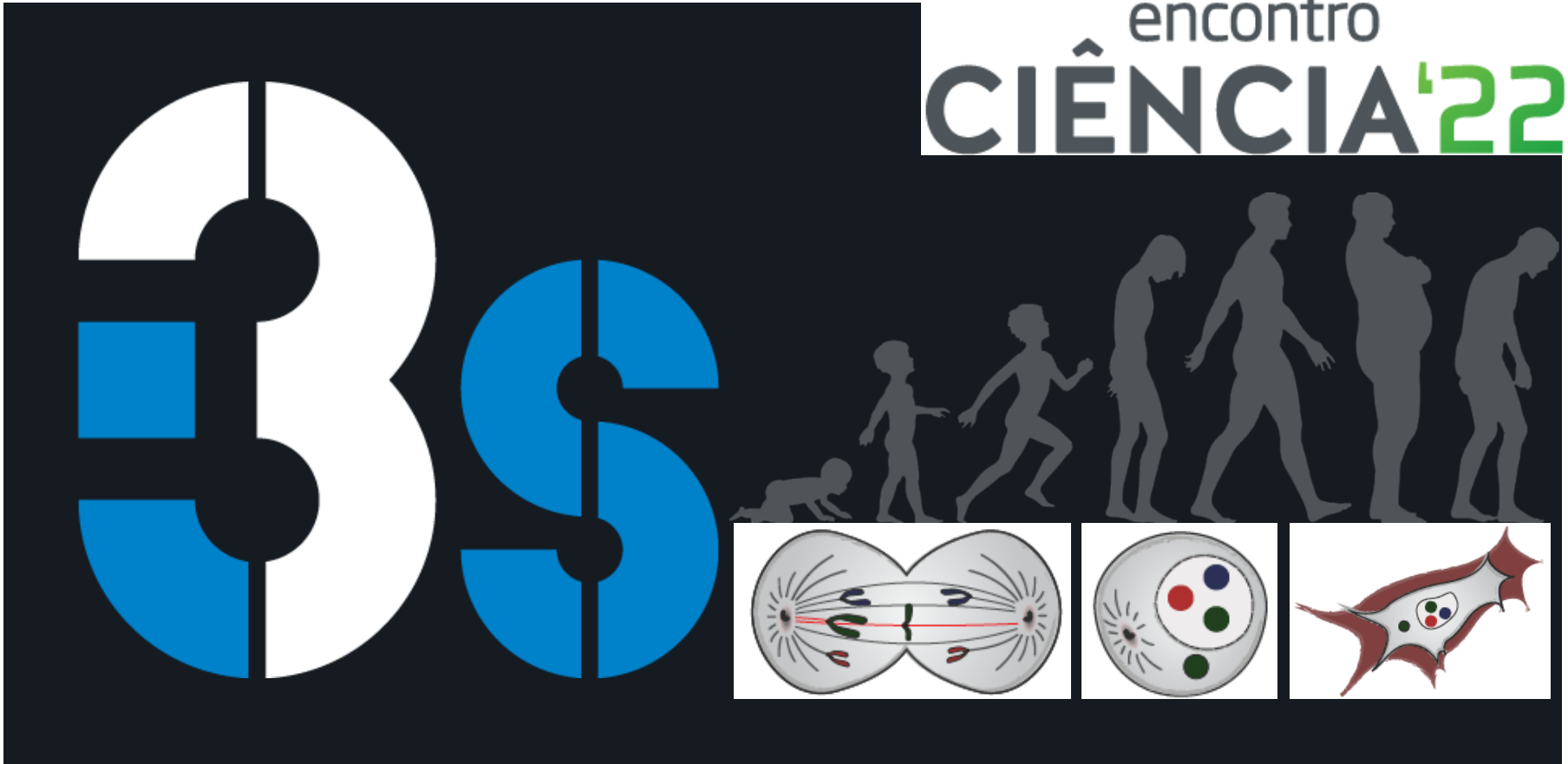


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CIÊNCIA'22



Inhibition of age-associated genomic instability as senotherapy against aging and age-related diseases

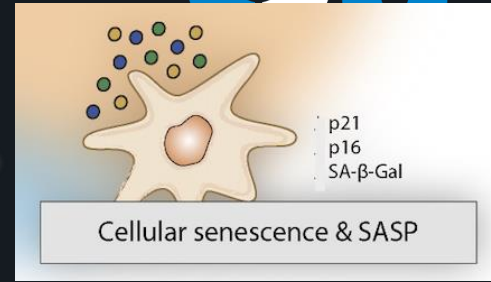
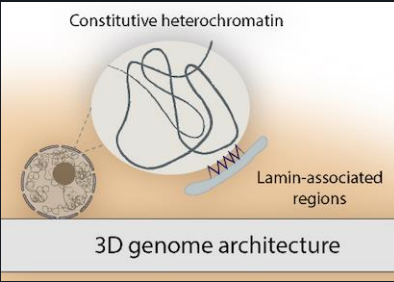
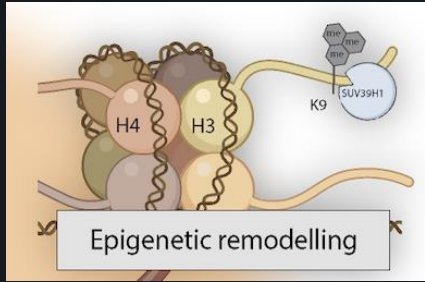
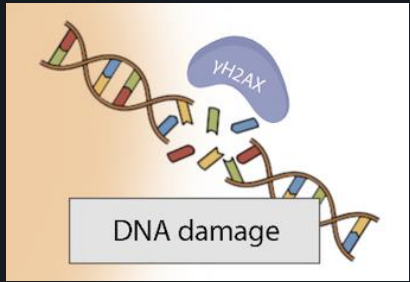


Elsa Logarinho
Aging and Aneuploidy Group @ i3S
Elsa.logarinho@ibmc.up.pt

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Why do we age?

A1100

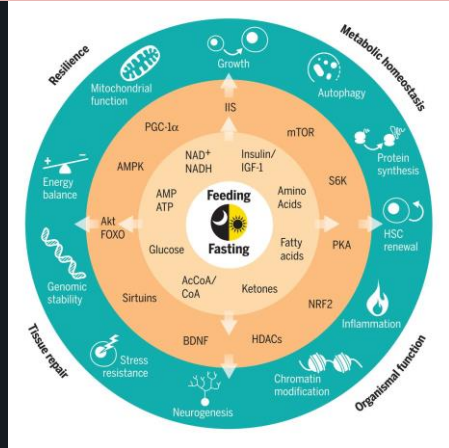


How can we postpone aging?

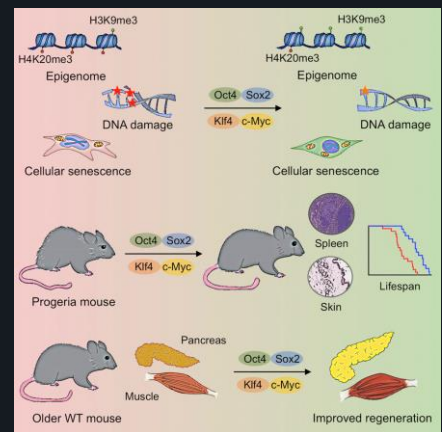


↑
Genomic instability targeting

Metabolic manipulation (diet regimens and dietary restriction mimetics)



Cellular reprogramming (partial reprogramming)



Ablation of senescent cells (genetic ablation or senolytic drugs)

ARTICLE

Naturally occurring p16^{Ink4a}-positive cells shorten healthy lifespan

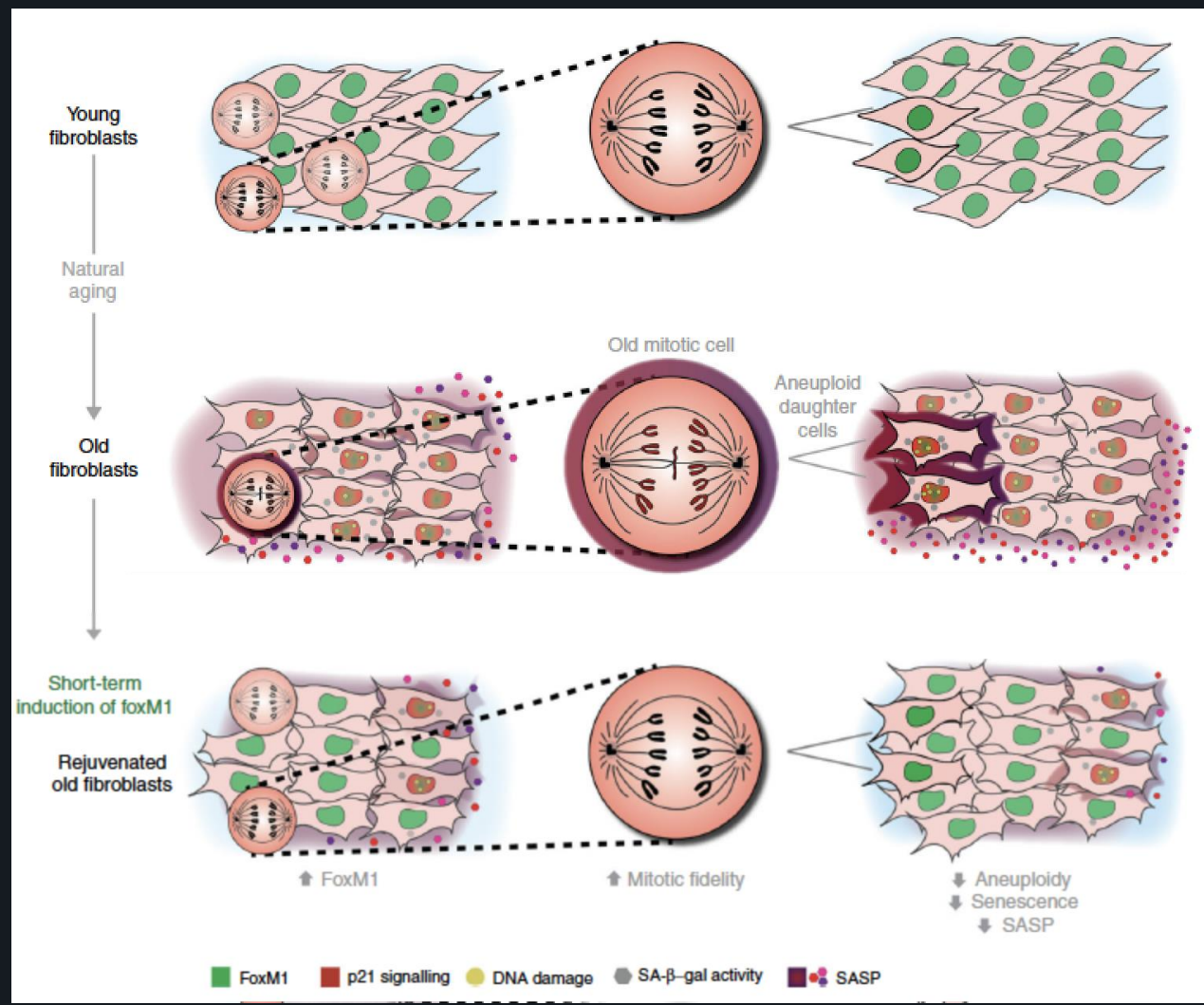
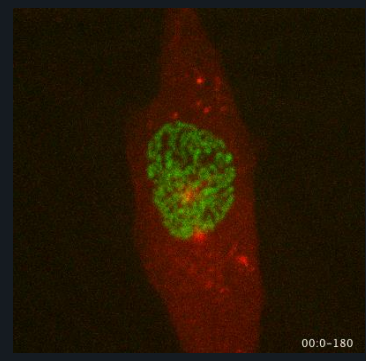
doi:10.1038/nature16932

Darren J. Baker¹, Bennett G. Childs², Matej Durik³, Melinde E. Wijers¹, Cynthia J. Sieben², Jian Zhong¹, Rachel A. Saltness¹, Karthik B. Jeganathan¹, Grace Casaccia Verzea², Abdulmohammad Pezeshki⁴, Khashayarsha Khazaei⁴, Jordan D. Miller¹ & Jan M. van Deursen^{1,2}

Before clearance of senescent cells After clearance of senescent cells

Before After

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- FOXMI is repressed during aging
 - Increased DNA damage
 - Increased chMS and aneuploidy
- Aged proliferating cells & SASP
 - ChMS/MN triggers full senescence
 - FACS sorted senescent cells are aneuploid
- FOXMI induction prevents genomic instability and senescence

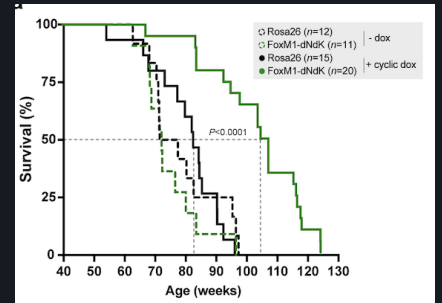
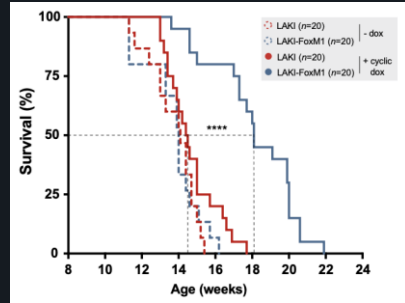
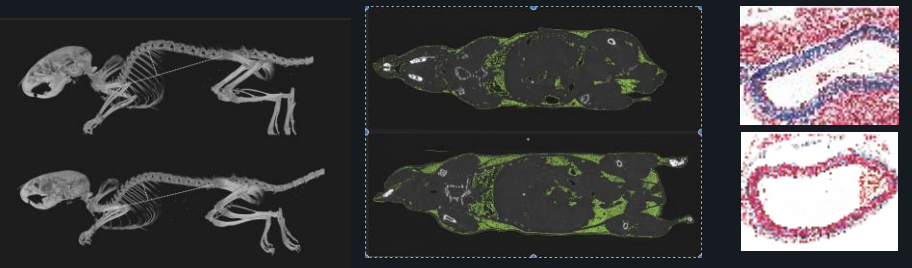
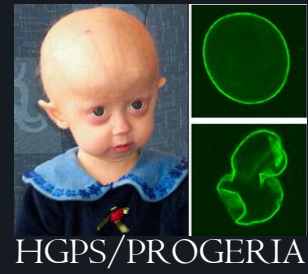
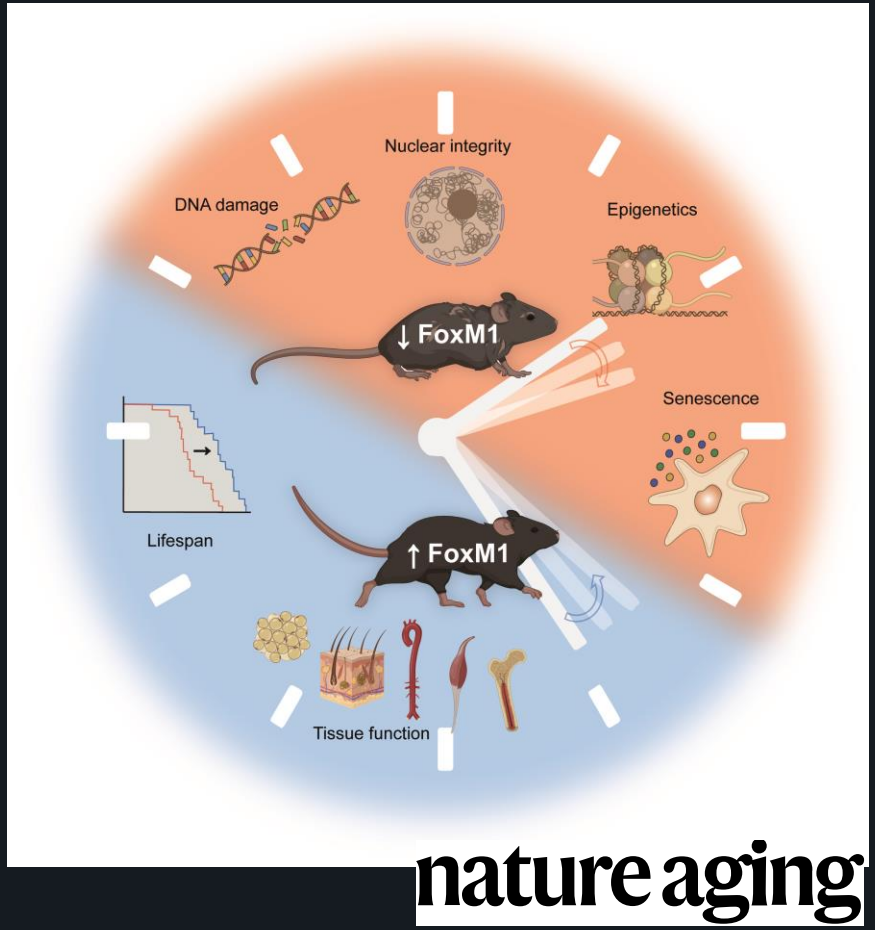


Macedo... & Logarinho, 2018

FoxMI: the youth gene?

Investigadores do i3S descobrem o “gene da juventude”





- *FoxM1* is repressed during aging and in HGPS
- *FOXMI*tg induction rescues genomic instability and senescence
- *FOXMI*tg induction rescues senescence-associated phenotypes and extends the lifespan



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Barroso-vilares et al,
 Embo Reports 2020