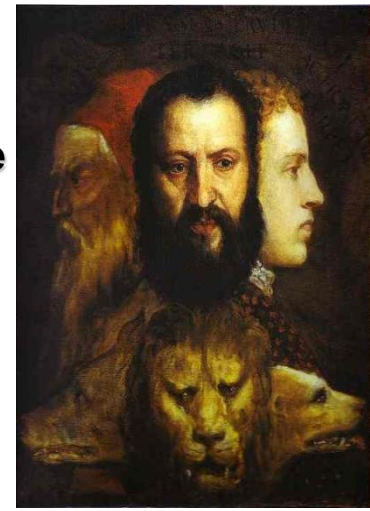


# Perte de l'audition liée au vieillessement

Jing Wang

Institute for Neurosciences of Montpellier  
Inserm U1051

Sagesse



Innocence

Maturité

## 1. Vieillesse:

- **Aspects physiologiques:** la perte progressive des fonctions physiologiques de l'organisme: respiration, circulation, locomotion, capacités sensorielles, fertilité...
- **Aspects émotionnels:** le sentiment d'inutilité, de la solitude et de l'abandon .

## 2. Maladies liées au vieillissement:

Alzheimer, Parkinson, cancers, presbycusie...

# Théories du Vieillissement

(plus de 300 théories)

## 1. Théories évolutionnistes du vieillissement (*Charles Darwin en 1859*):

Adaptation, sélection naturelle, renouvellement...

## 2. Théories métaboliques « Usure »: les cellules endommagées par leur sur-utilisation et les abus qu'elles subissent (toxines alimentaires, stress environnemental...)

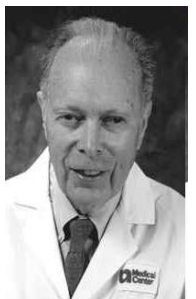
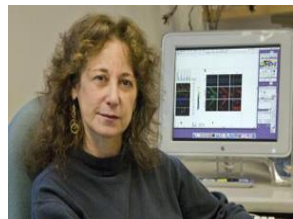
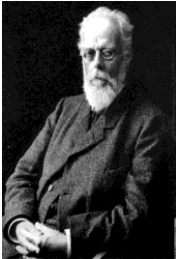
*Auguste Weismann en 1882*

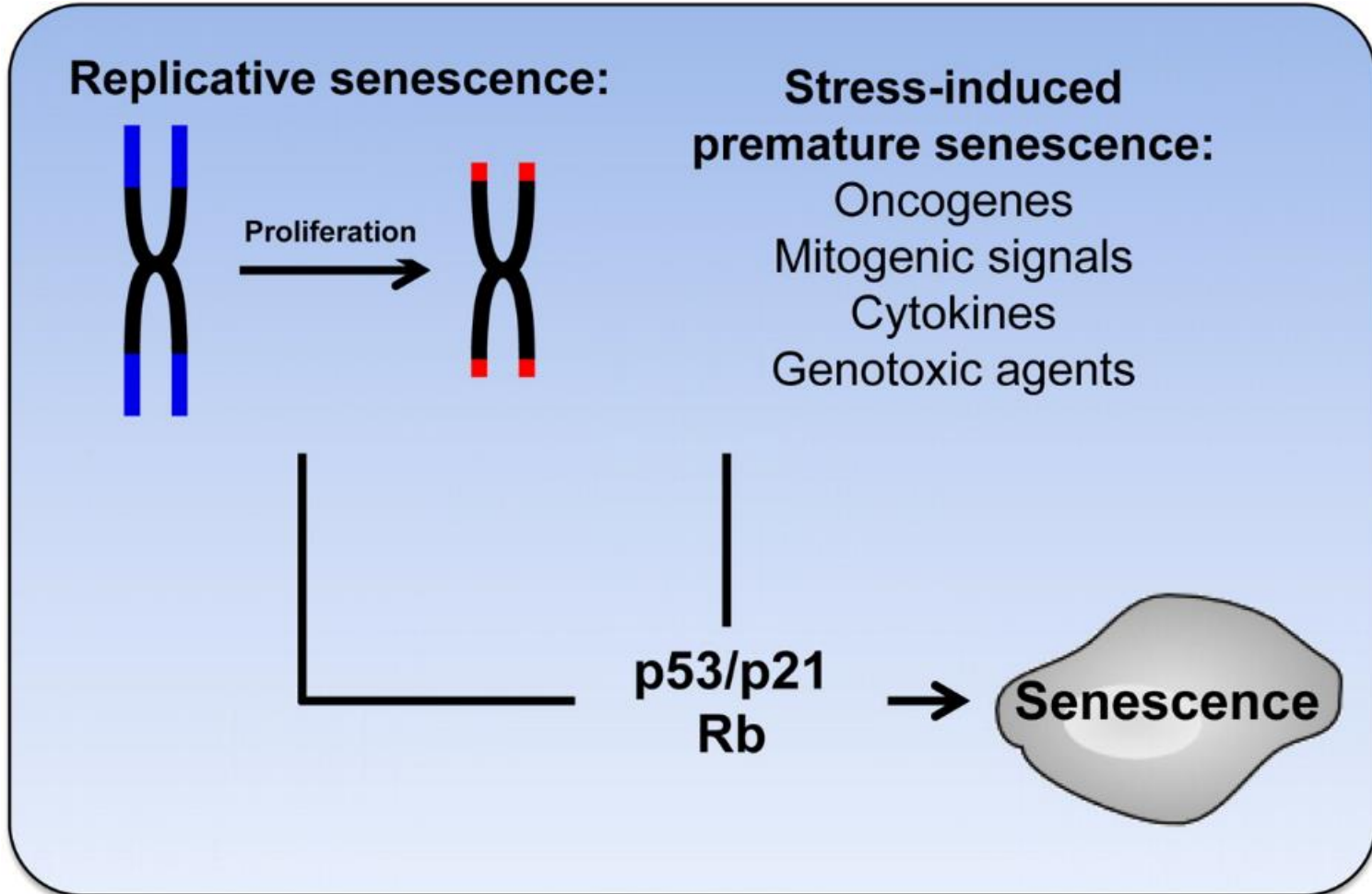
## 3. Théories génétiques:

- Horloges biologiques: raccourcissement des télomères (génétiquement programmés) *Campisi, 1997*
- Accumulation d'erreurs

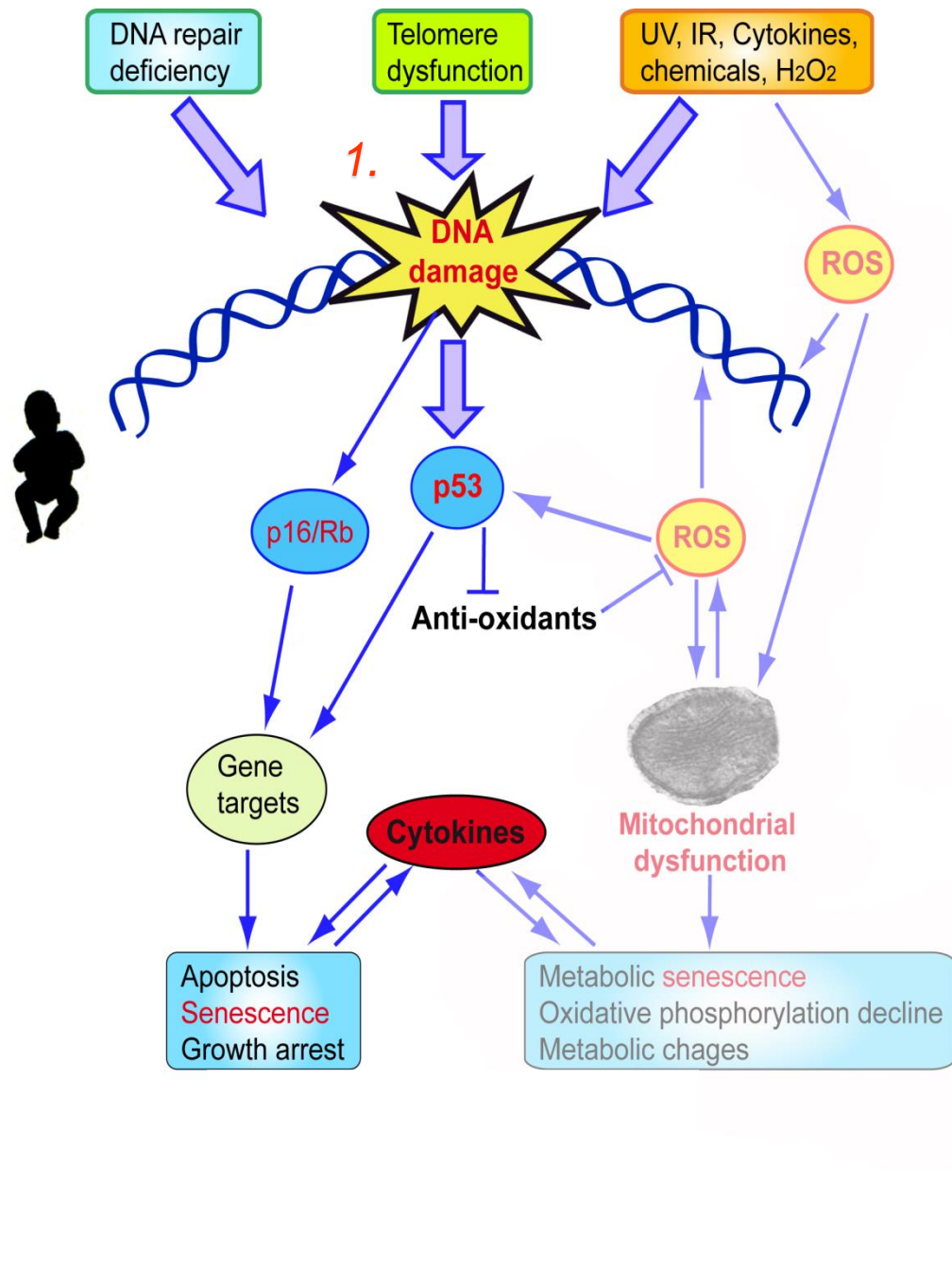
## 4. Théories environnementales:

- Radicaux libres de l'oxygène, *Harman, 1972*
- Pollution, radiations...





# Vieillessement



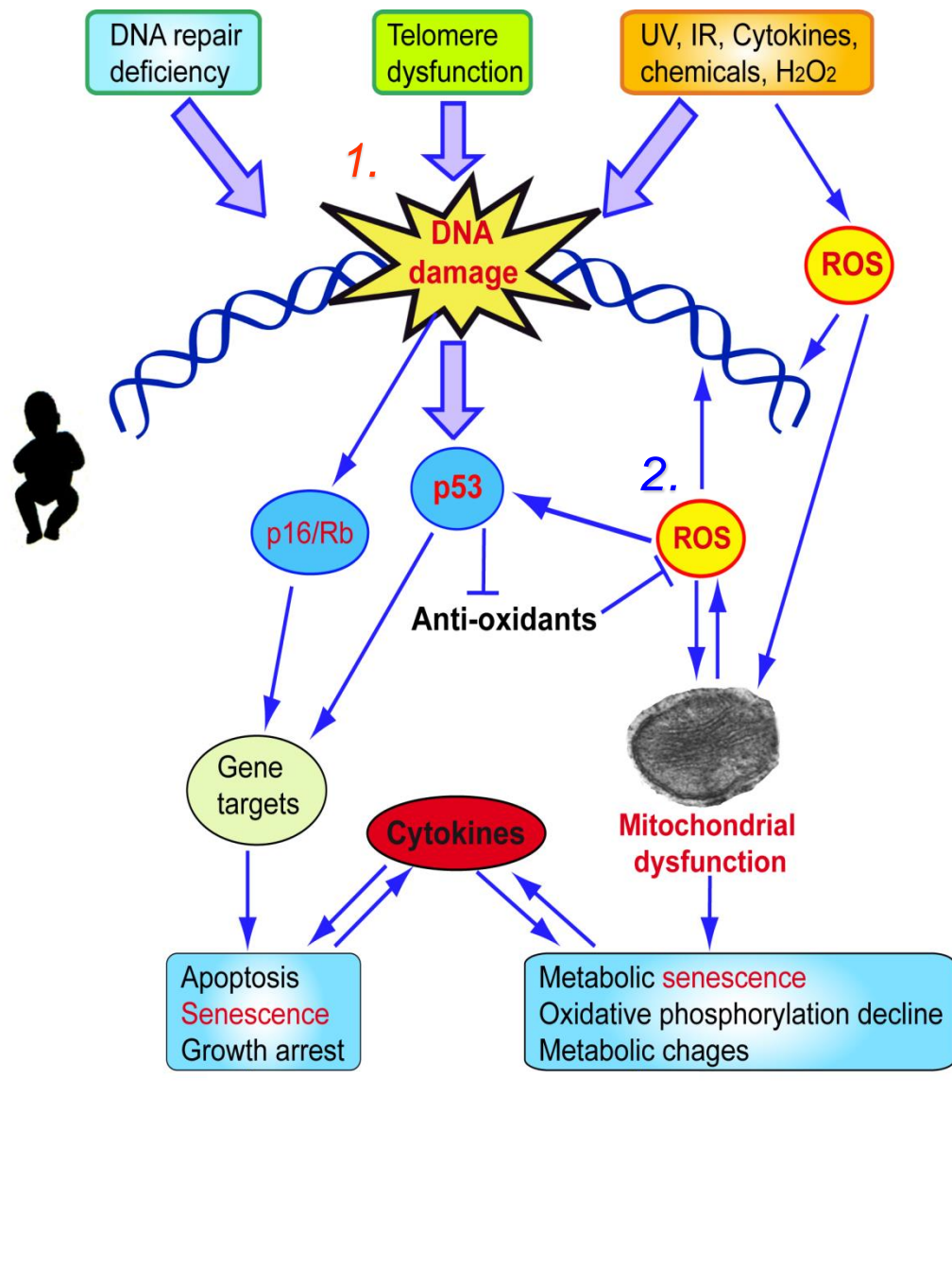
Adapté de :

Sahin E and Depinho RA, *Nature*, 464, 25, 2010;

Finkel T et al., *Nature*, 448, 16, 2007;

Nemoto S and Finkel T, *Nature*, 429, 13, 2004

# Vieillessement



Adapté de :

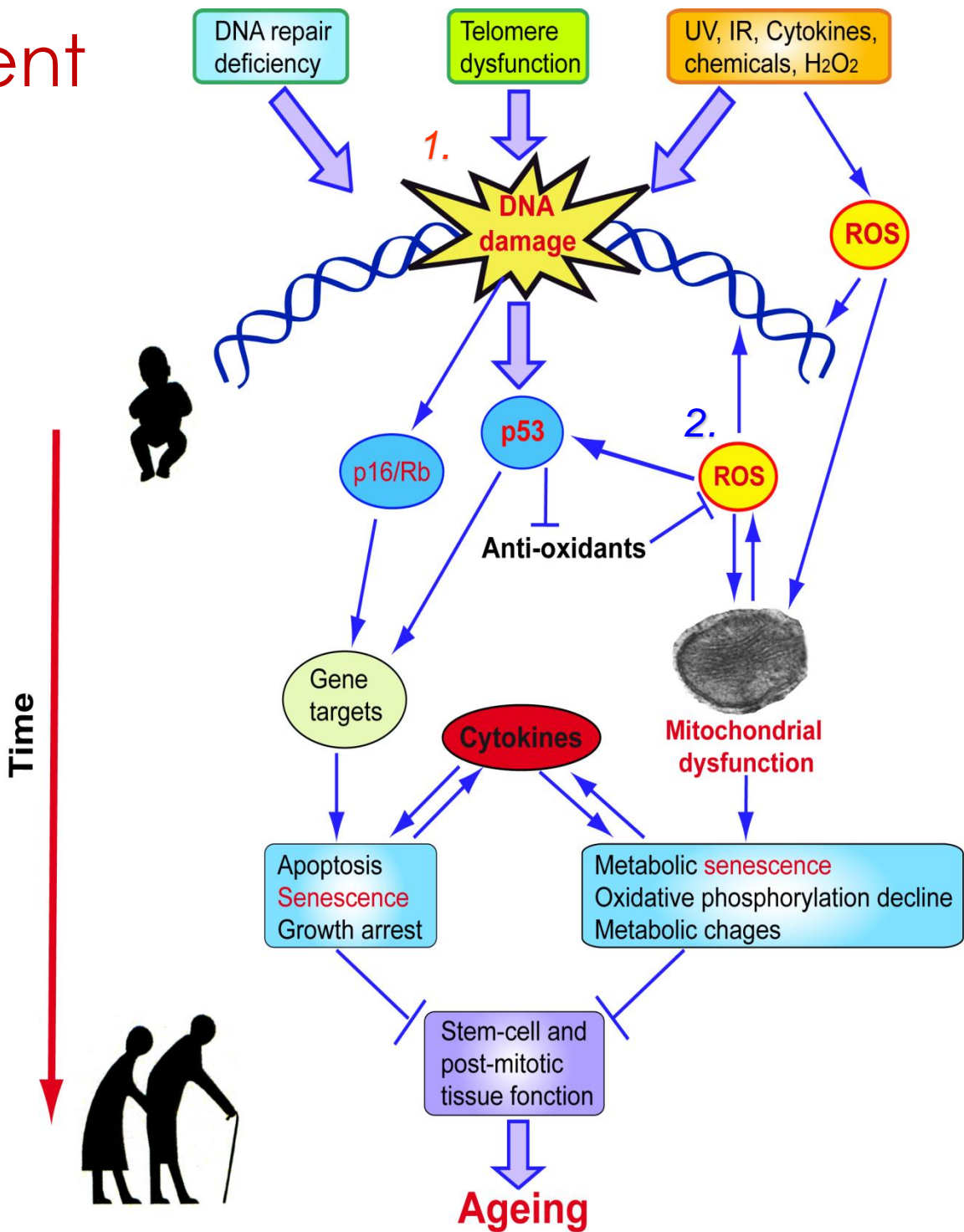
Sahin E and Depinho RA, *Nature*, 464, 25, 2010;

Finkel T et al., *Nature*, 448, 16, 2007;

Nemoto S and Finkel T, *Nature*, 429, 13, 2004



# Vieillessement



Adapté de :

Sahin E and Depinho RA, *Nature*, 464, 25, 2010;

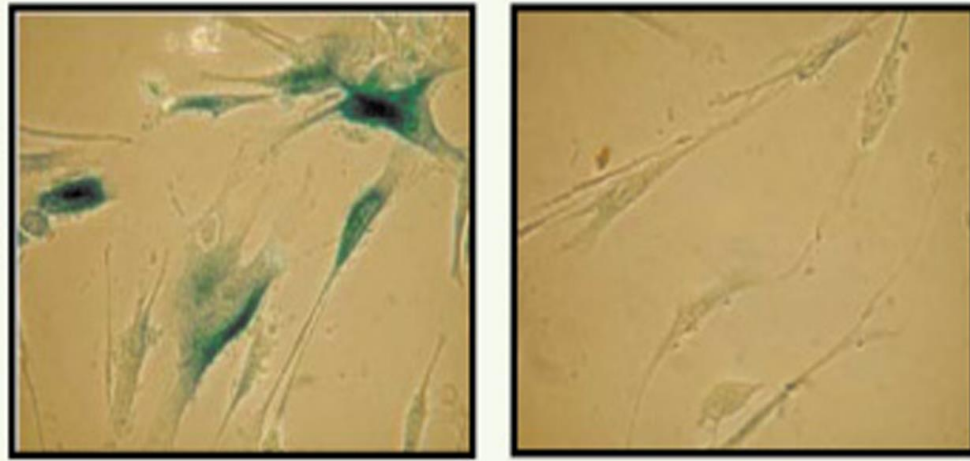
Finkel T et al., *Nature*, 448, 16, 2007;

Nemoto S and Finkel T, *Nature*, 429, 13, 2004

# Cellules sénescentes

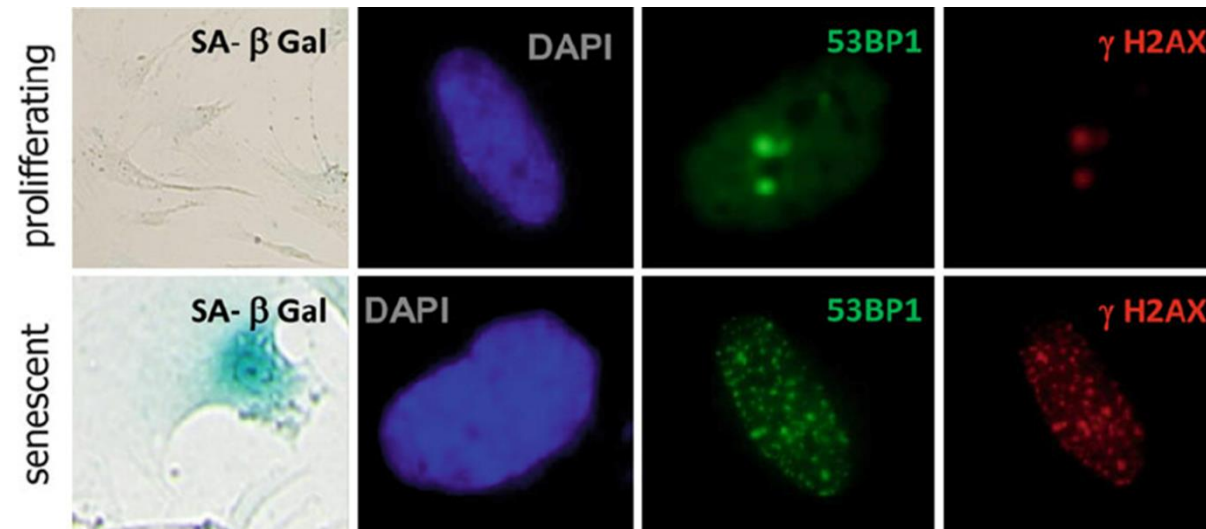
Sénescent

Pré-sénescence



**Morphologies:** *aplatissement, vacuolisation, lipofuscine....*

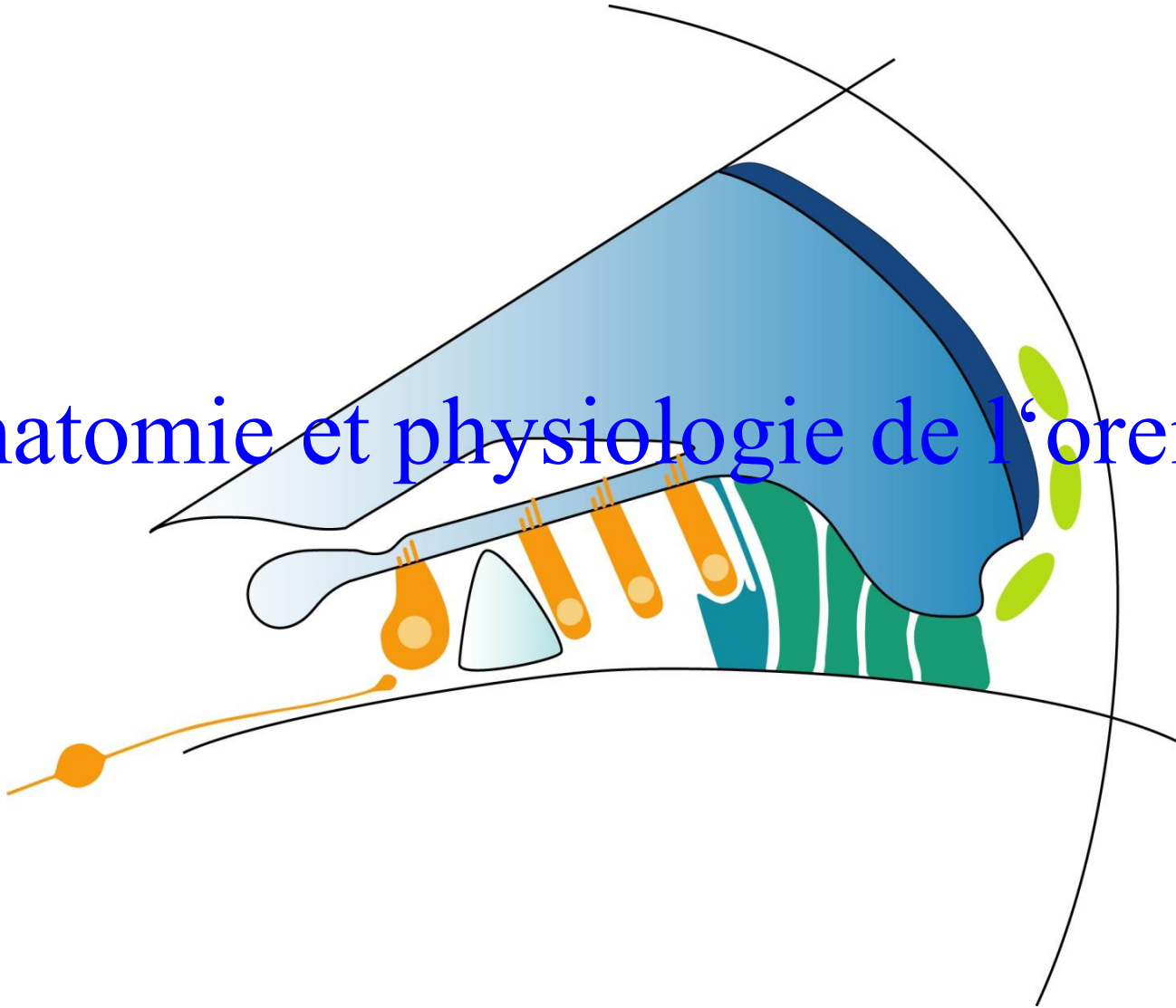
**Biochimies et moléculaire:** SA-β-Gal, p21, p53, p15...



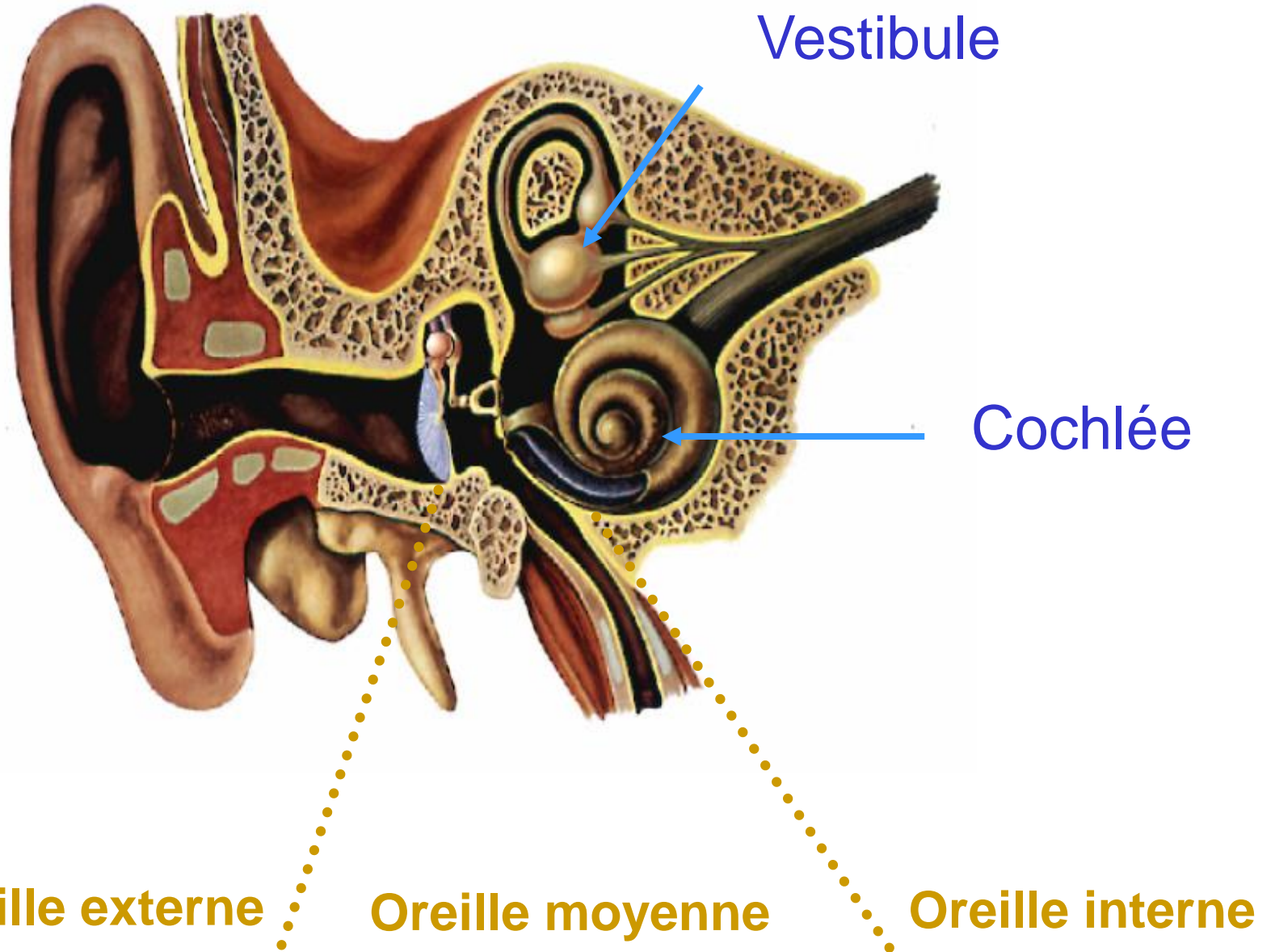
**Chromatine:** SAHFs, p-H2AX, 53BP1



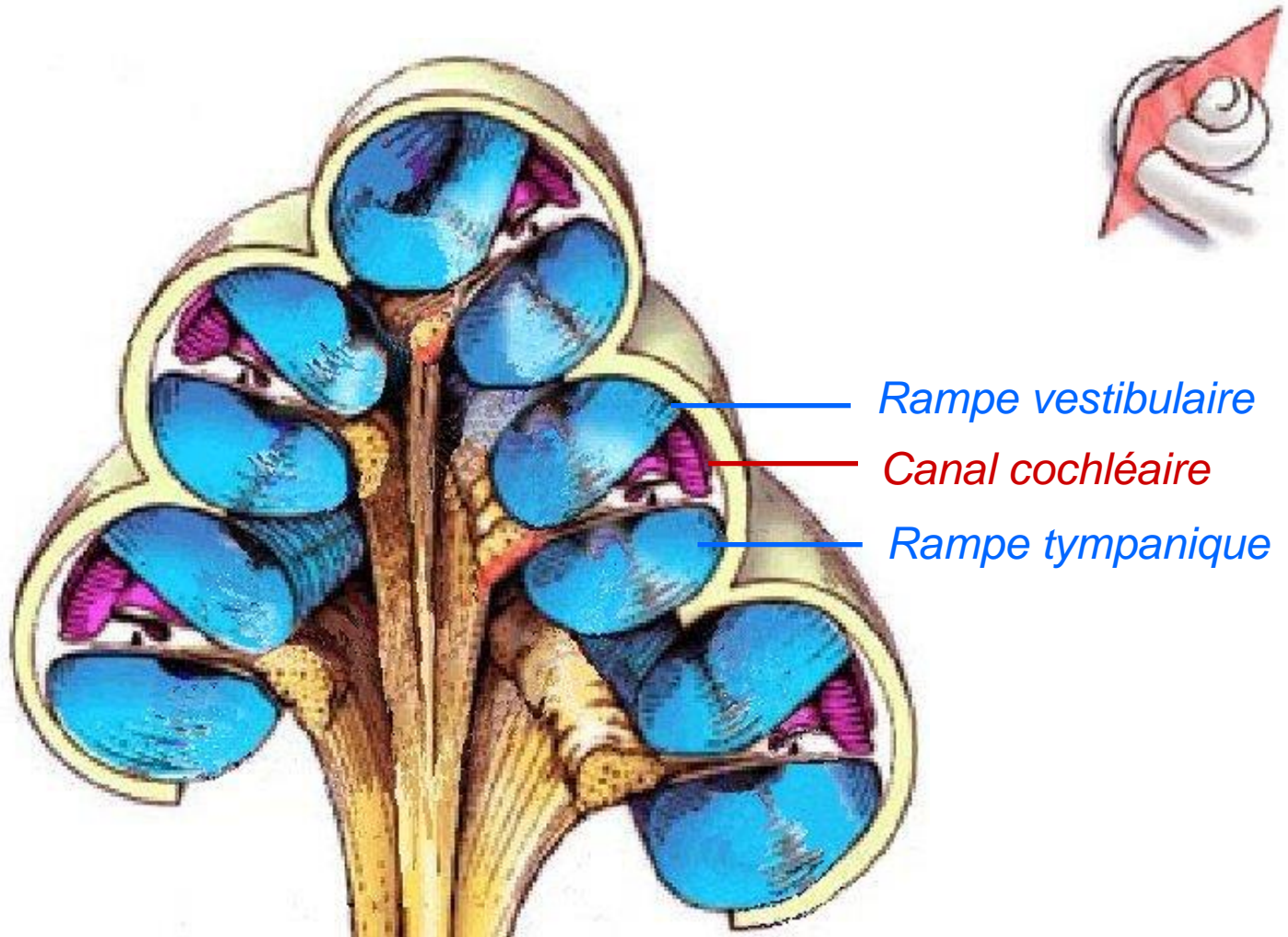
# Anatomie et physiologie de l'oreille



# L'oreille

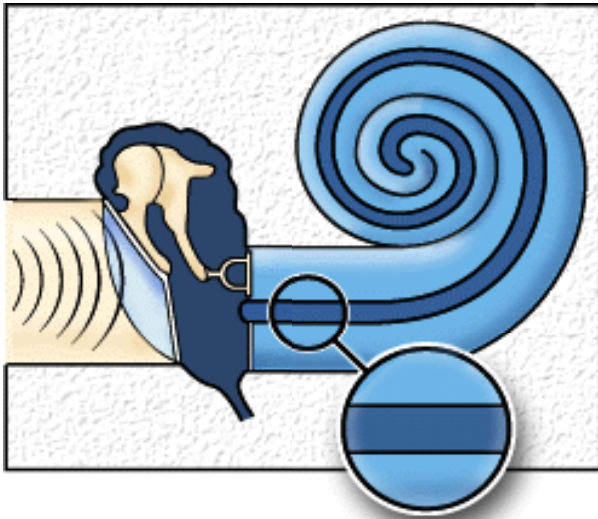


# L'oreille



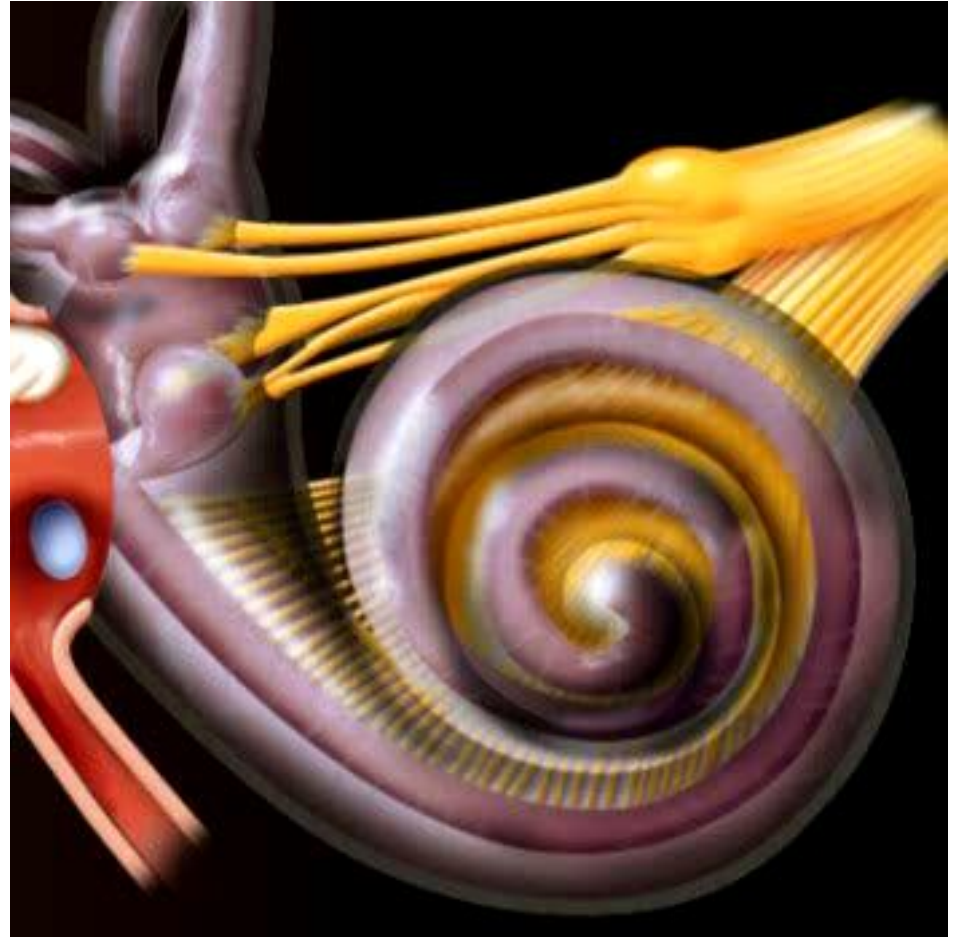
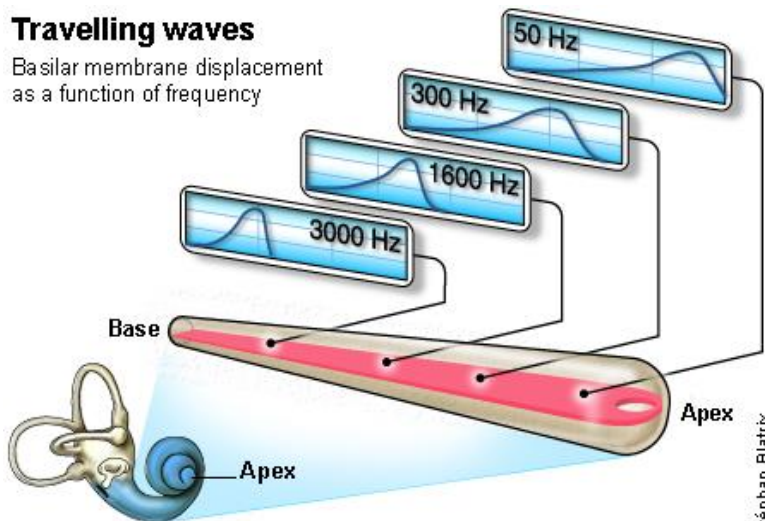


# Distribution des fréquences le long de la membrane basilaire



## Travelling waves

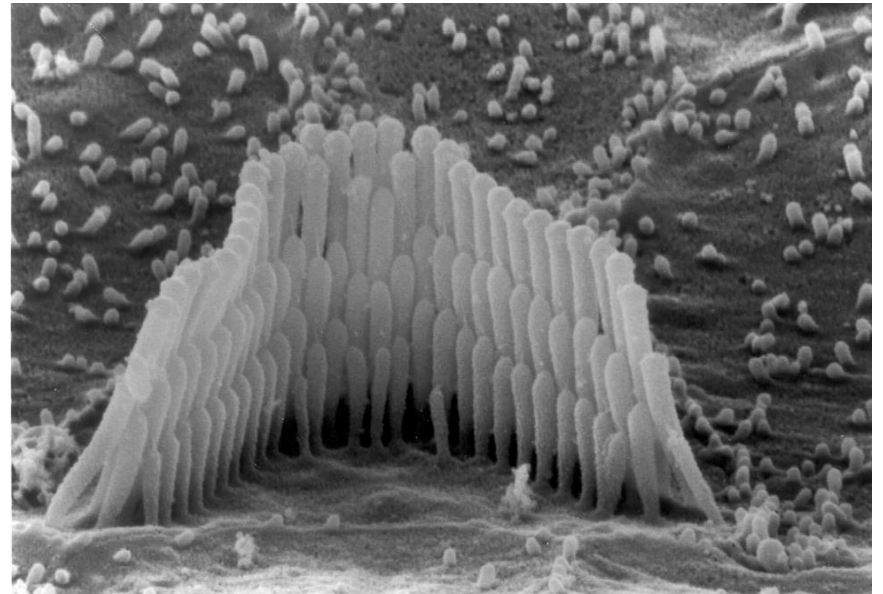
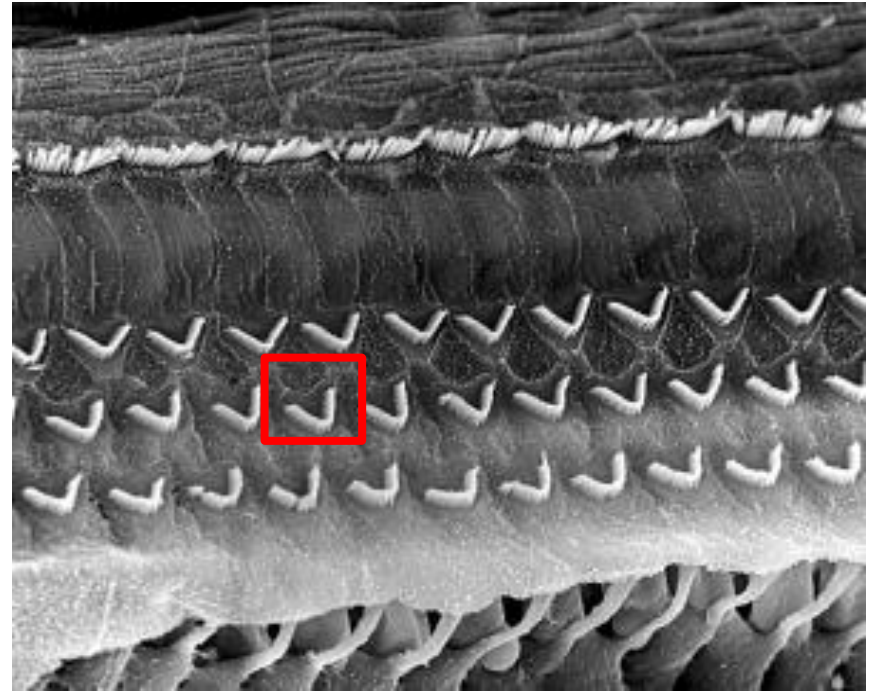
Basilar membrane displacement as a function of frequency



# Distribution des fréquences le long de la membrane basilaire

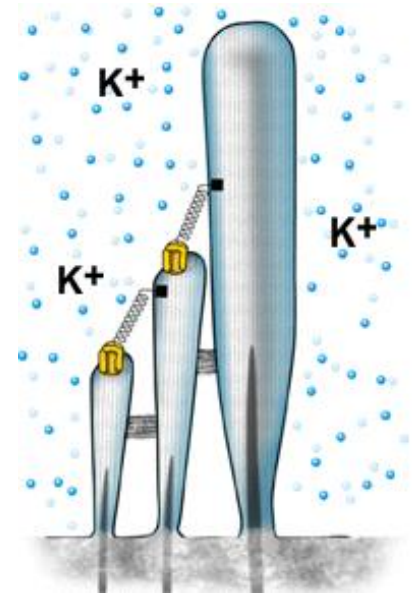
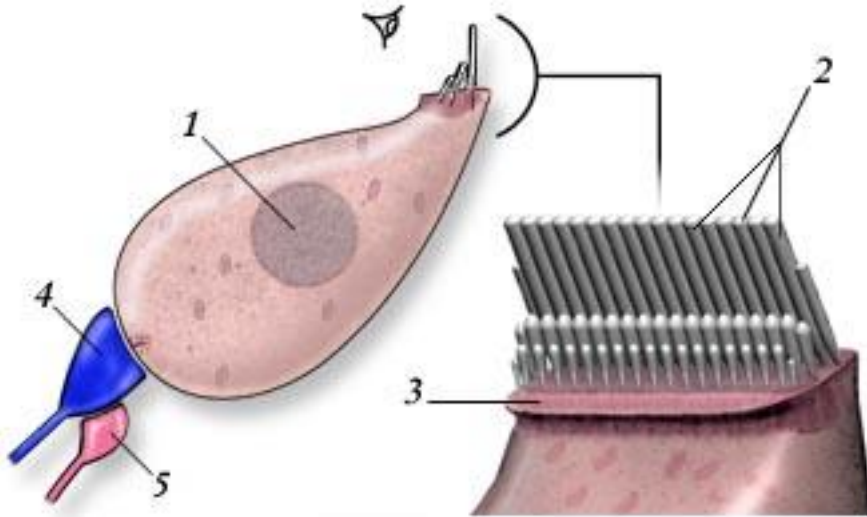


# L'organe de Corti

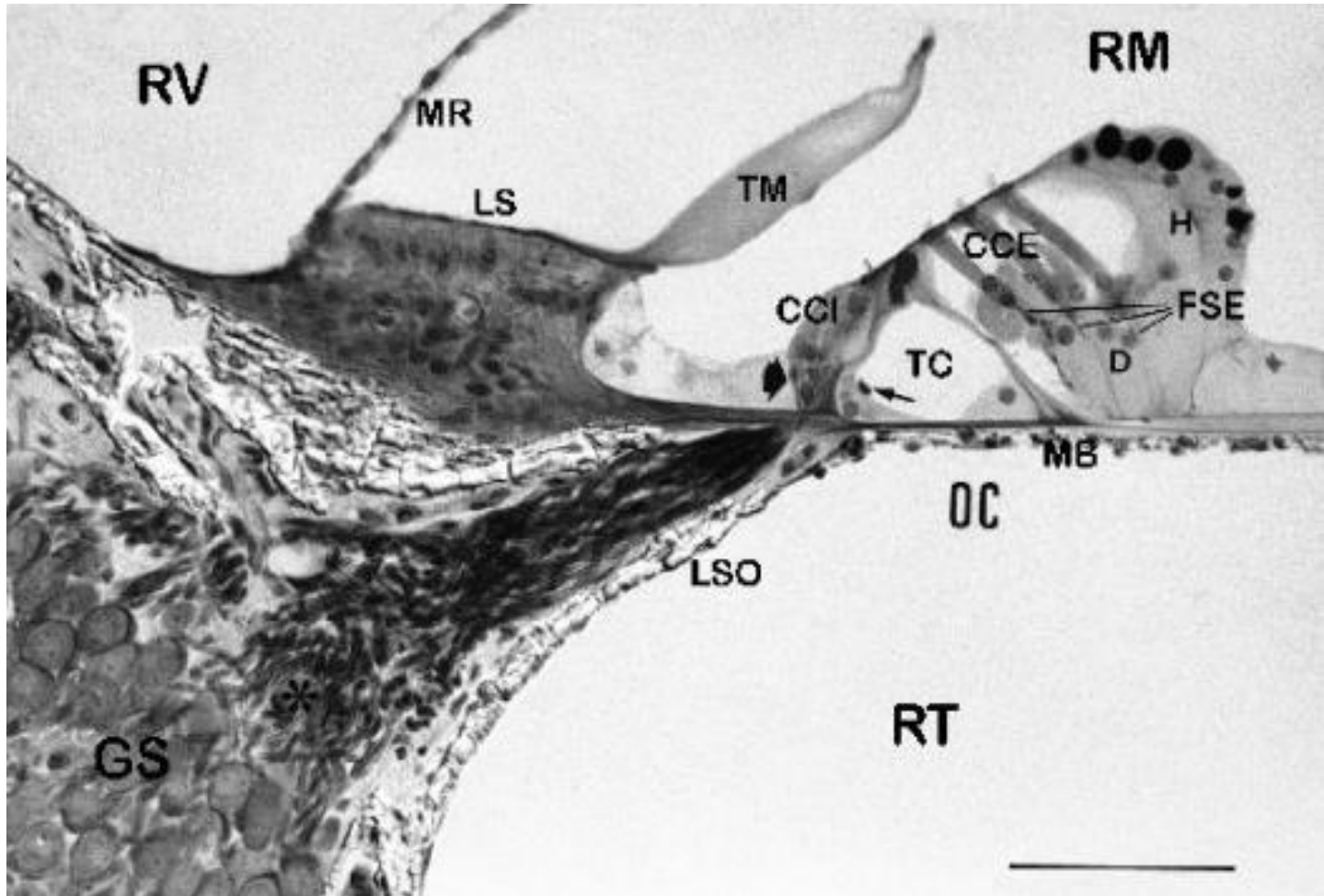




# Les cellules ciliées internes



# L'organe de Corti

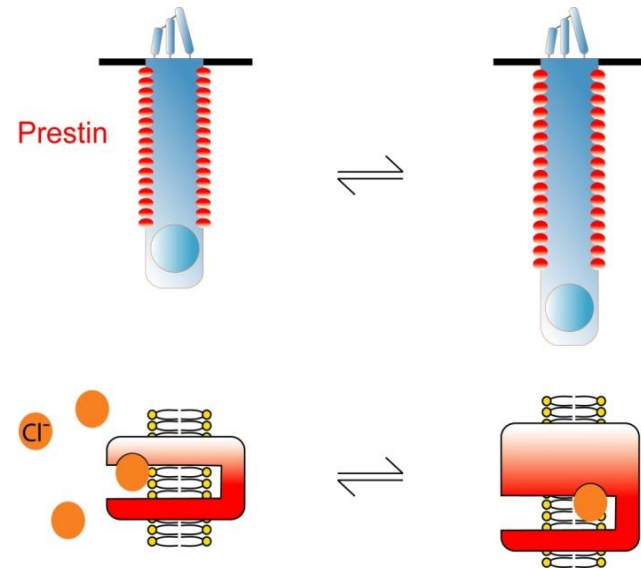


# Les cellules ciliées externes

## Electromotilité

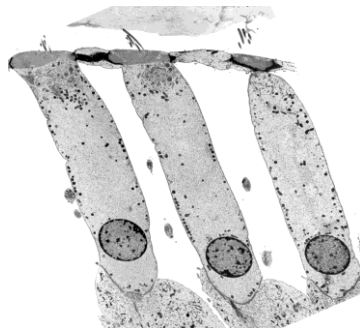
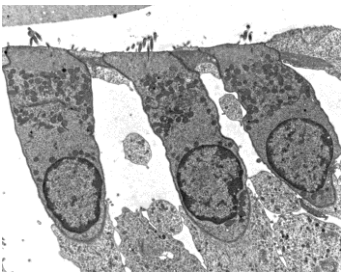


## Prestine



Base

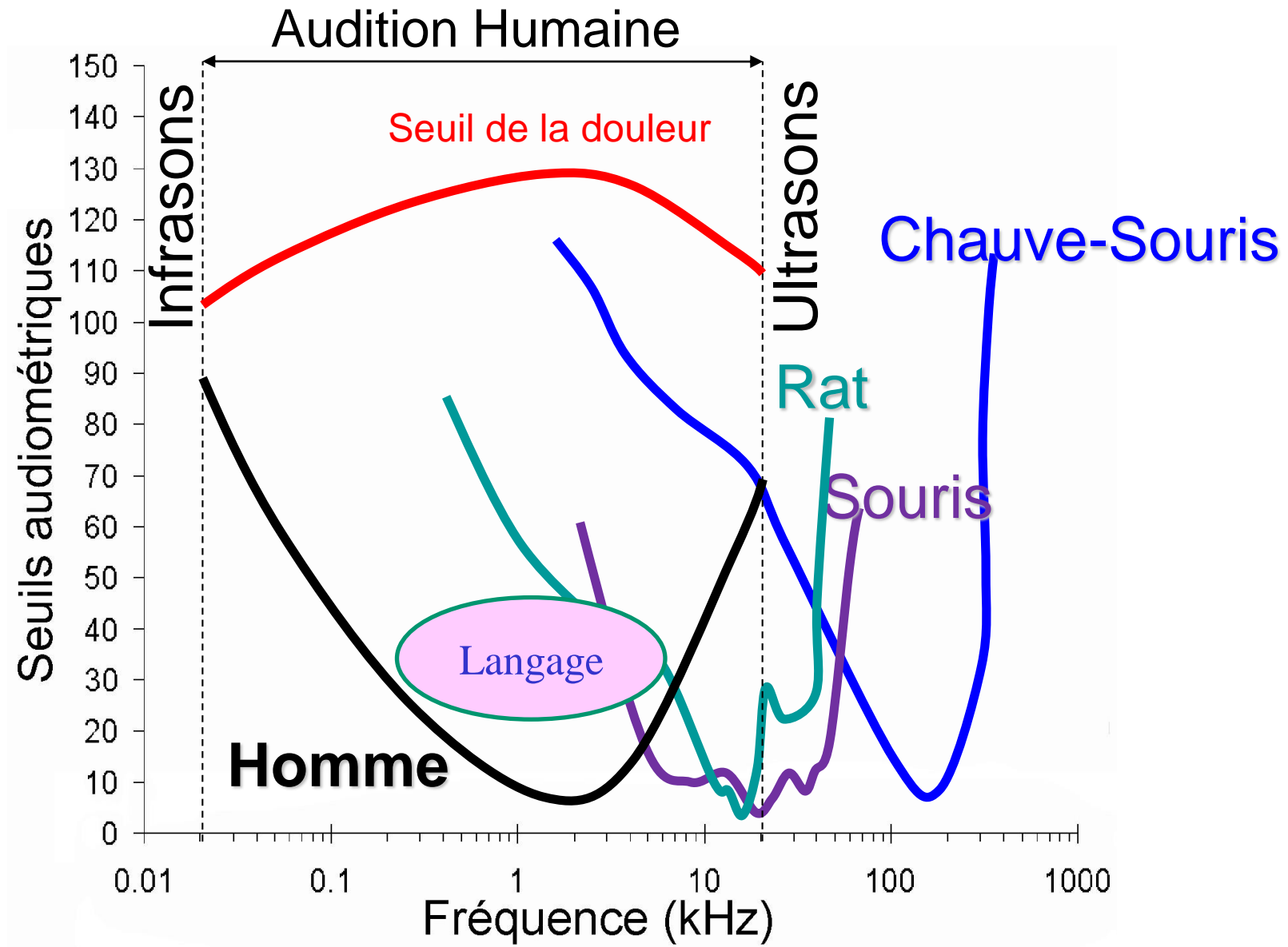
Apex



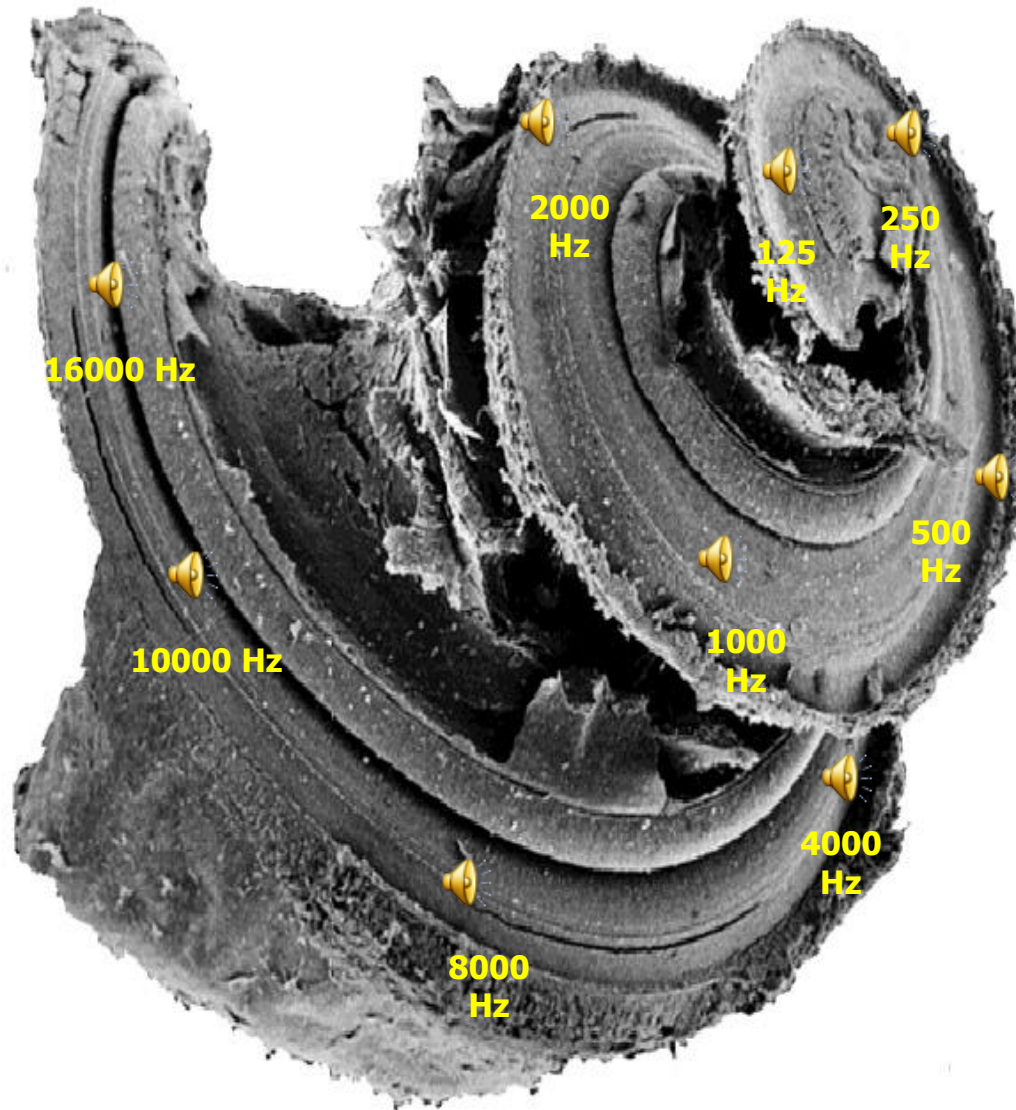
1. Amplification des vibrations + 60 dB
2. Filtrage sélectif des fréquences

**Tonotopie active**

# Audiogrammes

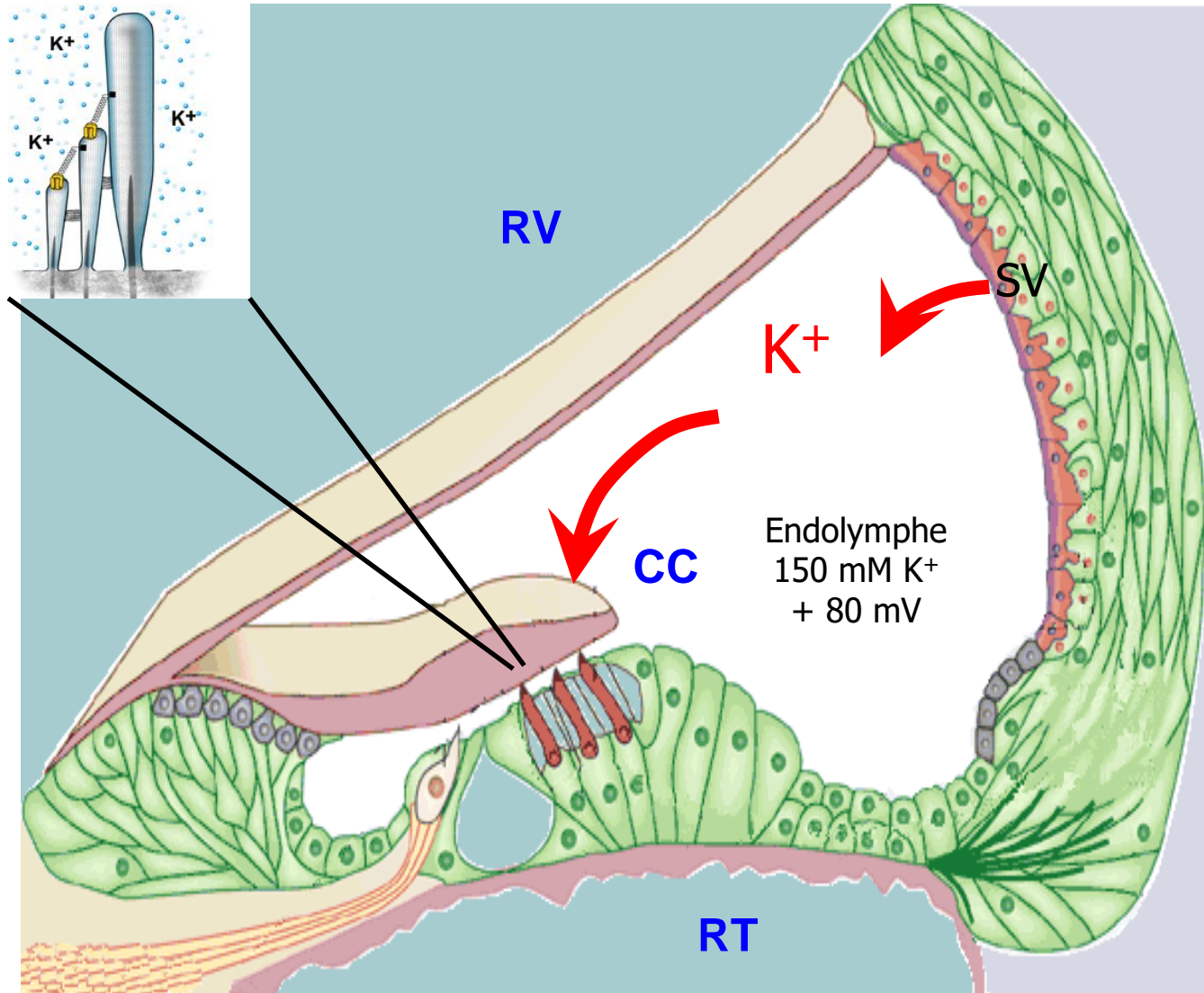


# Distribution des fréquences le long de la cochlée

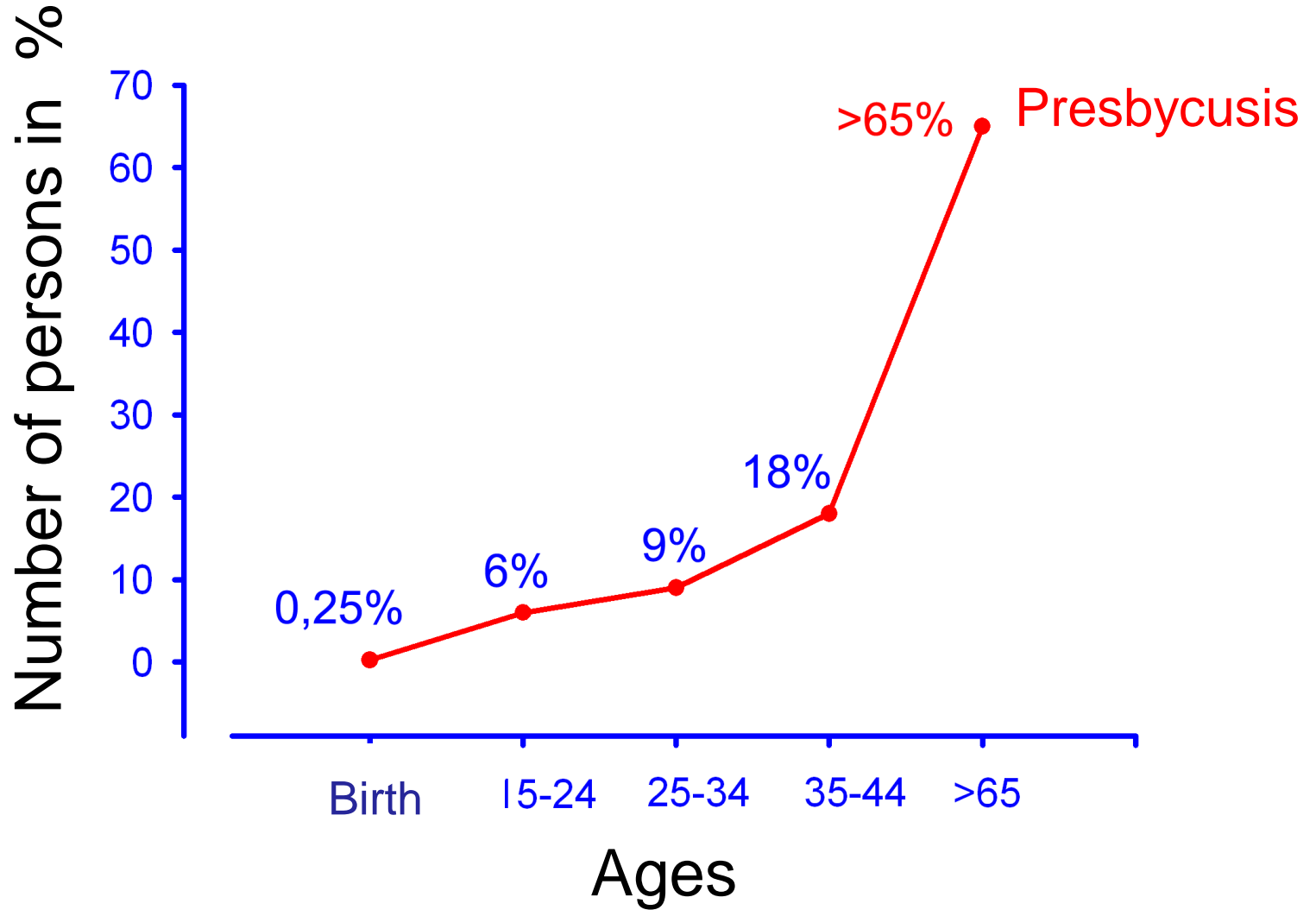




# La strie vasculaire



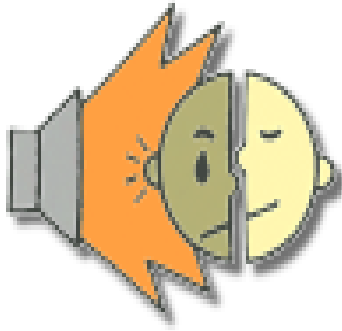




# Facteurs de risques

## Facteurs environnementaux

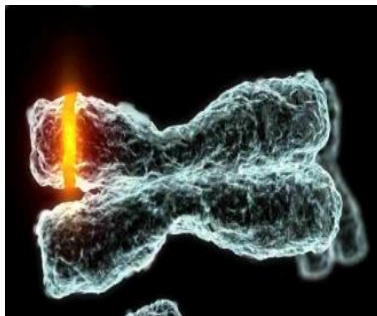
Bruits



Médicaments ototoxiques



Facteurs génétiques

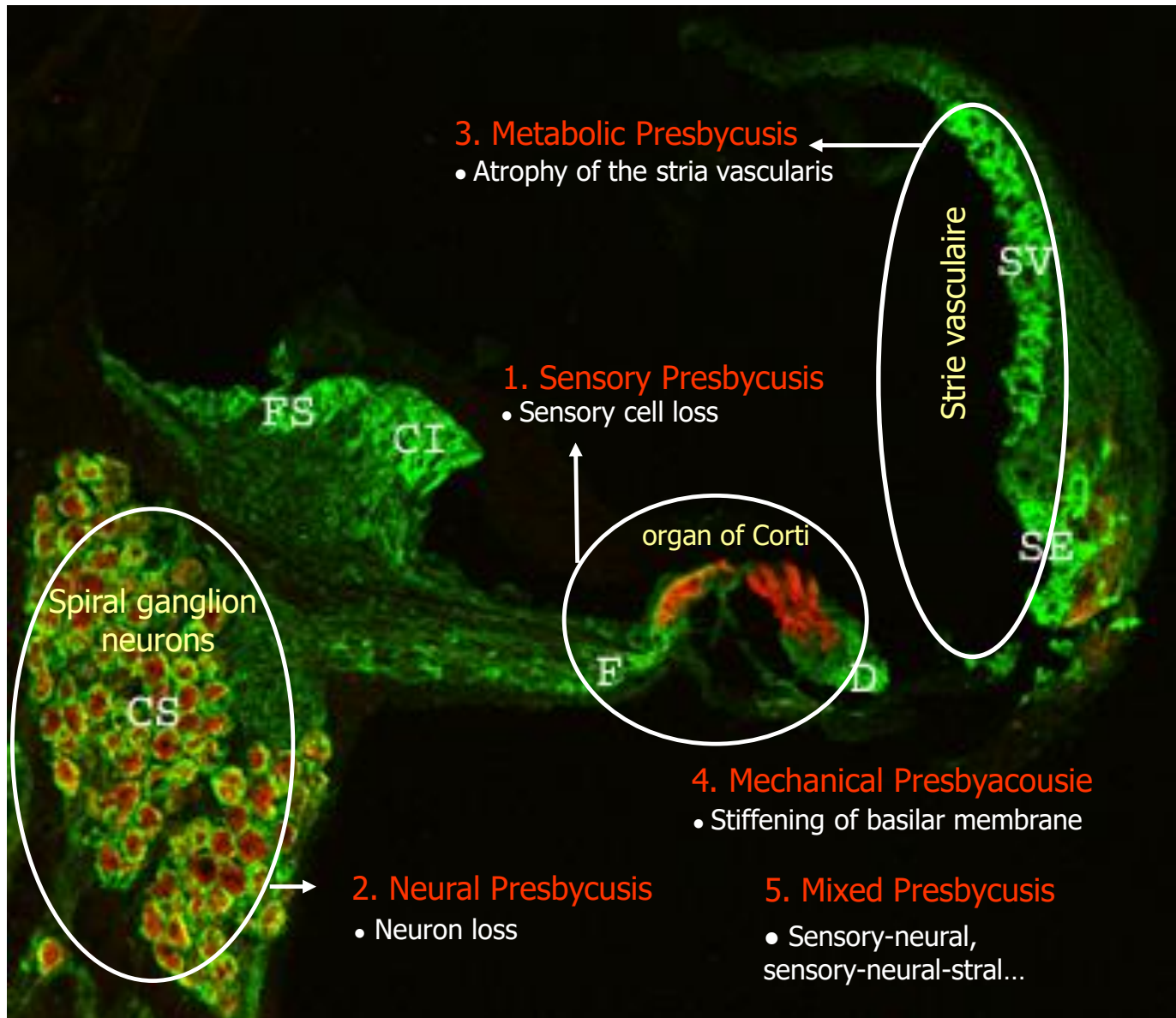


Âge



# Classifications

*Schuknecht and Gacek, 1993*



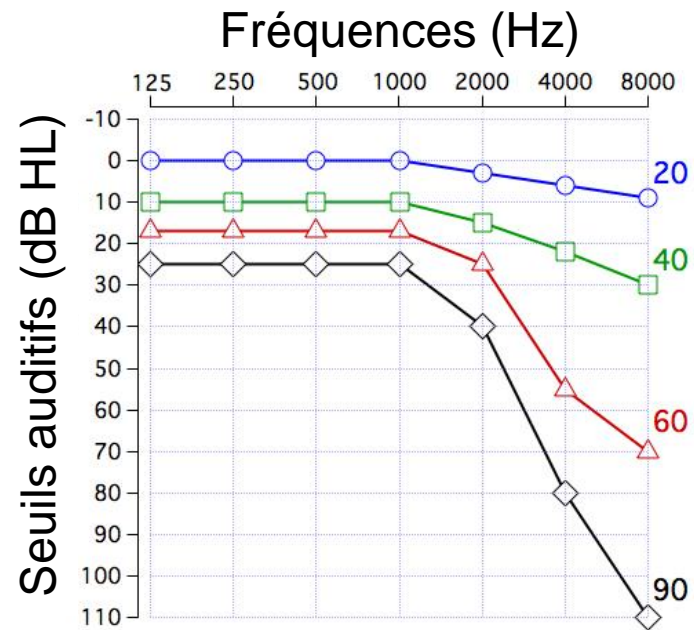
## Signes cliniques:

- **Stade de début** : Baisse de la perception des sons aigus et difficulté de compréhension dans un milieu bruyant
- **Stade suivant** : Difficulté de compréhension dans un milieu calme et intolérance aux sons forts
- **Stade final** : Surdit e invalidante, isolement social, d epression, anxi et e et m eme d emence.

**D'autres signes** : Acouph enes (1/3), instabilit e positionnelle...

# Perte de l'audition liée à l'âge

## Audiométrie tonale





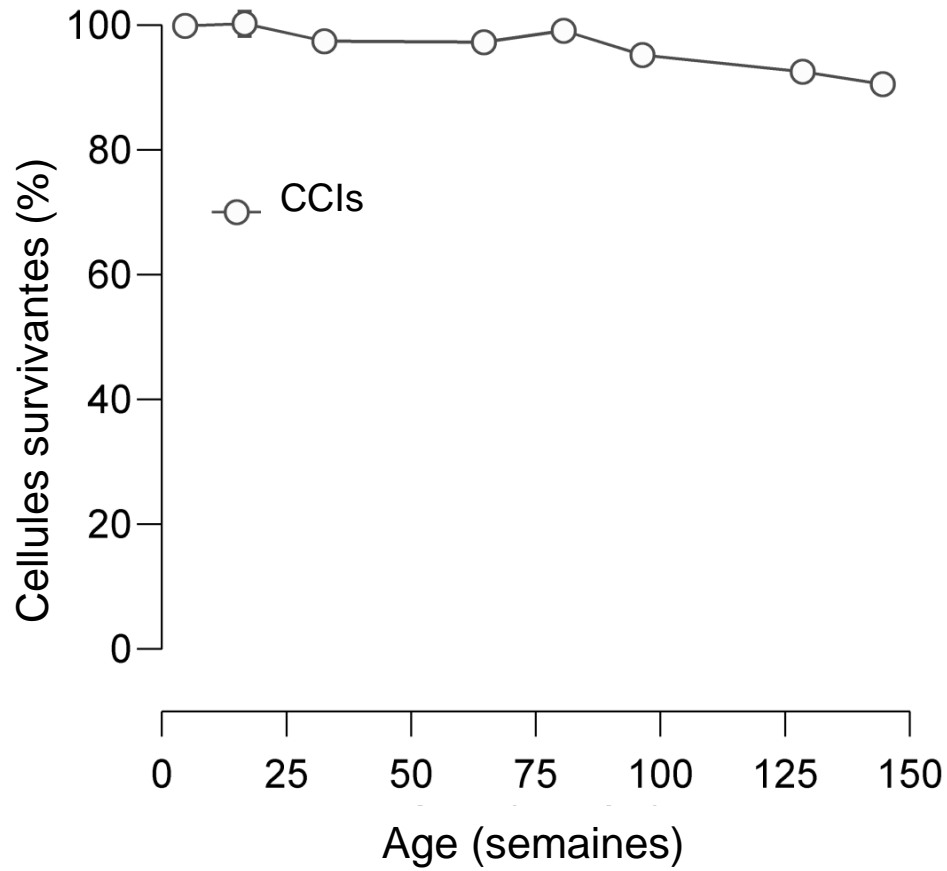
# Presbyacousie

*Données chez la souris*

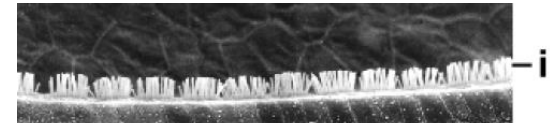


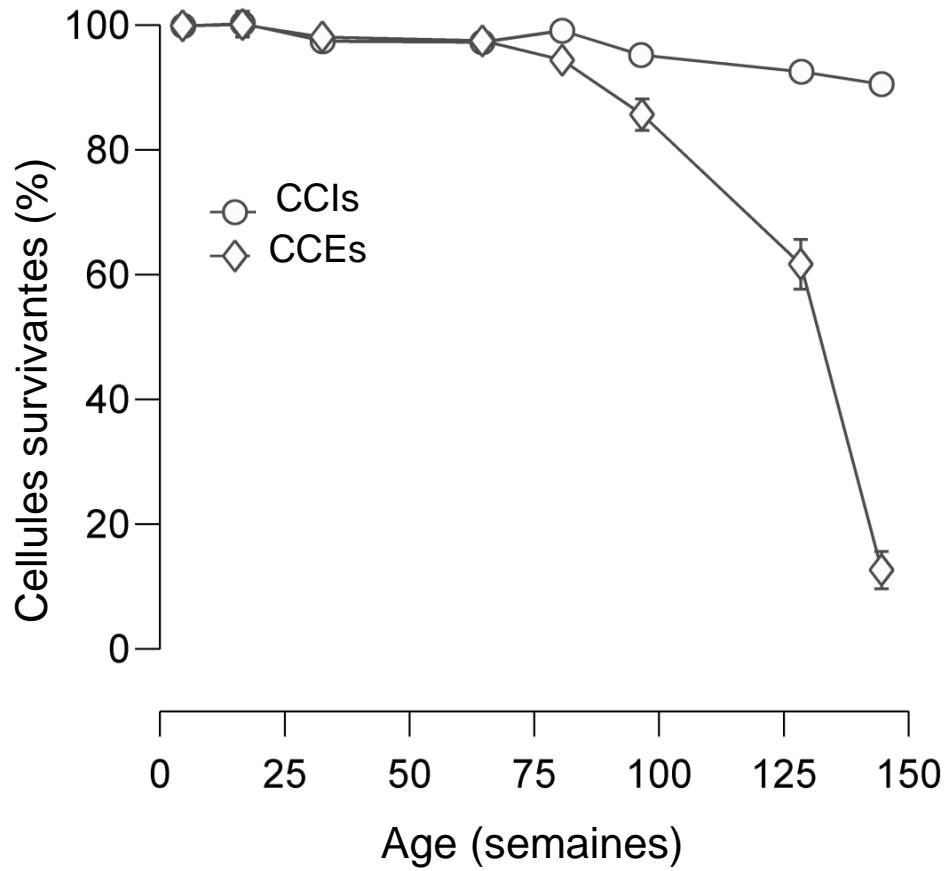
UNIVERSITÉ  
DE MONTPELLIER



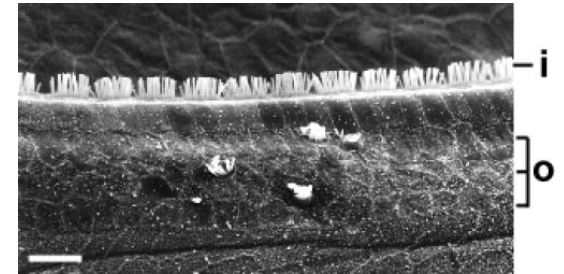


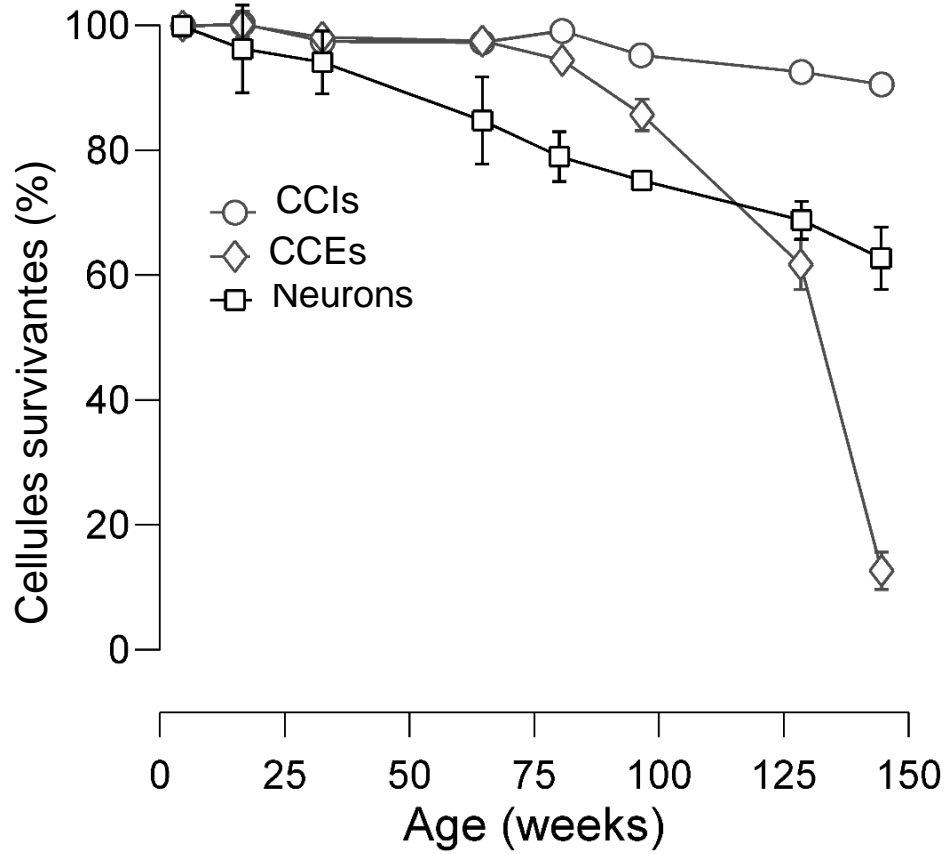
## Les cellules sensorielles



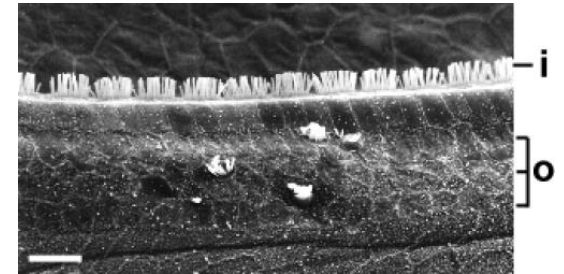


### Les cellules sensorielles

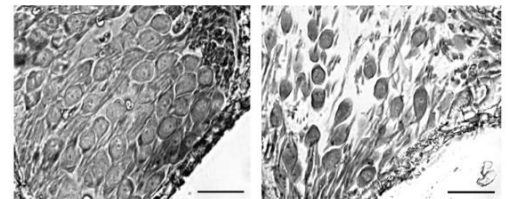


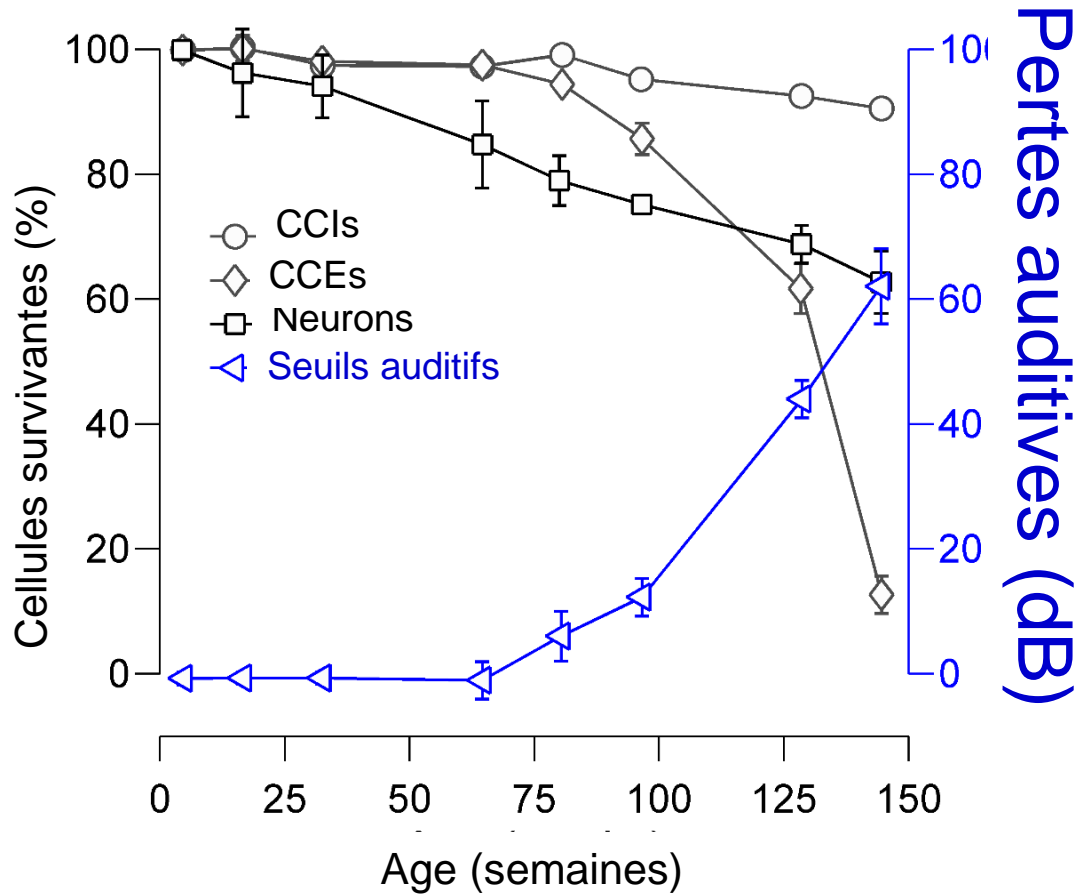


### Les cellules sensorielles

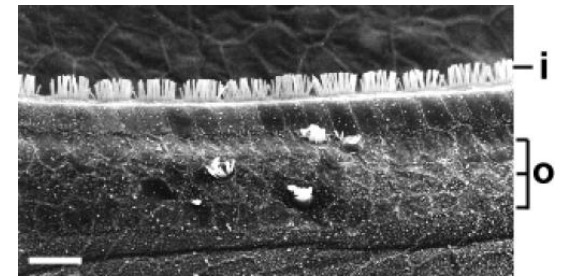


### Les neurones auditifs

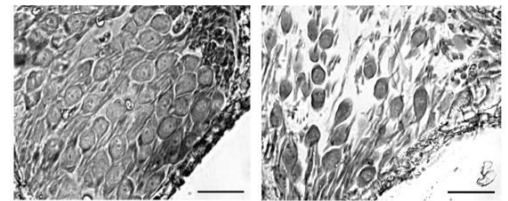


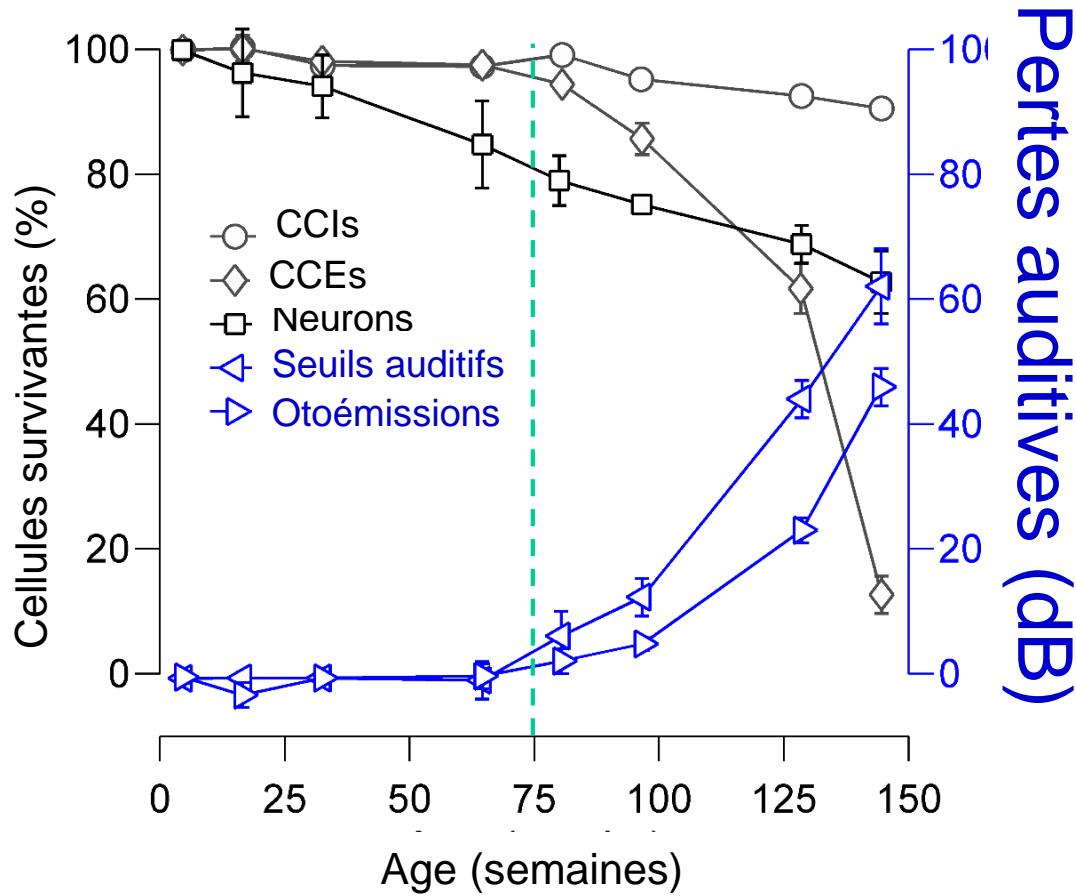


Les cellules sensorielles

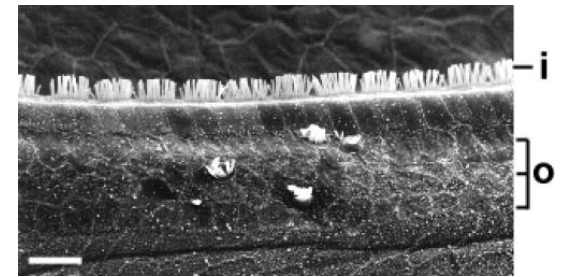


Les neurones auditifs

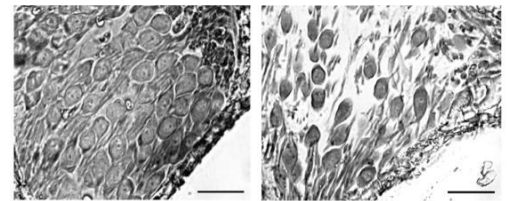




Les cellules sensorielles



Les neurones auditifs





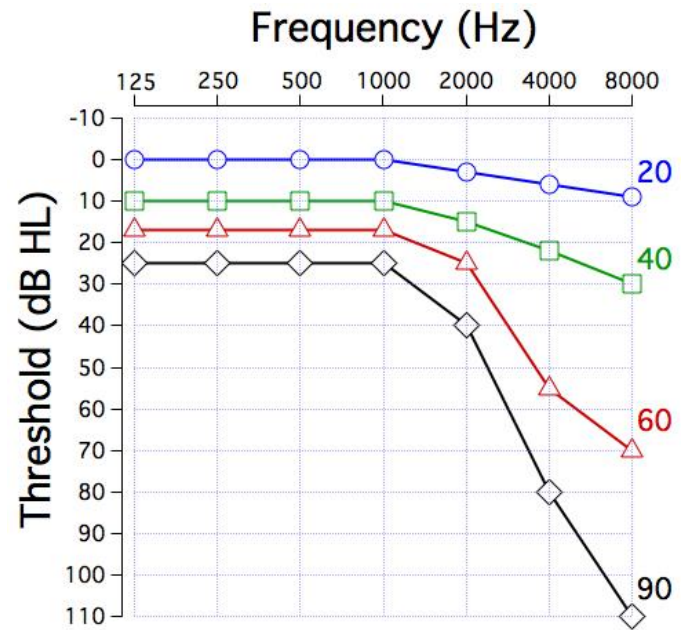
# Presbyacousie

*Données chez l'homme*

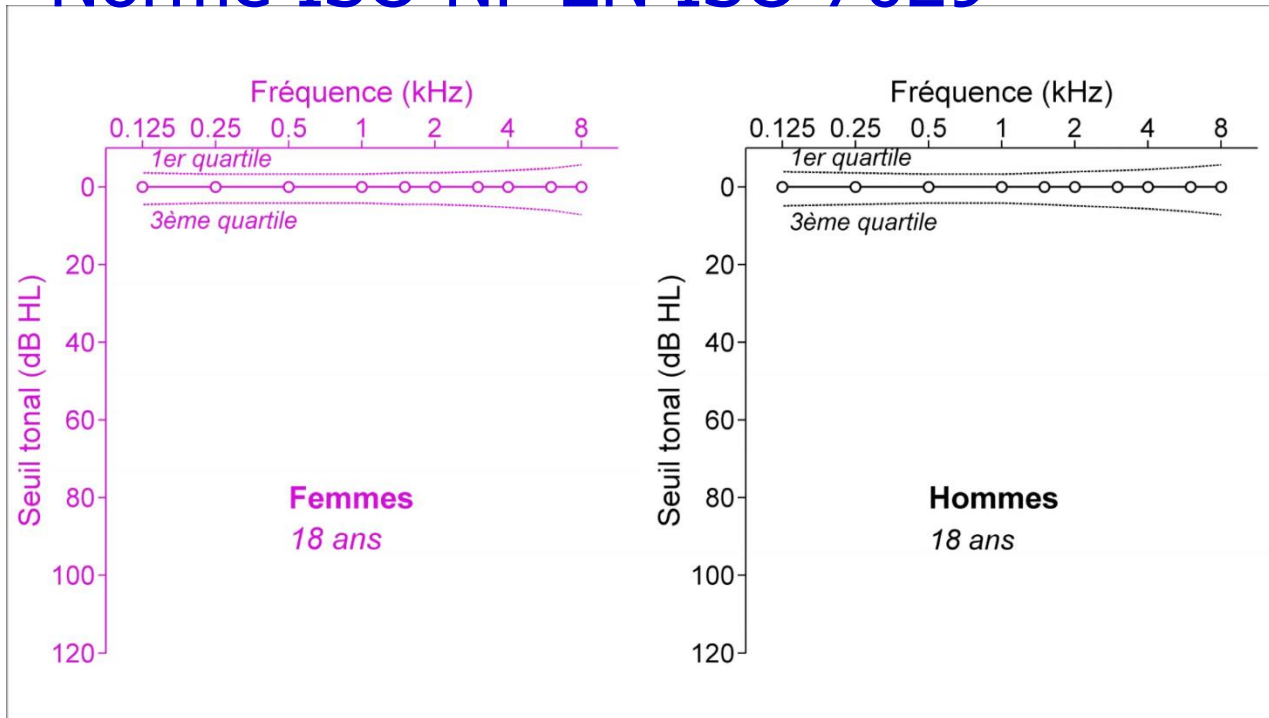


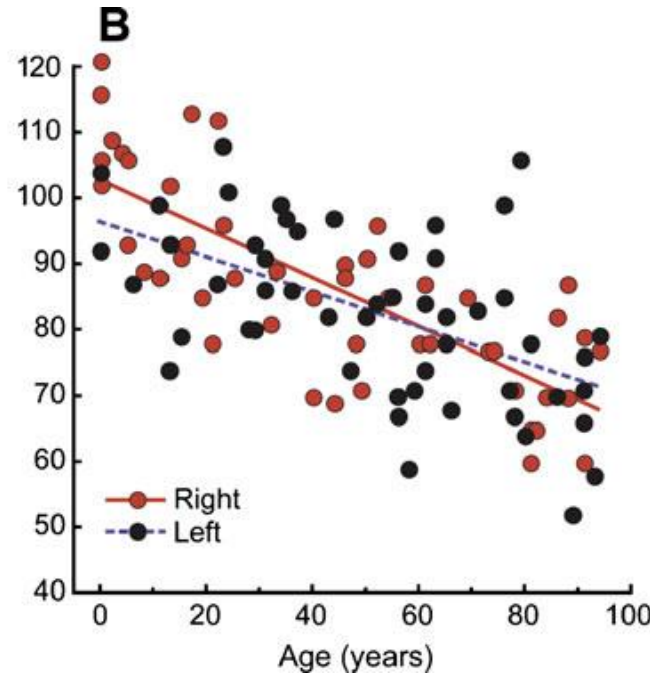
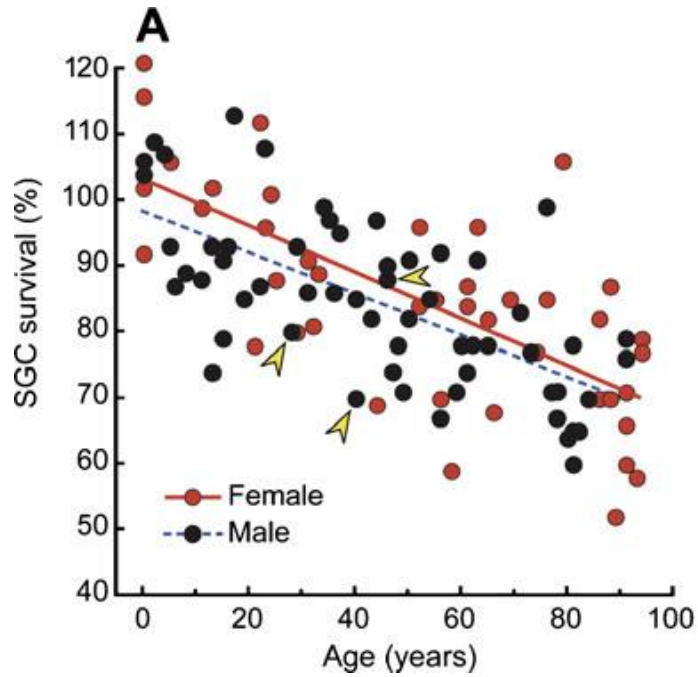
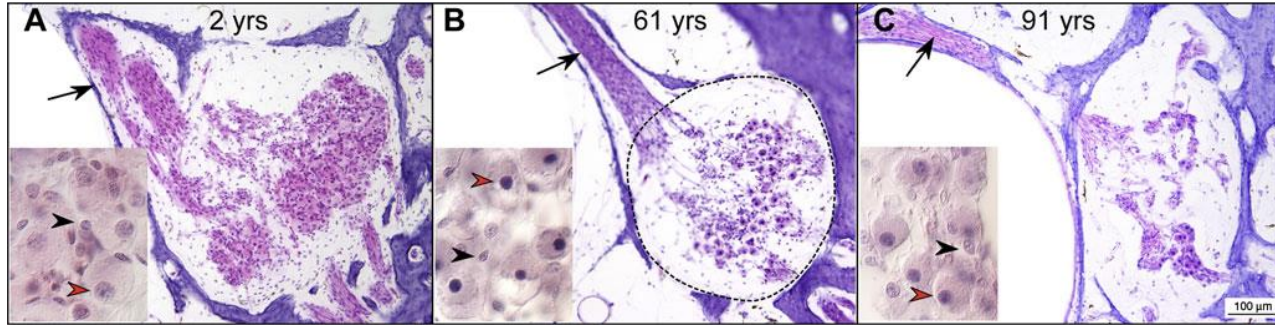
UNIVERSITÉ  
DE MONTPELLIER

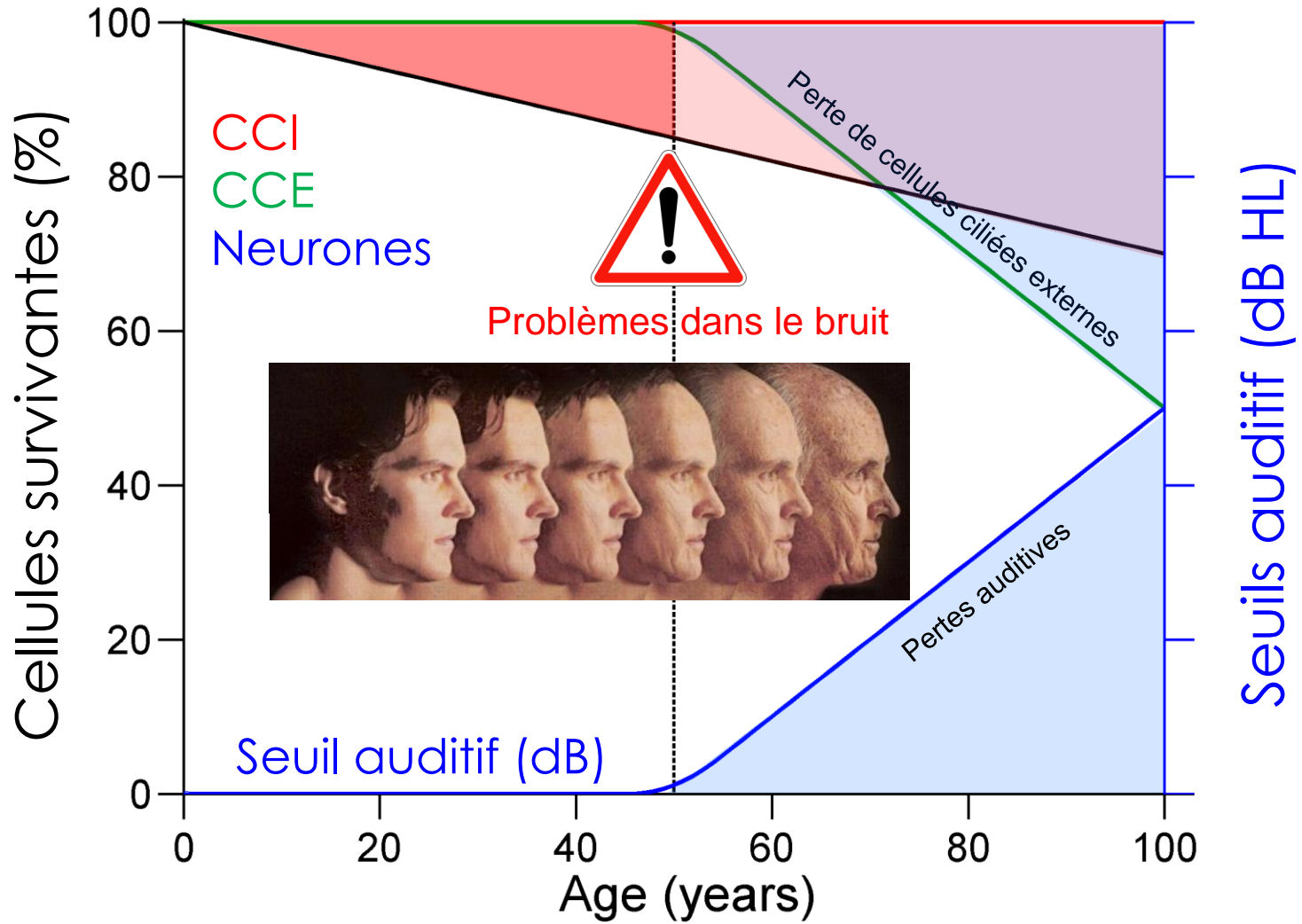




## Norme ISO NF EN ISO 7029



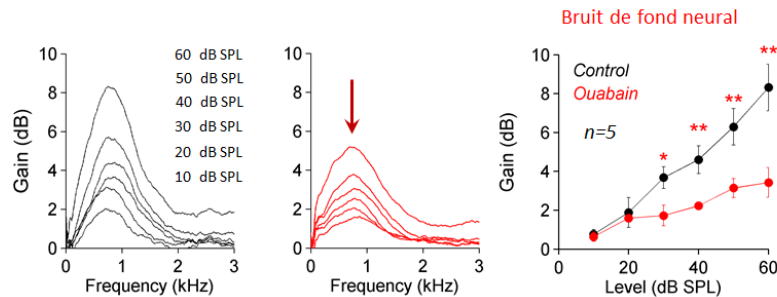




# Que faire?

## Médical

Développer de nouveaux outils diagnostiques précoces



Batrel et al., PlosOne., 2017

## Recherche

Développer des stratégies thérapeutiques adaptées

# Senescence-Accelerated Prone Mouse 8 (SAMP8):

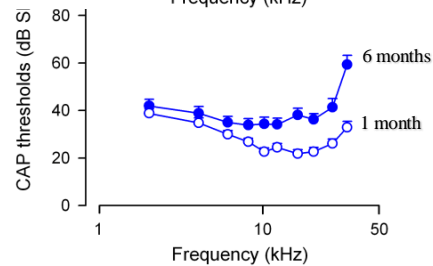
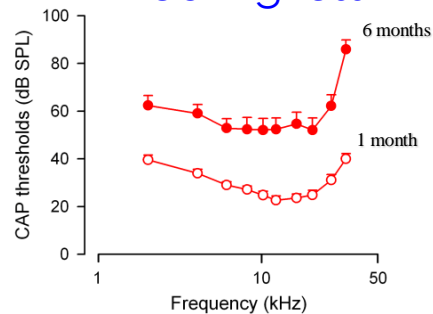
**SAMP8**



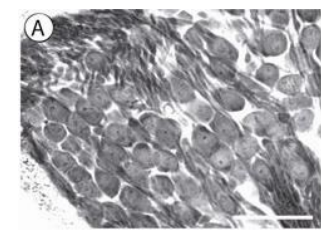
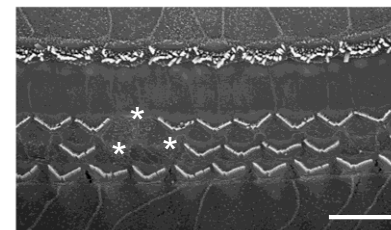
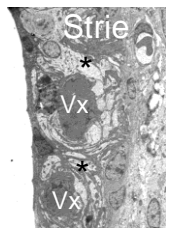
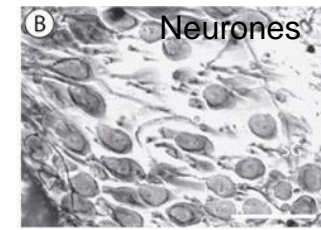
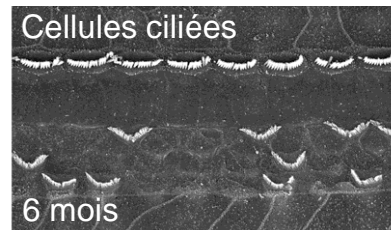
**SAMR1**



*Hearing loss*



*Cell degeneration*



Oxidative stress

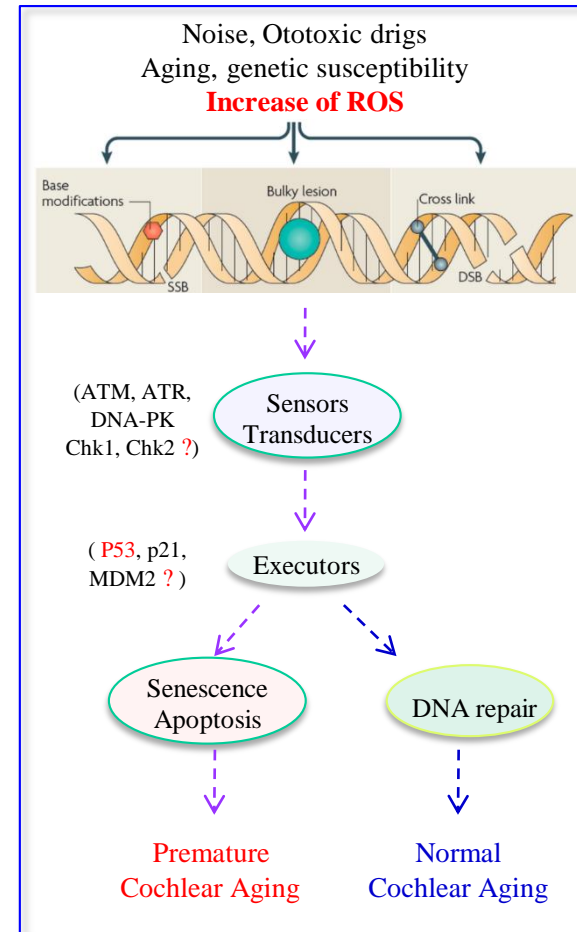
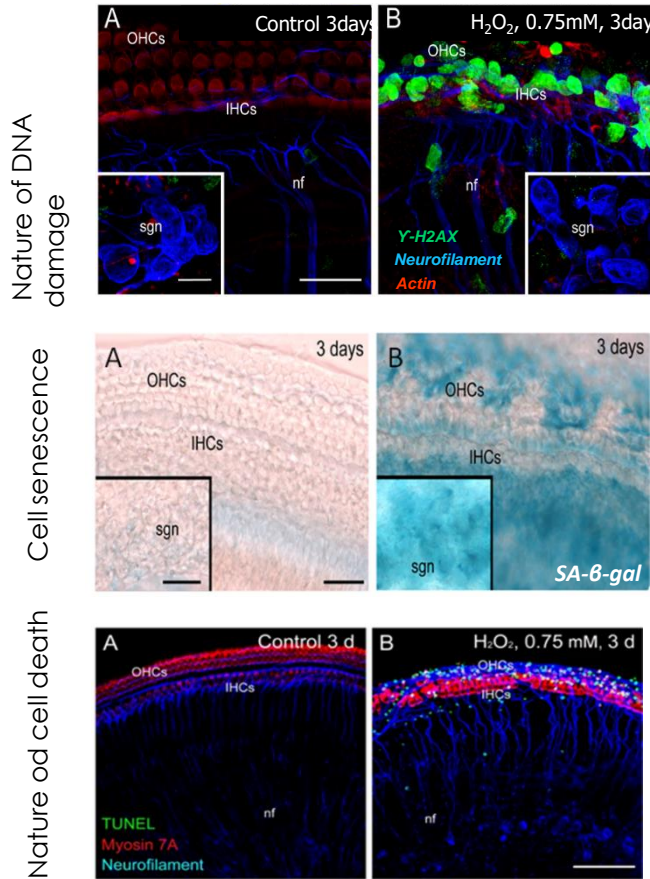
Inflammation

Autophagic stress



# Mecanismes moléculaires

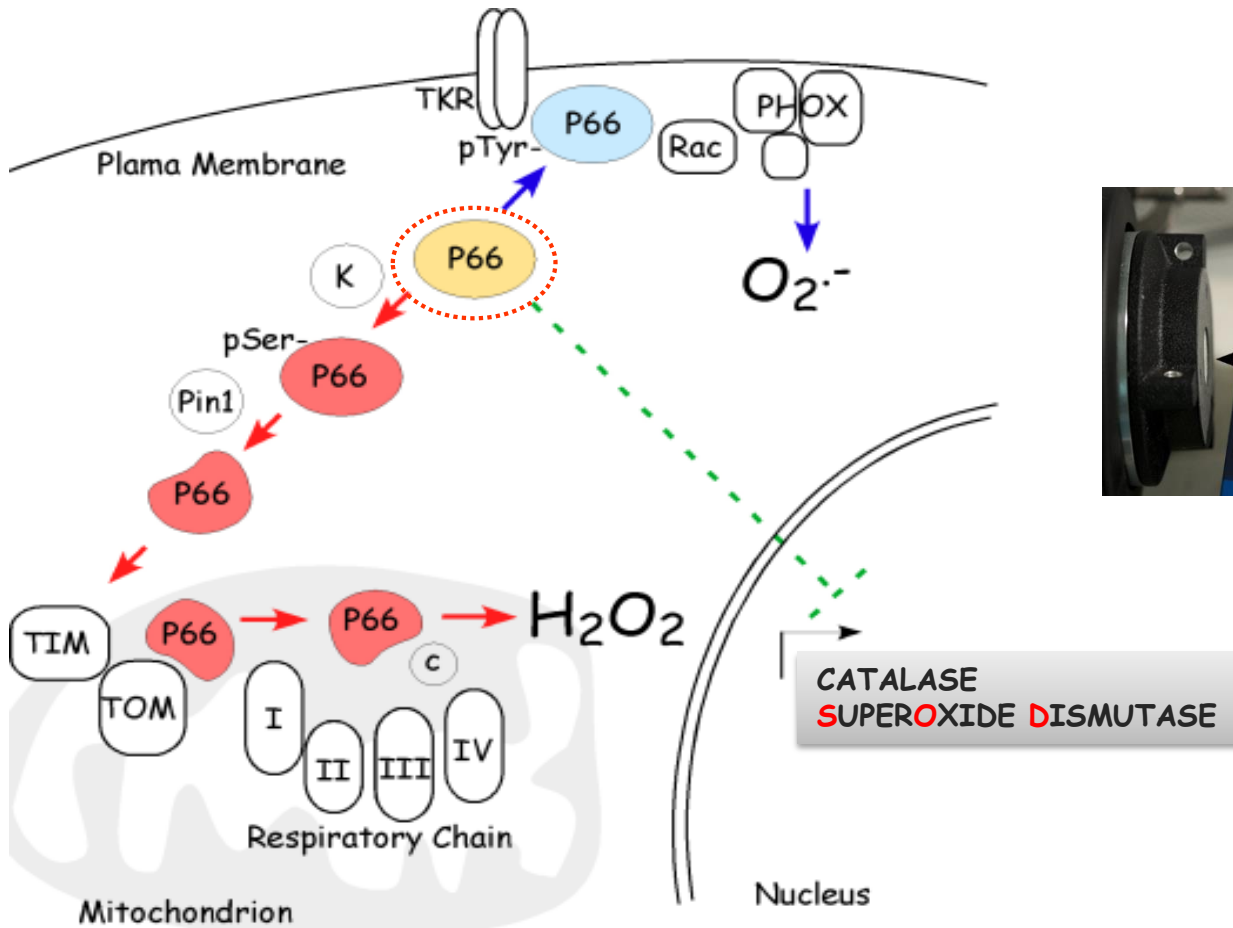
## Signaling pathway



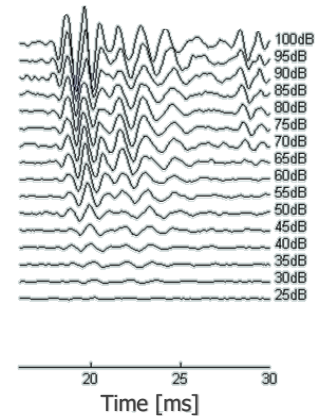
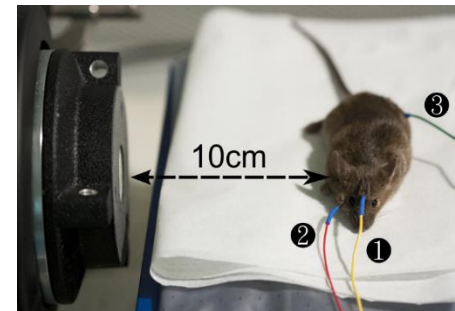


p66 KO mice  
C57BL/6J Background

## Oxidative stress, Ageing, Diseases

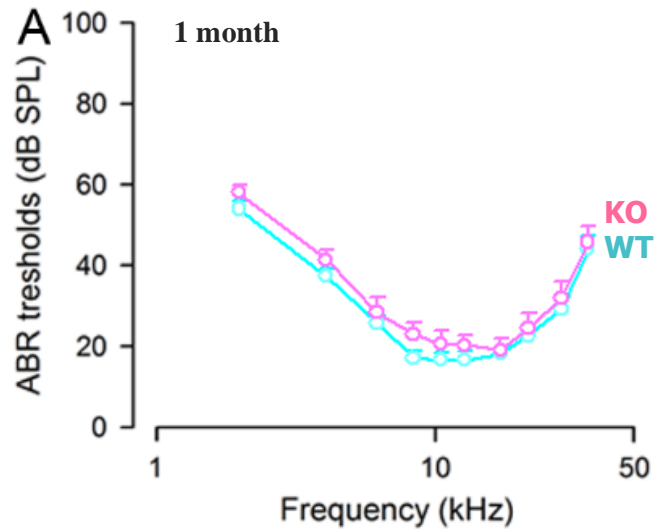


## Auditory Brainstem Response





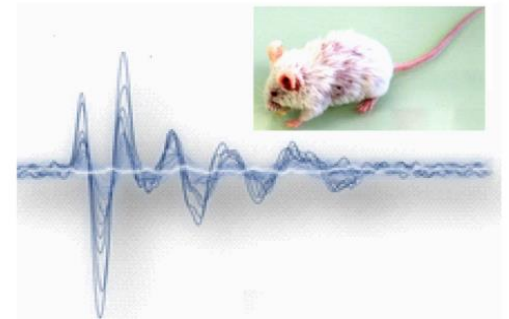
# Délétion du p66<sup>shc</sup> préserve l'audition



# Traitements ciblés



For 3 months



6-month-old SAMP8 mice

*Conception scientifique : Rémy Pujol*

# *Promenade autour de la Cochlée*

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