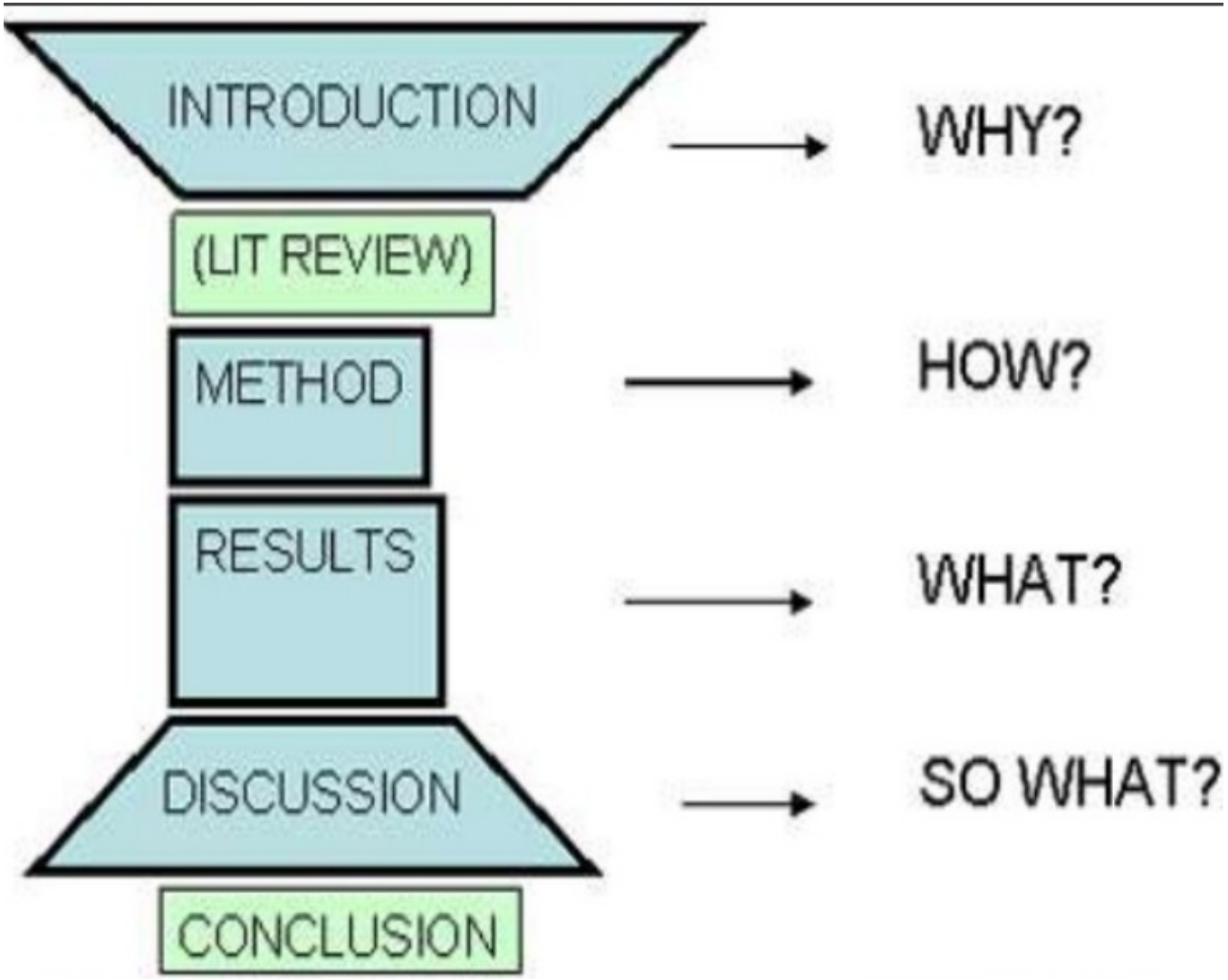
A SCIENTIFIC RESEARCH APPROACH TO LEARNING

Personalize your learning method by exploring several strategies

Teachers
Are trying to find the better method
But only
You, as learner,
makes your learning

https://youtu.be/t2K6mJkSWoA

https://youtu.be/M3aZNaPY88Y



- **Features of abstracts**

Abstracts usually contain four kinds of information:

- ✓ purpose or rationale of study (why they did it),
- ✓ methodology (how they did it),
- ✓ results (what they found),
- ✓ conclusion (what it means).

ANALITIC READING: INTRODUCTION

Reading the introduction is a test of whether or not you are ready to read the rest of the paper; if the introduction doesn't make sense to you, then the rest of the paper won't either.

Depending on the guidelines for that specific journal.

What problem is this author trying to solve?

Specific questions to be addressed by the authors.

Citations for previously published articles or reviews that discuss the same topic.

Background information about the topic of the paper.

If you find yourself confused by the introduction, try:

- Going to other sources for clarifying information about the topic before you go for the rest of the paper (scientific dictionaries, encyclopedias, texts books, on line tutorials, a mentor..)
- If even after trying all these sources you're still confused, it may be time to consider a new paper.

Task

Second task:

- Match the titles, abstracts and key words from the first task to the introductions provided.
- Were your anticipations from the first task correct or not?
- If the topic of your paper is not related to your professional interests, try interchanging it with another team in a similar situation, if possible.
- Scan the text to identify: (if necessary use supporting sources for comprehension)

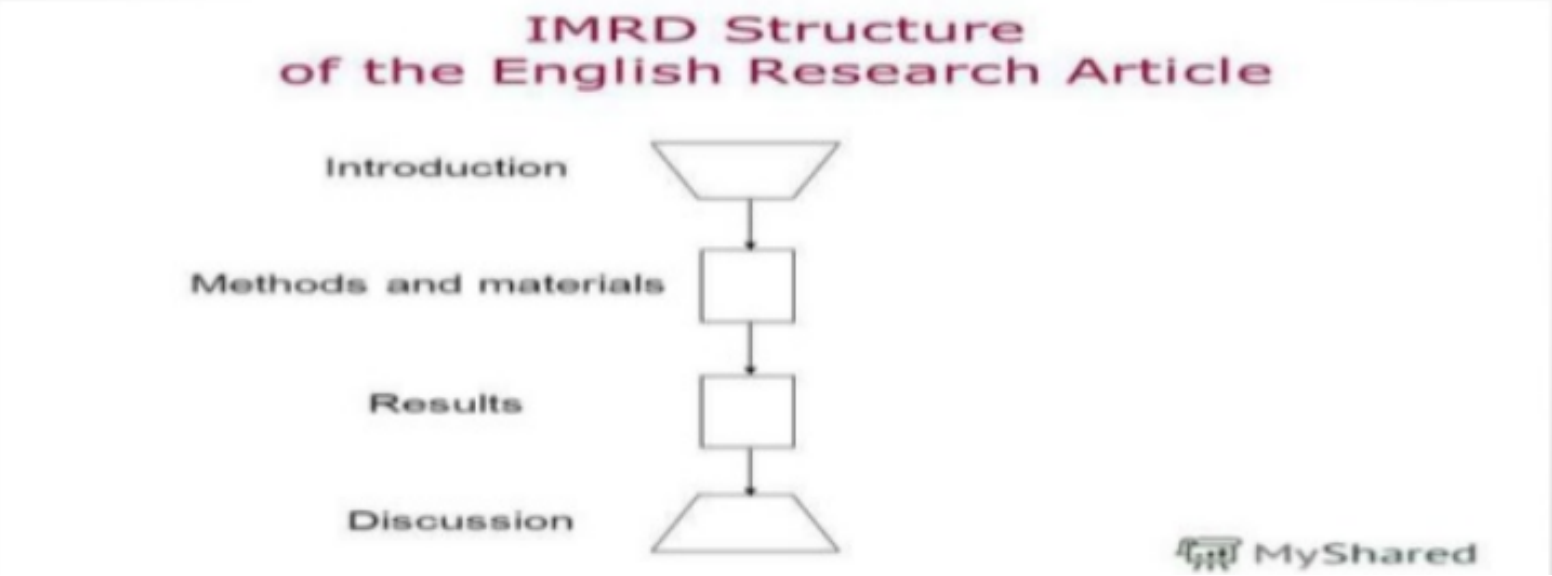
✓ Background information about the topic of the paper.
✓ Specific questions to be addressed by the authors.
✓ Citations of previously published articles or reviews that discuss the same topic.
✓ **What problem is this author trying to solve?**

-Would you finally read this paper or look for another one?

SKIMMING AND SCANNING: MAIN BODIES.

Conventional **IMRD** structure: an abstract followed by **I**ntroduction, **M**ethods, **R**esults, and **D**iscussion.

Each of these sections normally contains easily recognized conventional features, and if you read with an anticipation of these features, you will read an article more quickly and comprehend more.



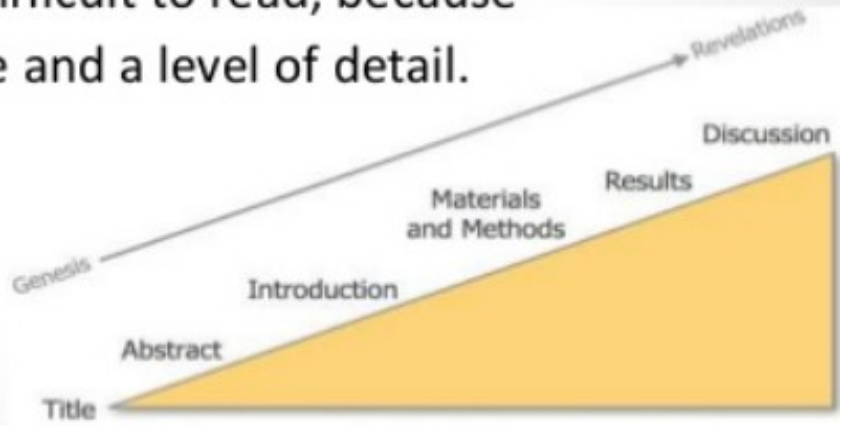
Materials and Methods

Helpful in understanding exactly *what* the authors did.

Technical details of how the experiments were carried out

"How-to" manual if you're interested in carrying out similar experiments.

Methods are often difficult to read, because of technical language and a level of detail.



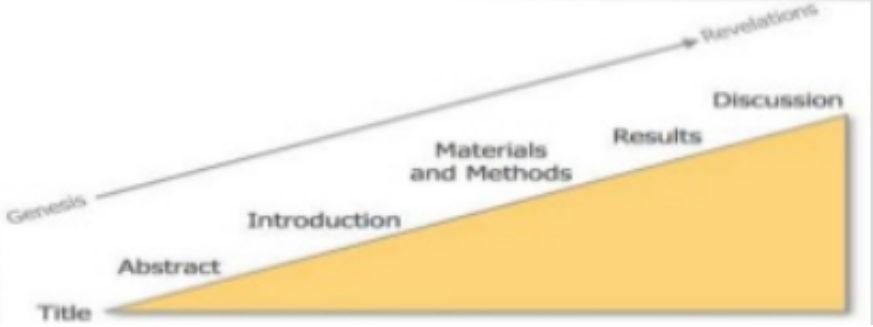
Results

Real meat of a **primary research article.**

The figures contain the majority of the data.

Accompanying text contains verbal descriptions of the pieces of data the authors feel were most critical.

Make sure to spend ample time thoroughly looking at all the graphs, pictures, and tables, and reading their accompanying legends!



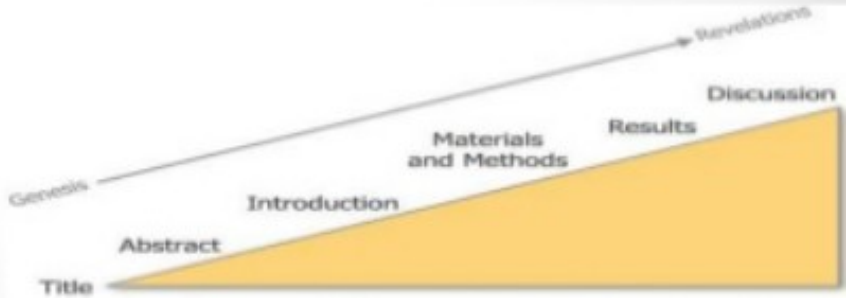
Discussion

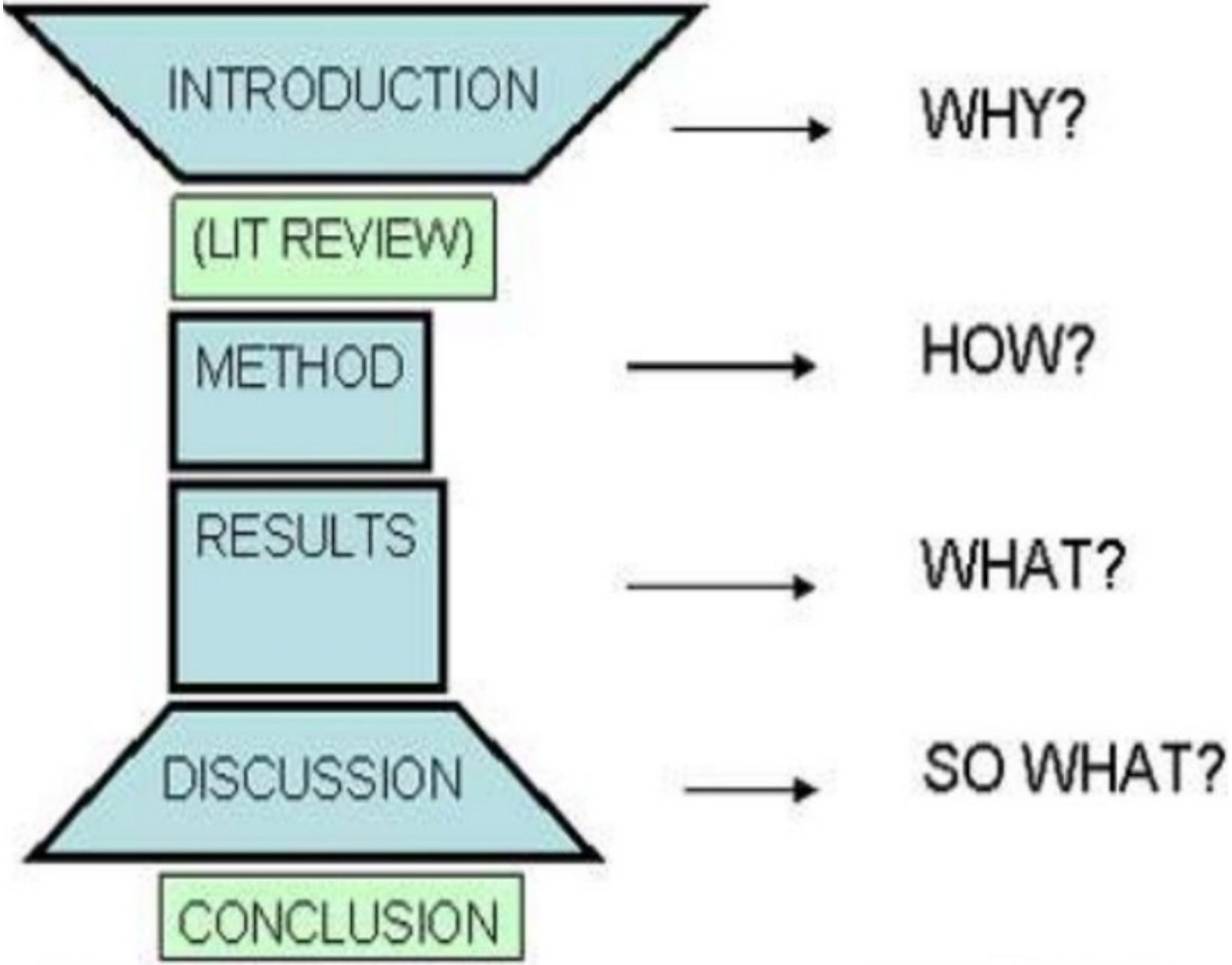
Authors' opportunity to give you their opinions.

They draw conclusions about the results.

Allows the exchange of ideas between scientists.

Provide a clear answer to the question posed in the Introduction.




INTRODUCTION
WHY?
(LIT REVIEW)
METHOD
HOW?
RESULTS
WHAT?
DISCUSSION
SO WHAT?
CONCLUSION

ARTICLE

DOI: 10.1038/s41467-018-03770-3 OPEN

Targeting of NAT10 enhances healthspan in a mouse model of human accelerated aging syndrome

Gabriel Balmus[1,2], Delphine Larrieu[1,9], Ana C. Barros[1,2], Casey Collins[2], Monica Abrudan[2], Mukerrem Demir[1], Nicola J. Geisler[1,2], Christopher J. Lelliott[2], Jacqueline K. White[2], Natasha A. Karp[2,3], James Atkinson[4], Andrea Kirton[2], Matt Jacobsen[4], Dean Clift[5], Raphael Rodriguez[6,7,8], Sanger Mouse Genetics Project, David J. Adams[2] & Stephen P. Jackson[1]

Hutchinson-Gilford Progeria Syndrome (HGPS) is a rare, but devastating genetic disease characterized by segmental premature aging, with cardiovascular disease being the main cause of death. Cells from HGPS patients accumulate progerin, a permanently farnesylated, toxic form of Lamin A, disrupting the nuclear shape and chromatin organization, leading to DNA-damage accumulation and senescence. Therapeutic approaches targeting farnesylation or aiming to reduce progerin levels have provided only partial health improvements. Recently, we identified Remodelin, a small-molecule agent that leads to amelioration of HGPS cellular defects through inhibition of the enzyme N-acetyltransferase 10 (NAT10). Here, we show the preclinical data demonstrating that targeting NAT10 in vivo, either via chemical inhibition or genetic depletion, significantly enhances the healthspan in a *Lmna*^{G609G} HGPS mouse model. Collectively, the data provided here highlights NAT10 as a potential therapeutic target for HGPS.

What is the main goal of this article?

Hutchinson-Gilford Progeria Syndrome (HGPS) is a rare, but devastating genetic disease characterized by segmental premature aging, with cardiovascular disease being the main cause of death. Cells from HGPS patients accumulate progerin, a permanently farnesylated, toxic form of Lamin A, disrupting the nuclear shape and chromatin organization, leading to DNA-damage accumulation and senescence. Therapeutic approaches targeting farnesylation or aiming to reduce progerin levels have provided only partial health improvements. Recently, we identified Remodelin, a small-molecule agent that leads to amelioration of HGPS cellular defects through inhibition of the enzyme N-acetyltransferase 10 (NAT10). Here, we show the preclinical data demonstrating that targeting NAT10 in vivo, either via chemical inhibition or genetic depletion, significantly enhances the healthspan in a *Lmna*^{G609G} HGPS mouse model. Collectively, the data provided here highlights NAT10 as a potential therapeutic target for HGPS.

Look the figures and identify the steps of experiments

Why did the authors perform these experiment?
(Remember the progeria model phenotype)

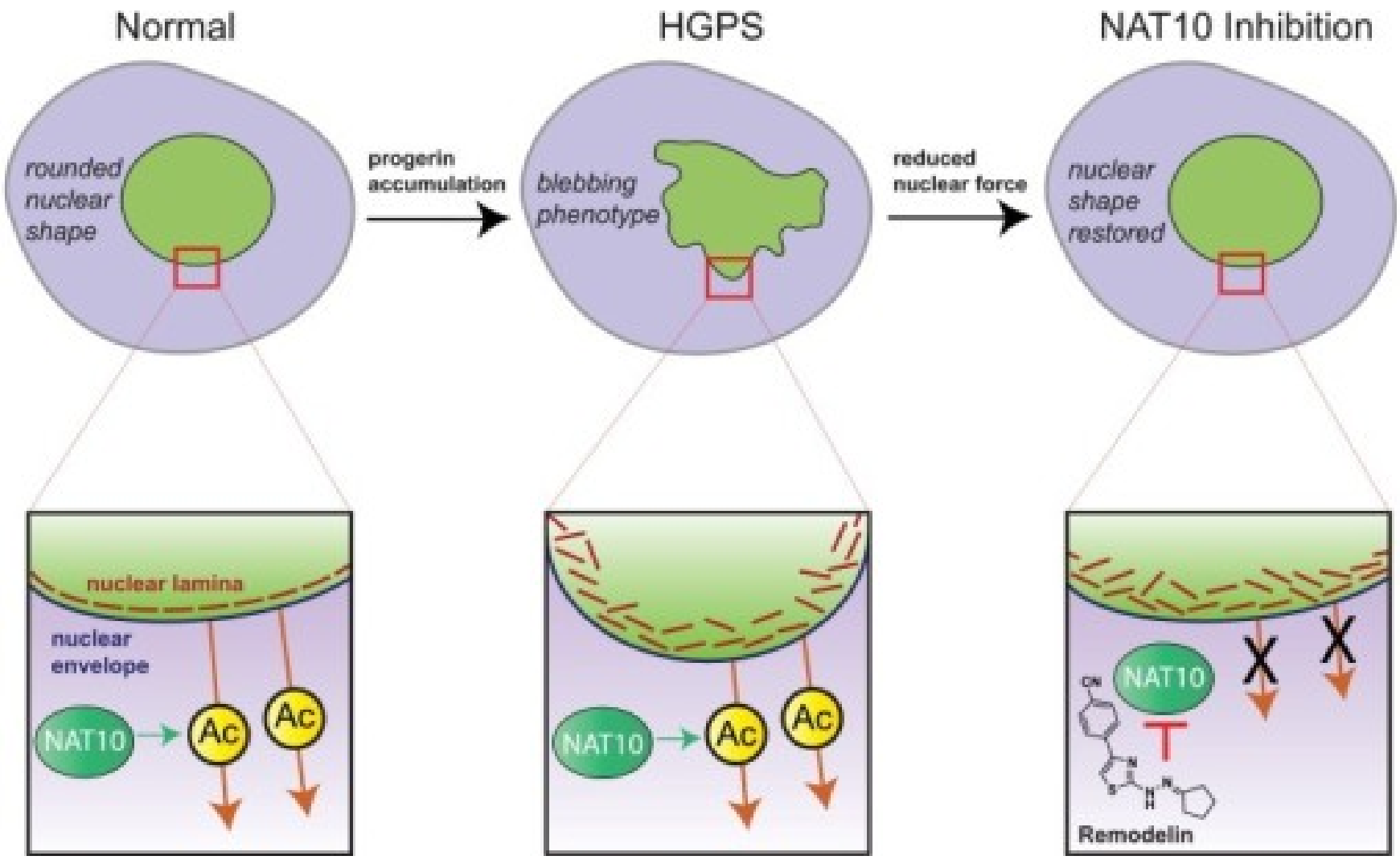
Look the figures and identify the steps of experiments

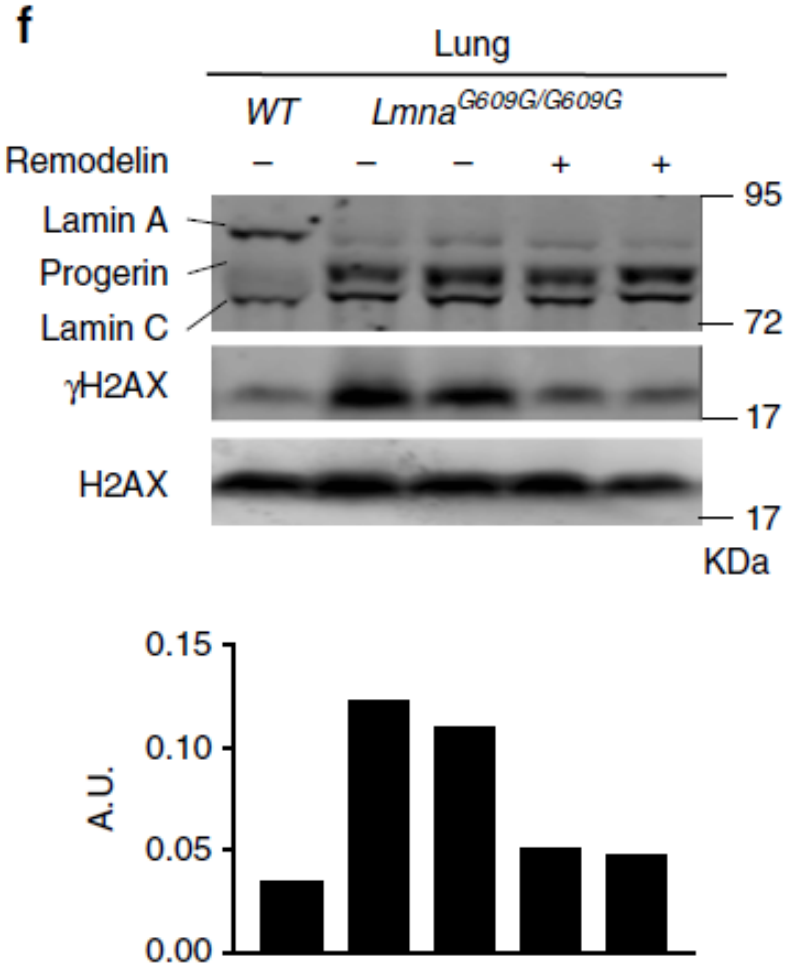
Why did the authors create a new mice model?

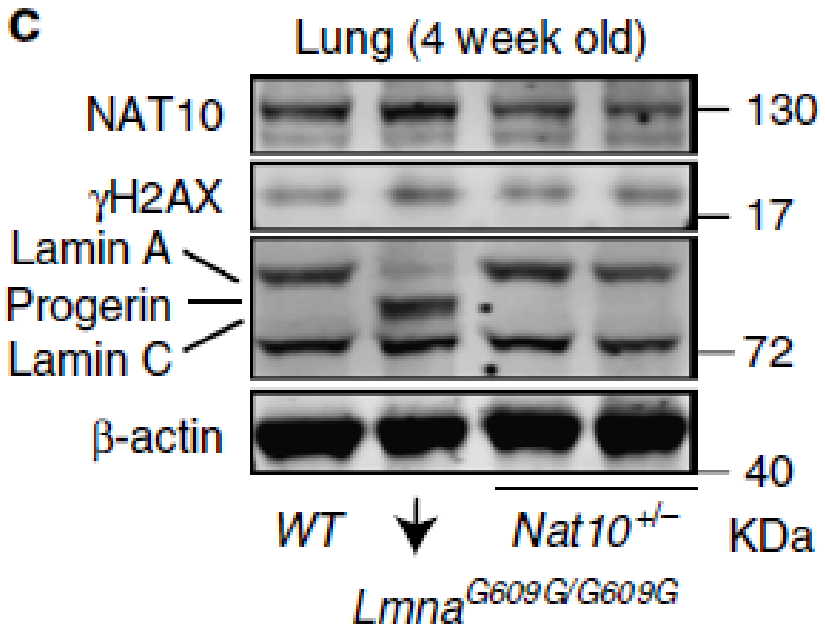
Engineering and characterization of a *Nat10*$^{+/-}$ mouse model.

DISCUSSION

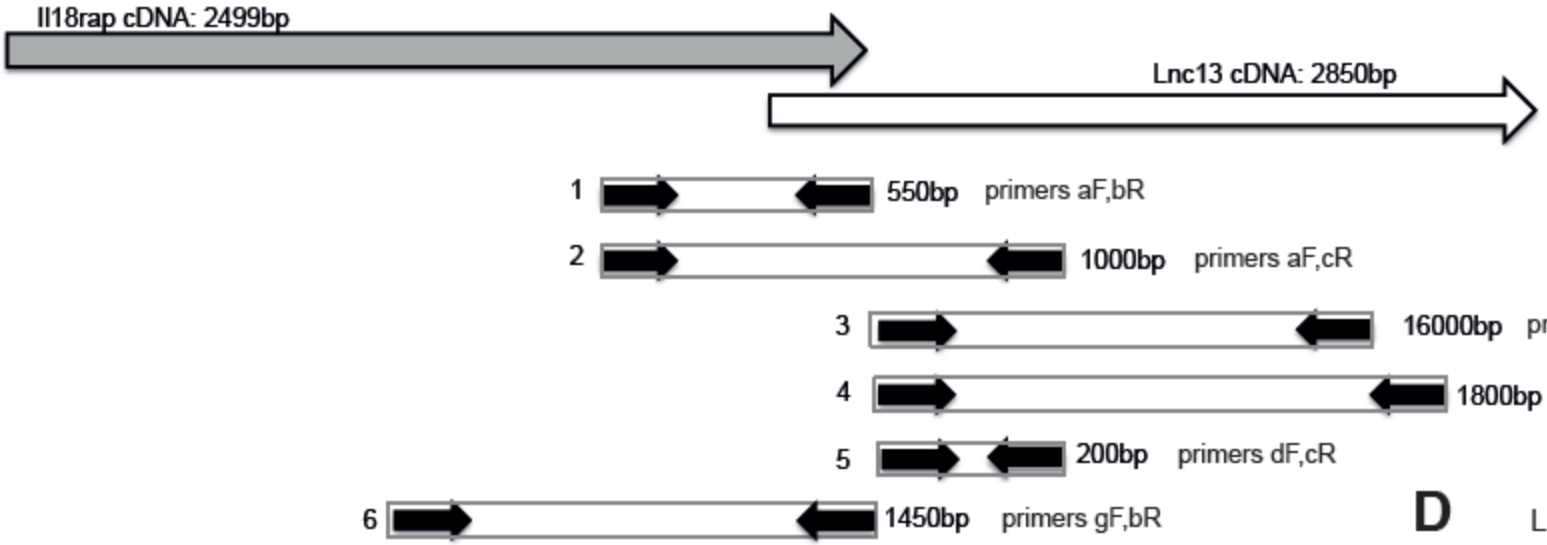
that acetylated α-tubulin lysine 40 (K40), a known NAT10 target[31,32], might also be used as a readout for NAT10 inhibition in cells and in vivo. These findings also correlated with our previous data, indicating that NAT10 inhibition ameliorates HGPS cellular phenotypes, at least in part, by mediating microtubule destabilization[25]. As α-tubulin acetylation at K40 is elevated in HGPS tissues and the cells are compared to controls, it will be of interest to explore whether this could be used to monitor disease progression and also enhance our understanding of disease pathobiology. Finally, we speculate that because the hallmarks of HGPS are present at lower levels in the vasculature and other tissues of aged-normal individuals[33], NAT10 targeting might offer therapeutic opportunities in broader settings. In accord with such a possibility, we have recently reported the effects of NAT10 inhibition in normally aged smooth muscle cells[26], that might suggest the potential for NAT10 inhibition in the context of normal ageing.

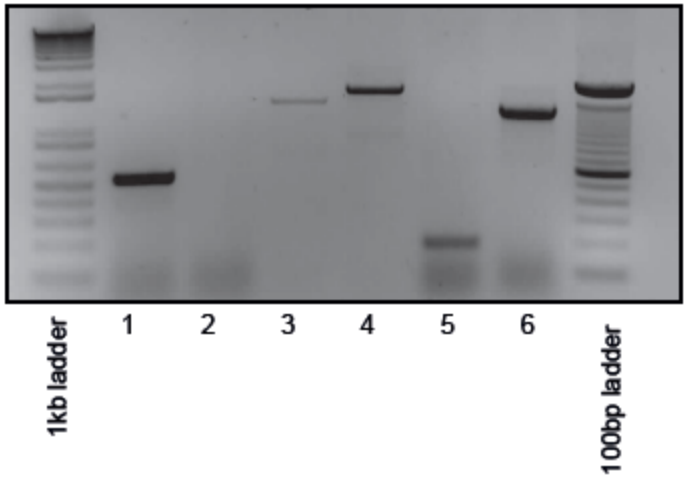

Normal
HGPS
NAT10 Inhibition
rounded nuclear shape
progerin accumulation
blebbing phenotype
reduced nuclear force
nuclear shape restored
nuclear lamina
nuclear envelope
NAT10
Ac
Ac
NAT10
Ac
Ac
NAT10
Remodelin

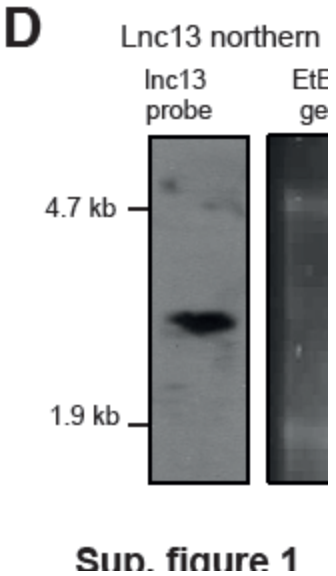

f
Lung
WT
Lmna G609G/G609G
Remodelin
– – – + +
Lamin A
Progerin
Lamin C
γH2AX
H2AX
95
72
17
17
KDa
0.15
0.10
0.05
0.00
A.U.


c
Lung (4 week old)
NAT10
γH2AX
Lamin A
Progerin
Lamin C
β-actin
130
17
72
40
KDa
WT
Nat10 +/–
Lmna G609G/G609G

IL18rap and Lnc13 transcripts are indipendent, two different transcripts







Sup. figure 1

fig. S1C

Thank you very much
for your collaboration and patience

I hope that these lessons are been a good experience and will be a useful tool