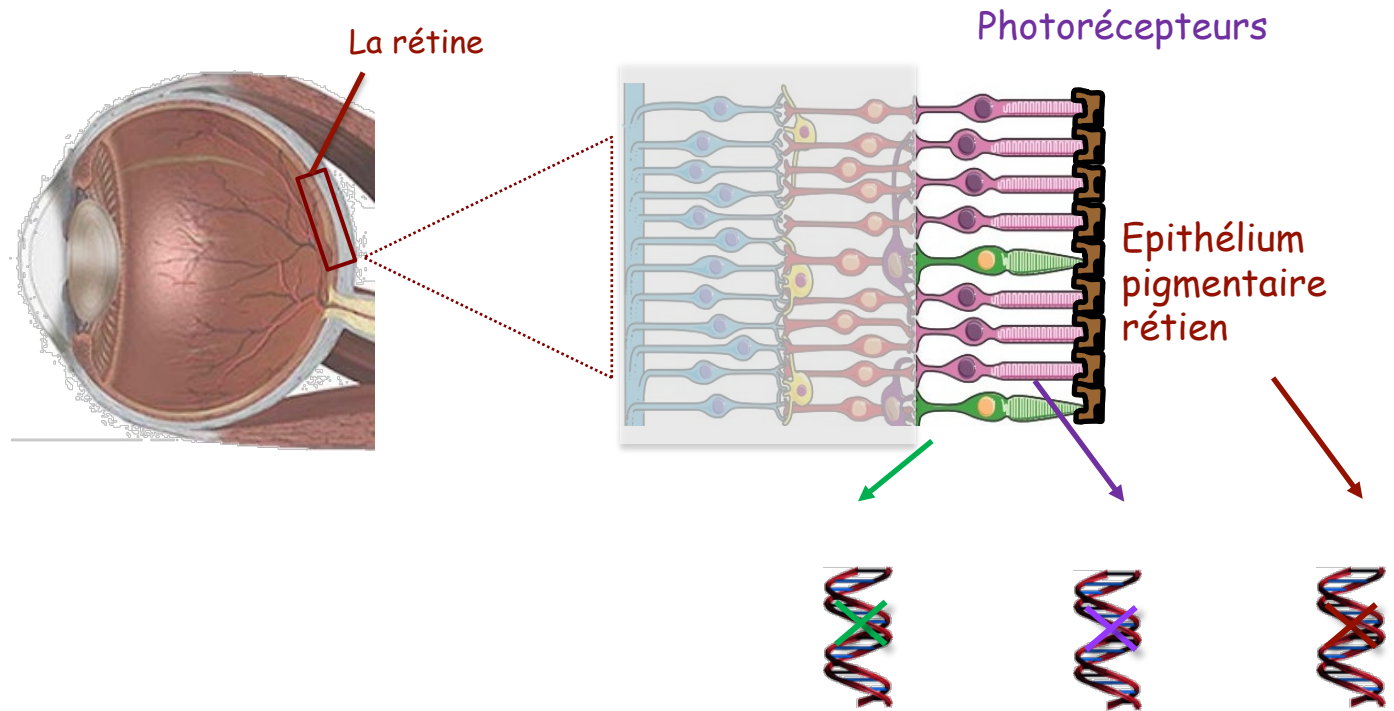
- Bâtonnet-cône



- Challenges pour la compréhension



# Les maladies rétiniennes héréditaires



- Hétérogénéité génétique

- => 270 gènes en cause = 270 différents maladies

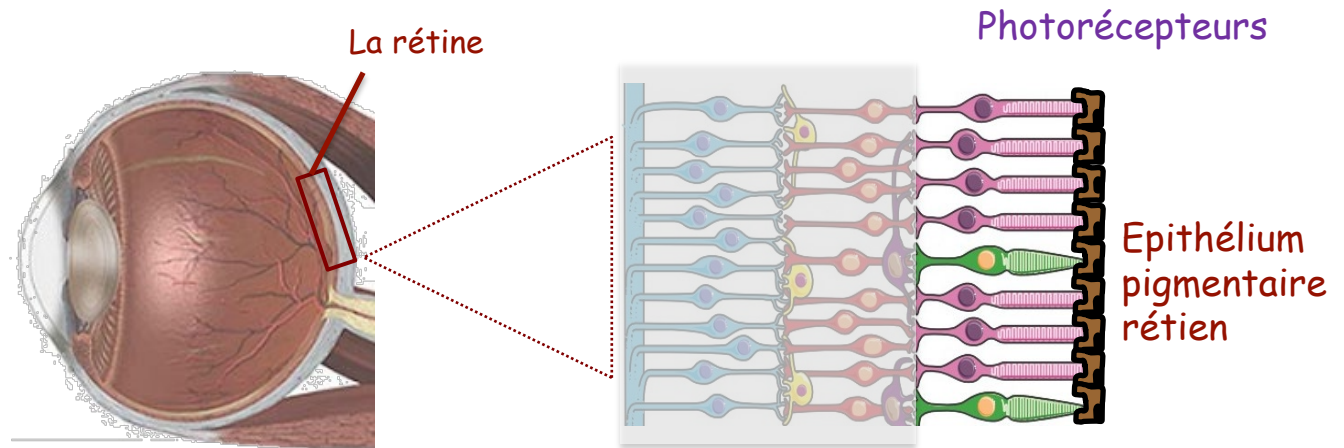
- => Mutations même gène, maladies cliniquement distinctes



- Challenges pour développer des traitements



# Modélisation des maladies rétiniennes



- Structure, distribution

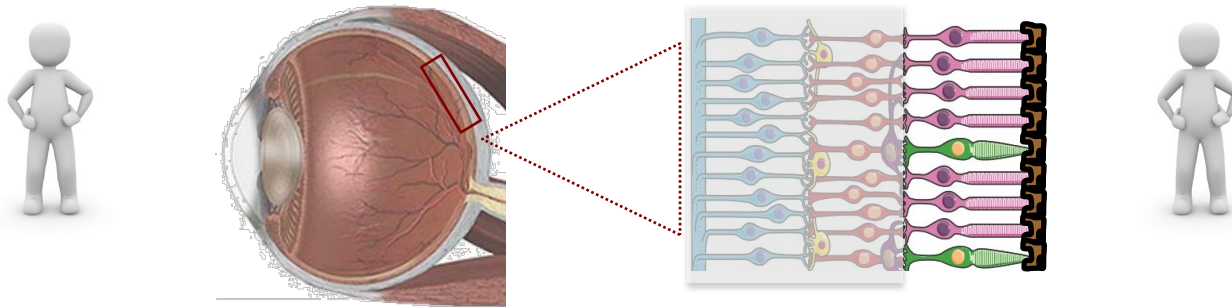


- Taille



(7x plus petit)

# Modèles rétiniennes humains

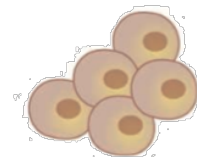


- Etudier la physiopathologie
- Tester molécules thérapeutiques

• Comment générés

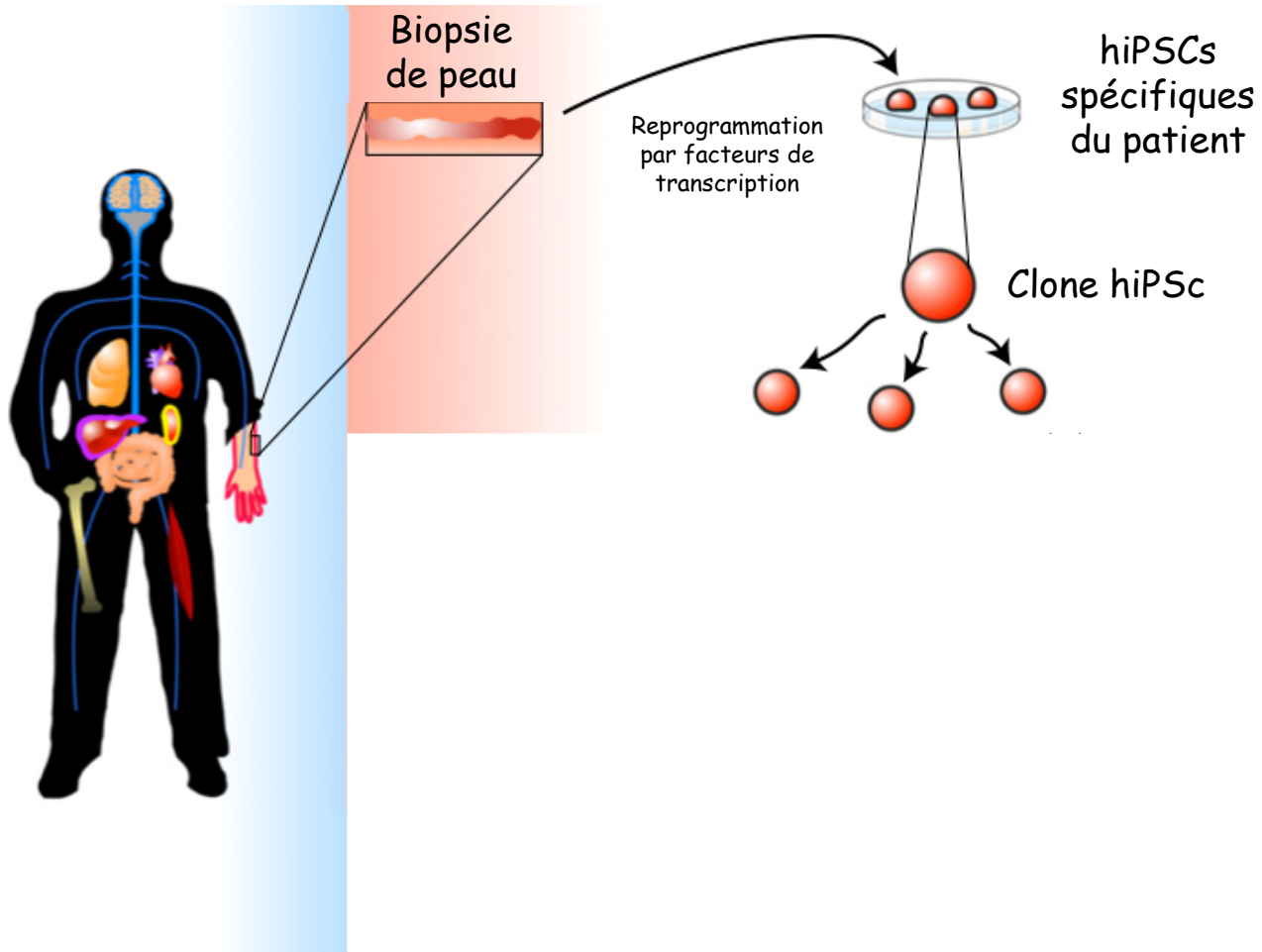


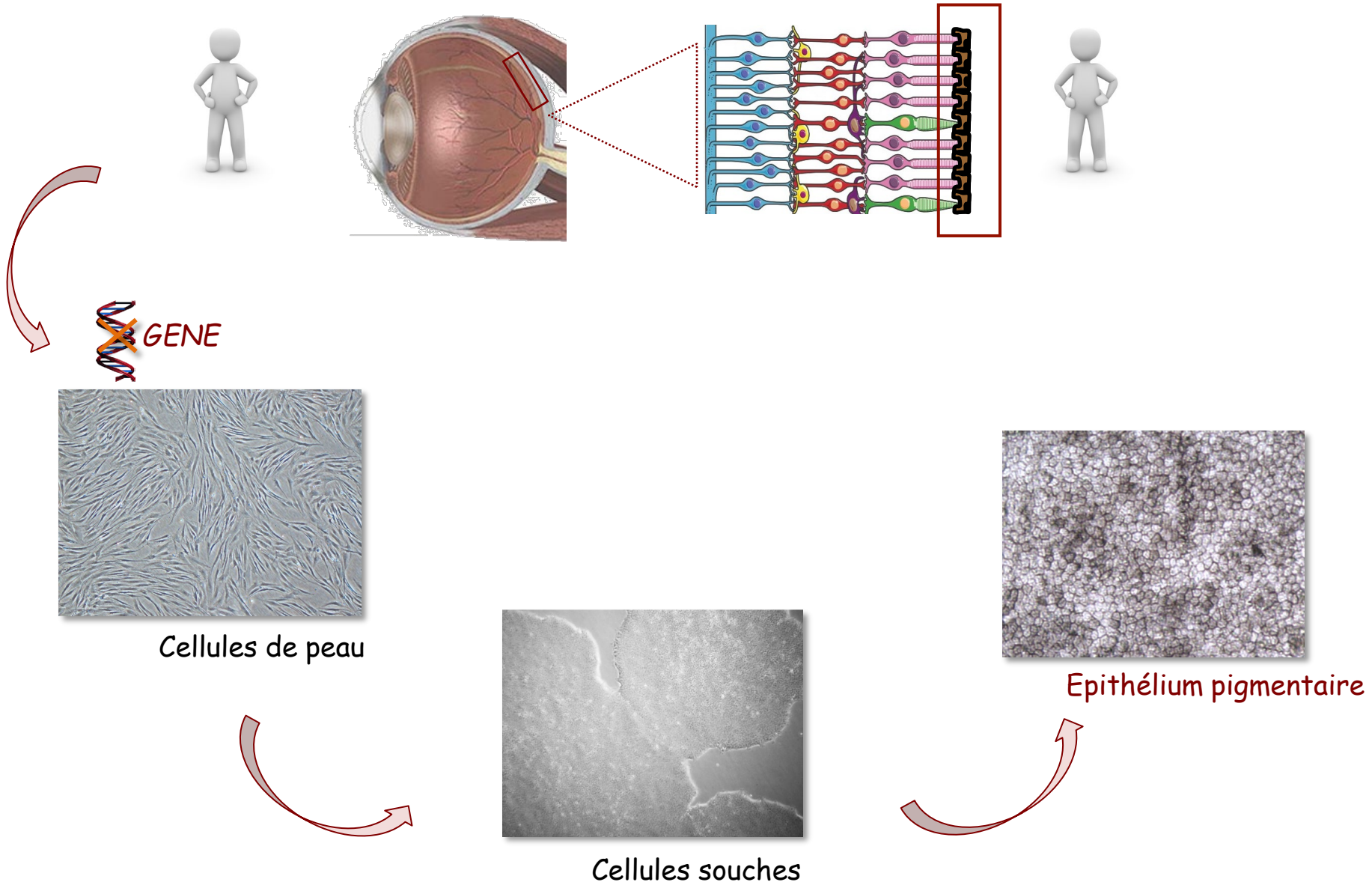
• Cellules souches





# Cellules souches pluripotentes induites (iPSC)

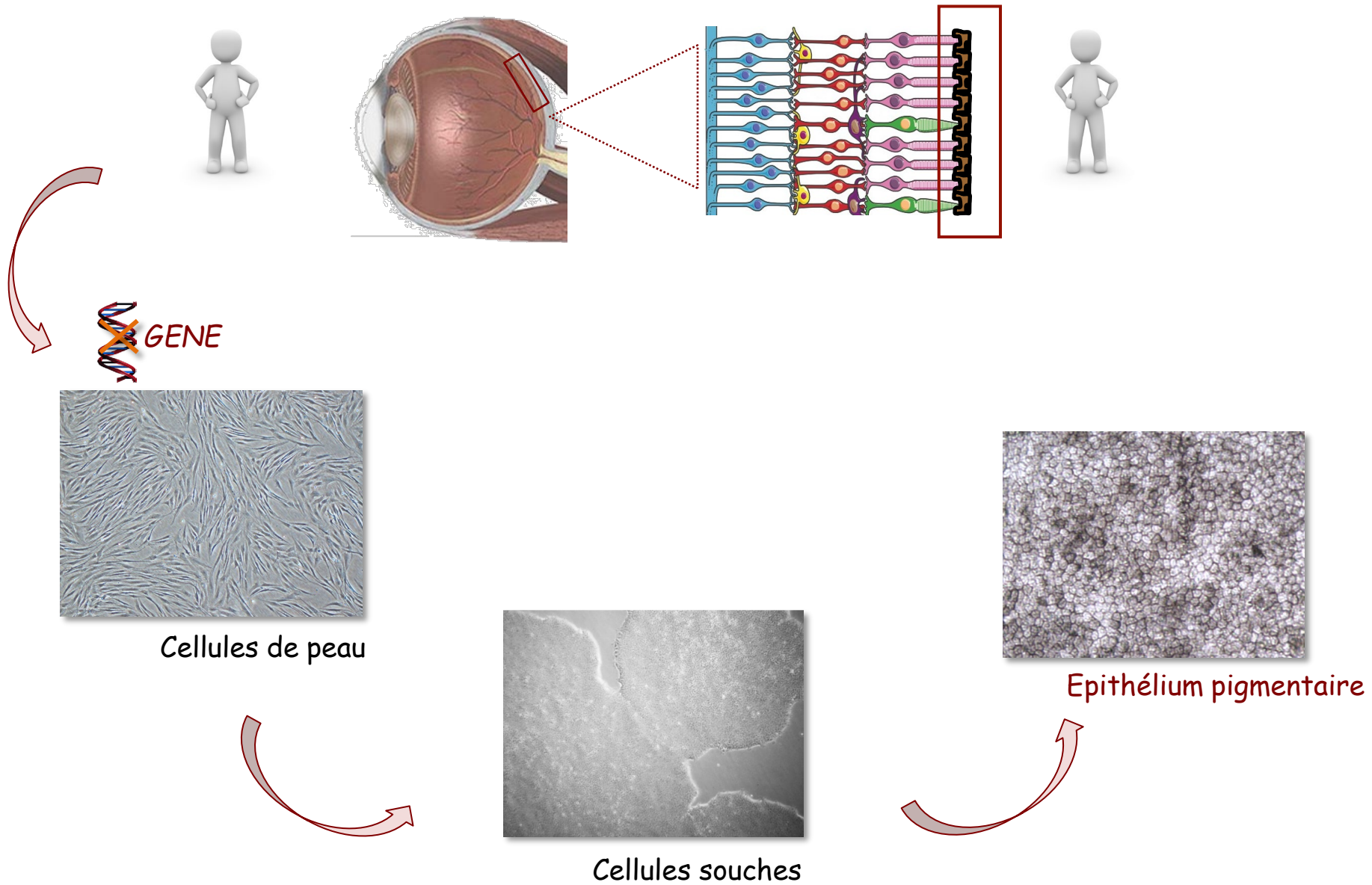






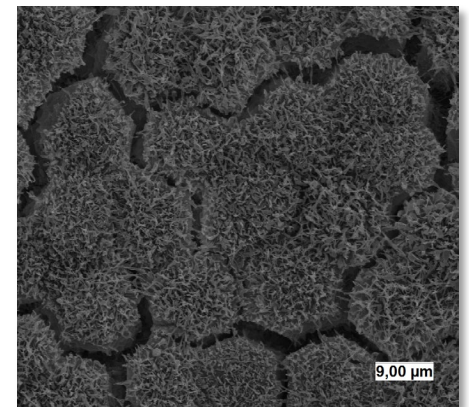
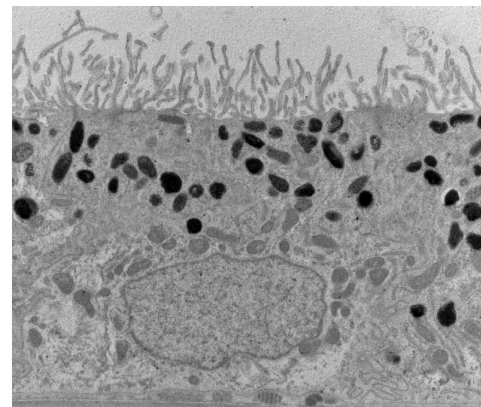
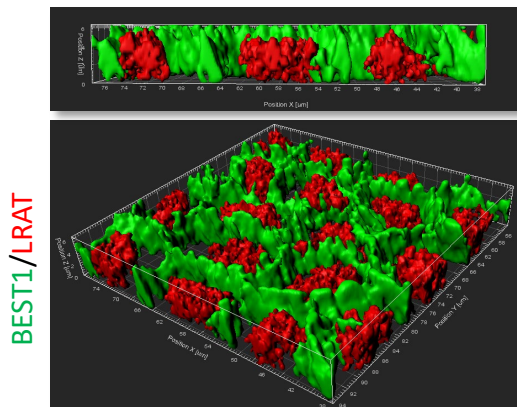
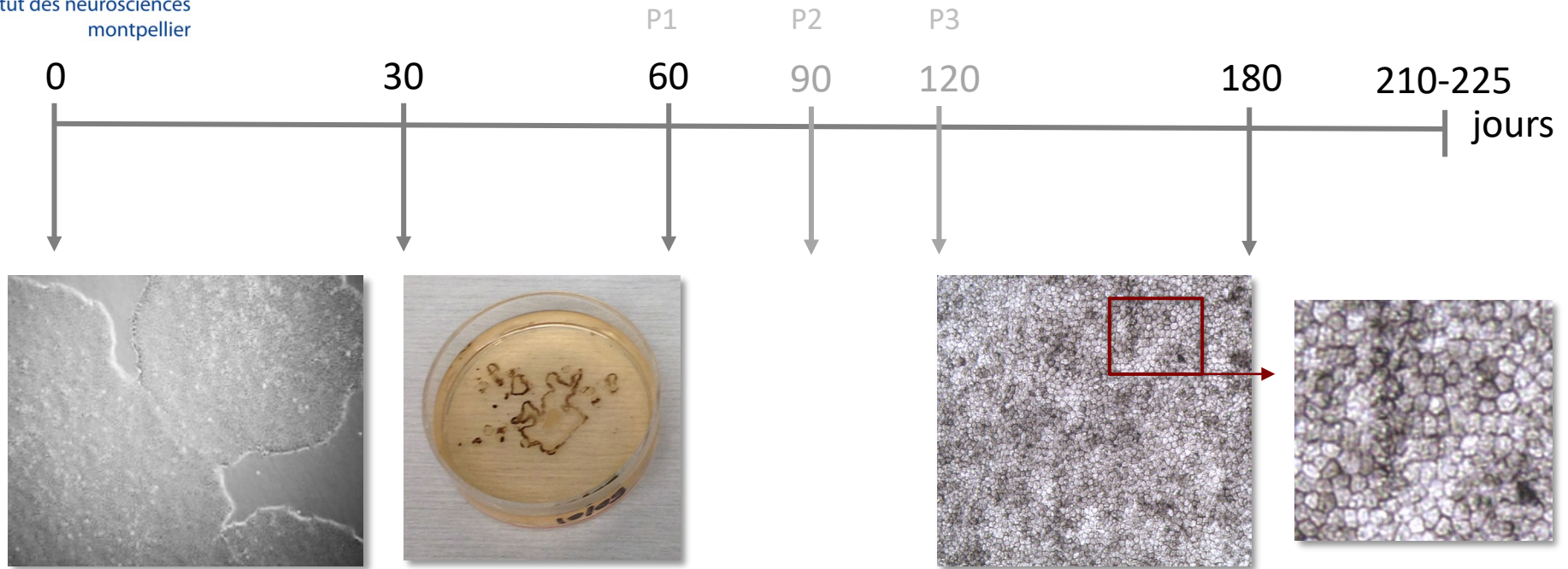


# Epithélium pigmentaire rétinien



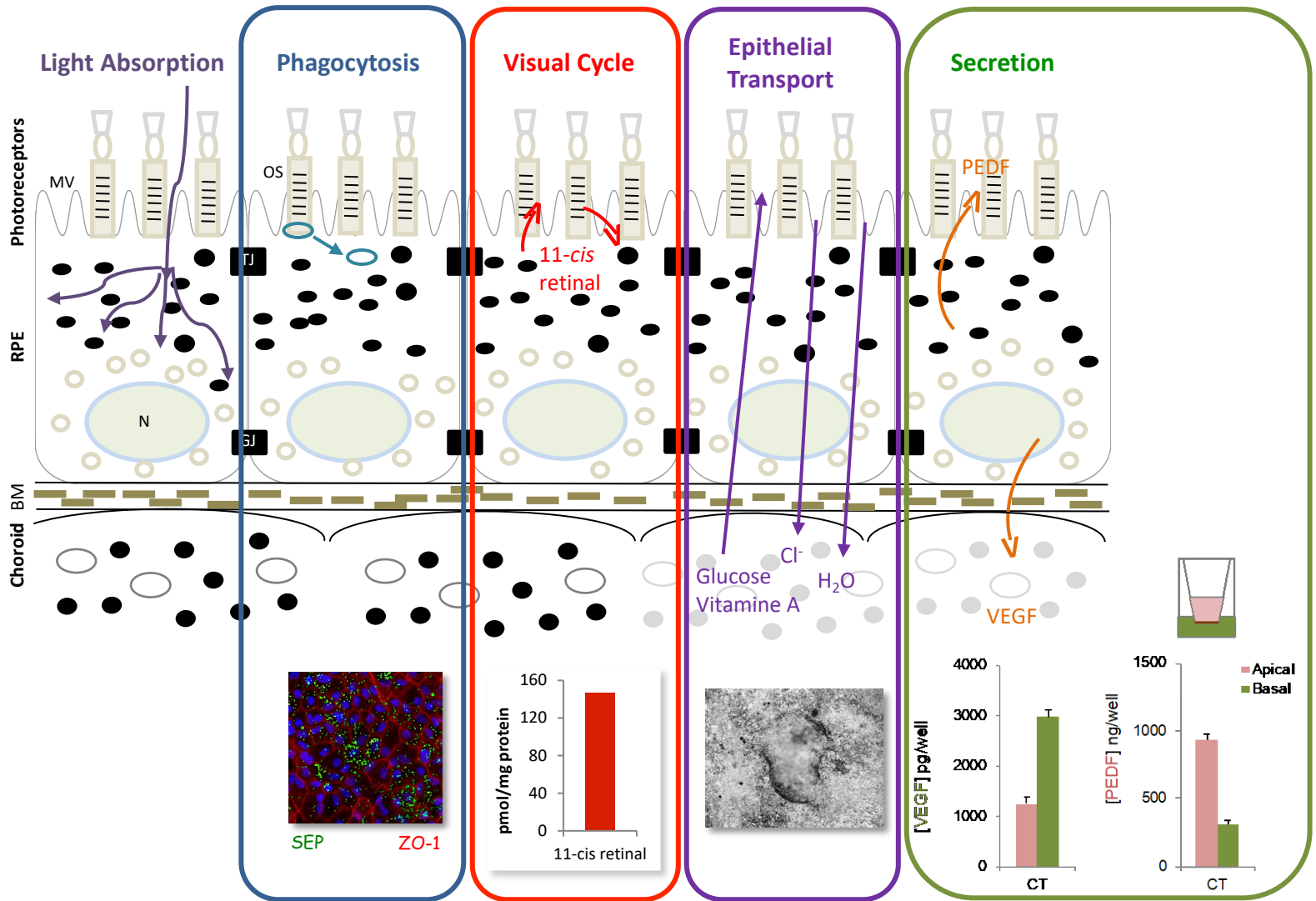


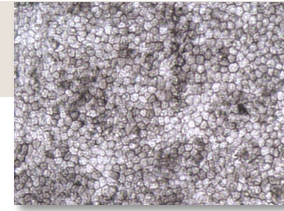
# Epithélium pigmentaire rétinien



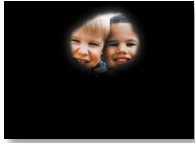
# Fonctionnalité de l'épithélium pigmentaire

De : Jazouli et al, 2021 Adv Stem Cell Biol





• Maladies rétiniennes



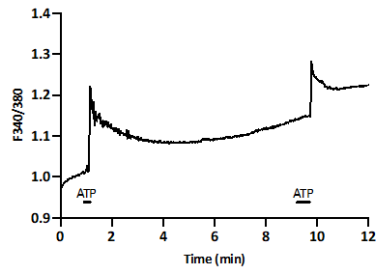
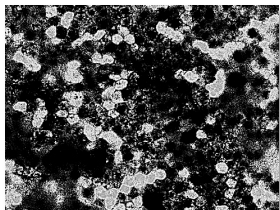
- CHM
- RLBP1
- CPH-RP

× 5  
× 3  
× 1



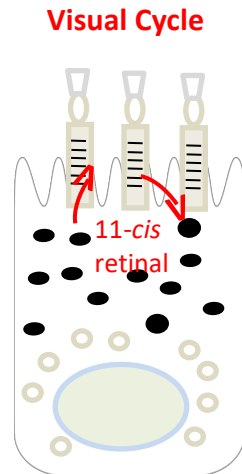
• Contrôle

• CHM



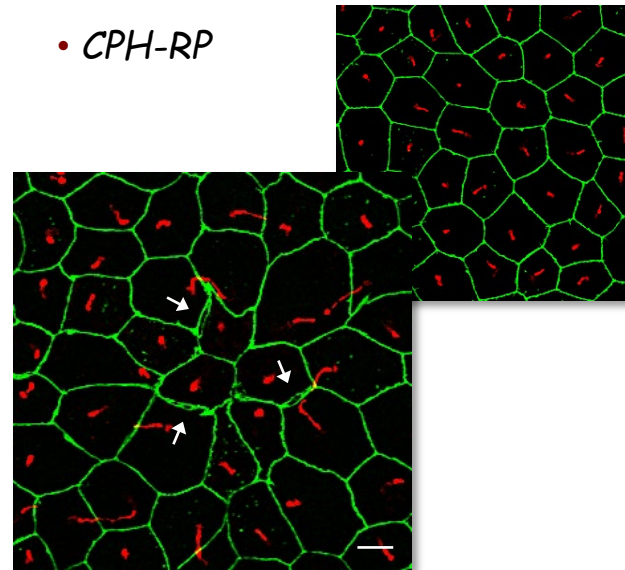
Jazouli *et al*, non publié

• RLBP1



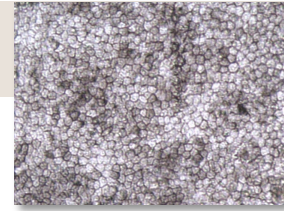
Damodar *et al*, en preparation

• CPH-RP

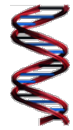
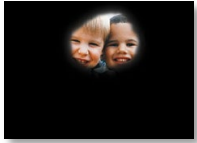


Bocquet *et al*, sous revue

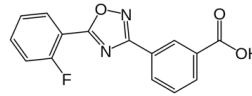
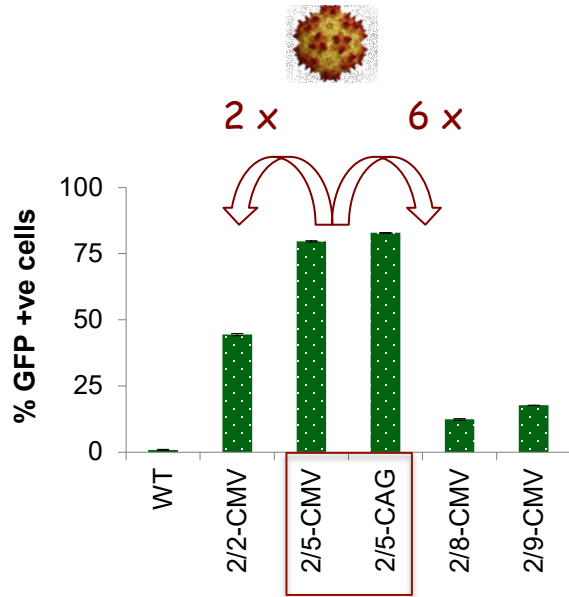




• Maladies rétinienne

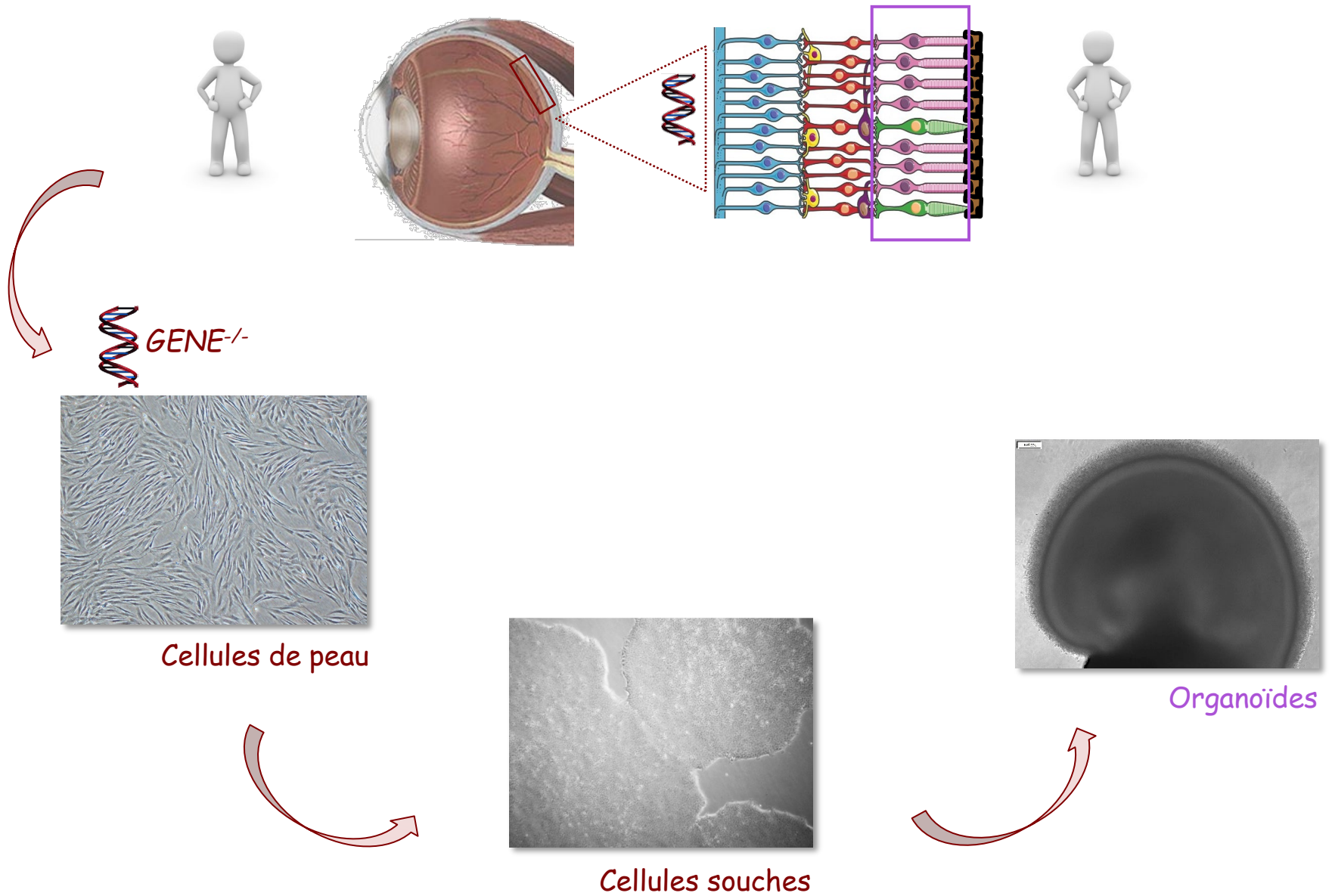


- CHM x 5
- RLBP1 x 3
- CPH-RP x 1

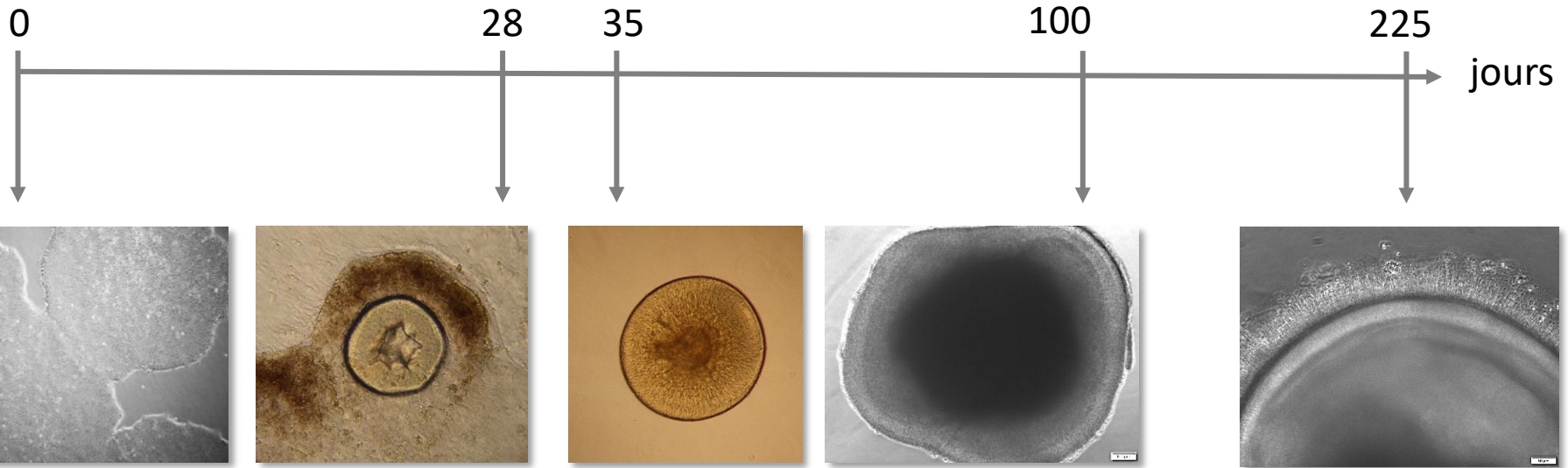


• Contexte génétique humain important

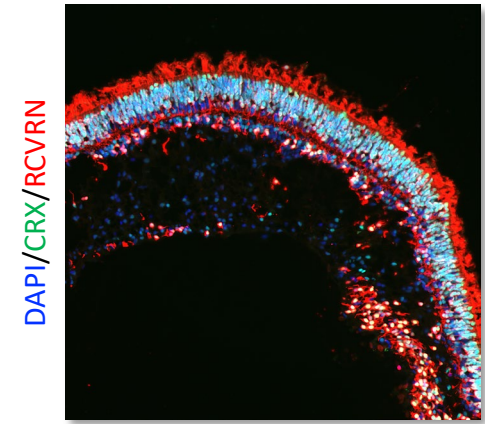
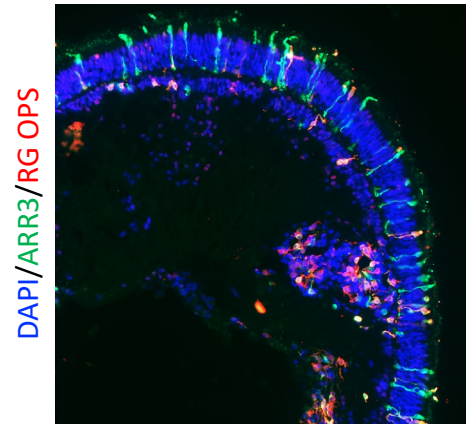
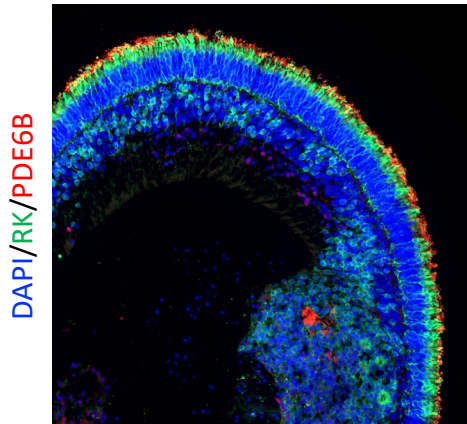
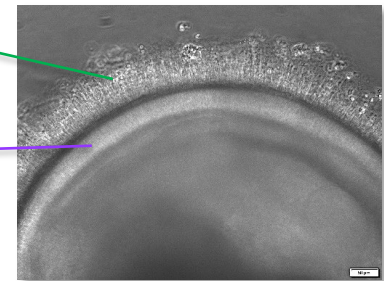
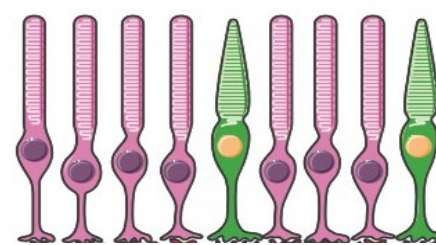
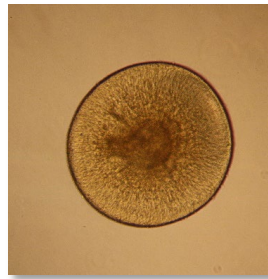
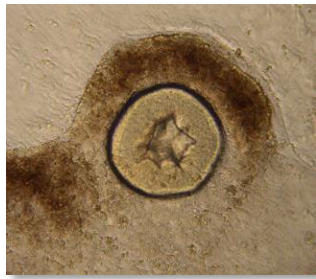
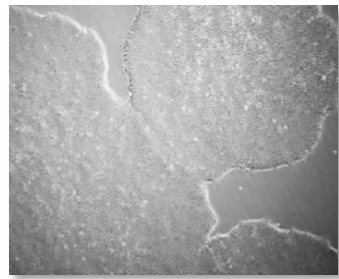
# Organoïdes rétiniens



# Organoïde rétinién avec photorecepteurs

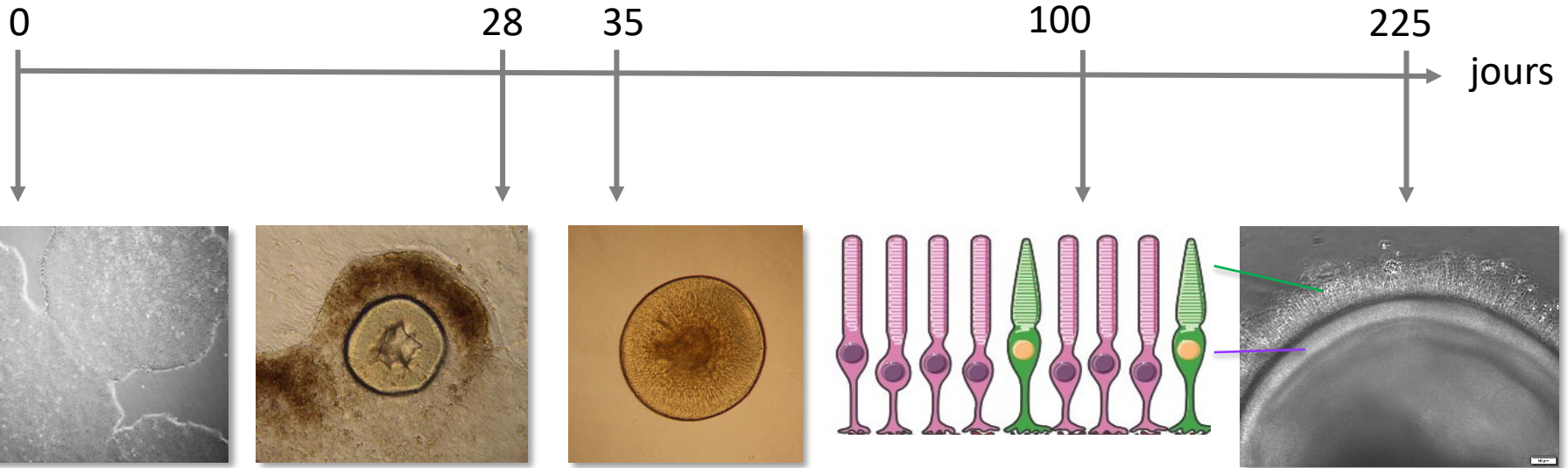


# Organoïde rétinien avec photorecepteurs

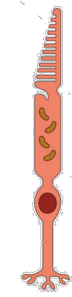




# Organoïde rétinien avec photorecepteurs

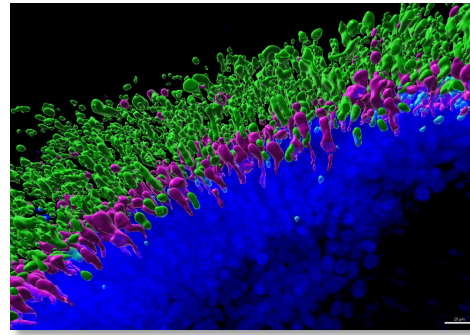


Batônnet

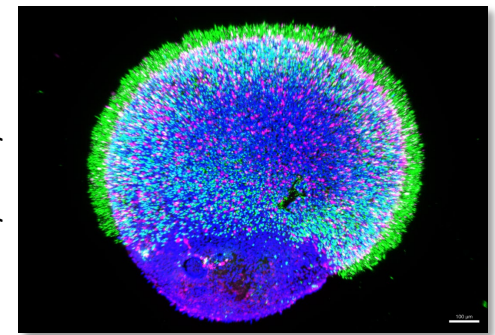


Cône

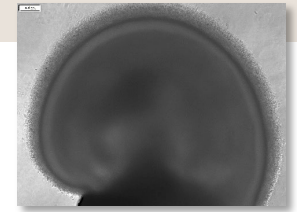
DAPI/ARR3/RHO



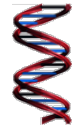
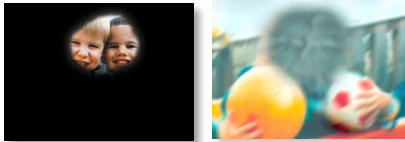
DAPI/ARR3/RHO







• Maladies rétinienne



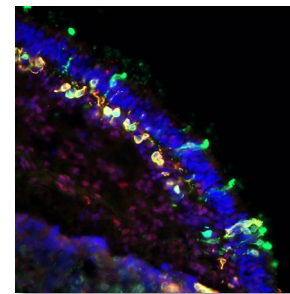
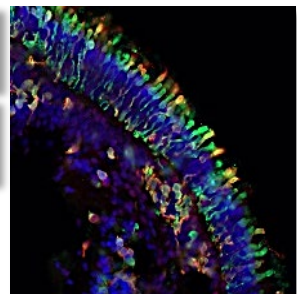
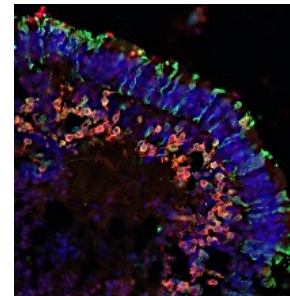
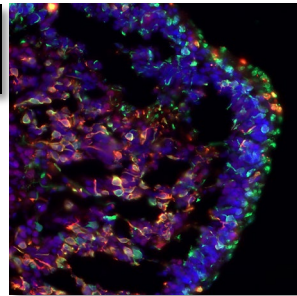
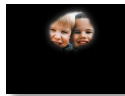
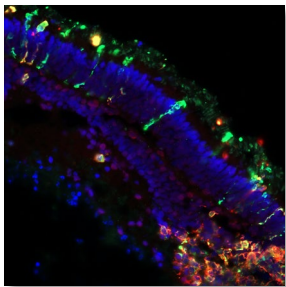
- *USH2A* × 6
- *NR2E3* × 2
- *CRX* × 3
- *ABCA4* × 1



Sanjurjo-Soriano *et al*, 2018a Stem Cell Res  
 Sanjurjo-Soriano *et al*, 2018b Stem Cell Res  
 Erkilic *et al*, 2019a Stem Cell Res  
 Erkilic *et al*, 2019b Stem Cell Res  
 Diakatou *et al*, 2021 Int J Mol Sci

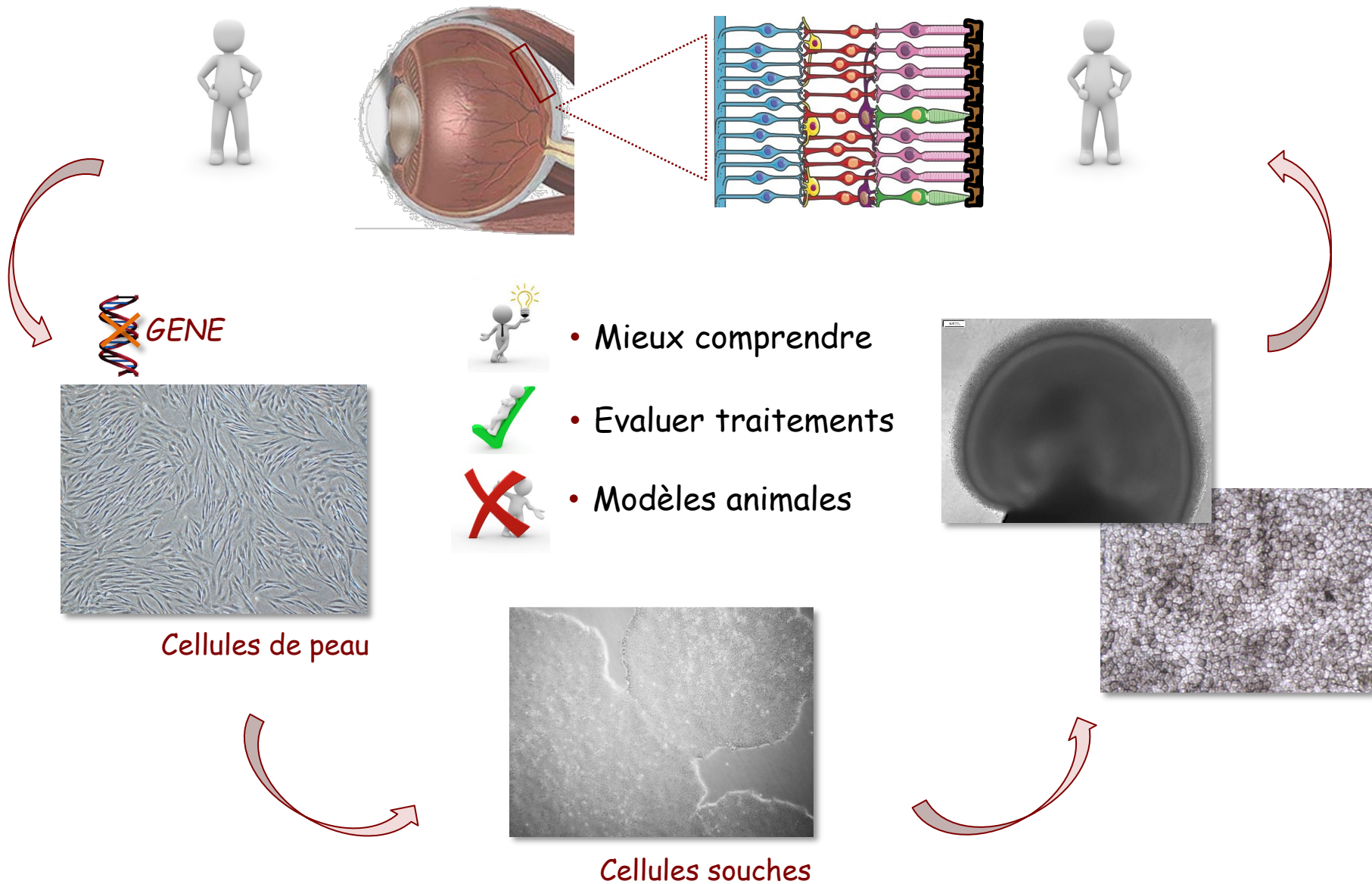


Contrôle



Sanjurjo-Soriano *et al*, 2019 Mol Ther MCD  
 Sanjurjo-Soriano *et al*, 2021 Methods Mol Biol

# Conclusion





- Equipe Vision



- Anciens membres



- En mémoire de...



Pr Christian Hamel



- Collaborateurs

S. Salinas, Montpellier  
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 H. Dollfus, Strasbourg  
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 K. Nagel-Wolfrum, Mainz, Allemagne  
 E. Van Wijk, Neijmegen, Pays-Bas  
 I. MacDonald, Alberta, Canada

- Financeurs



- Patients

