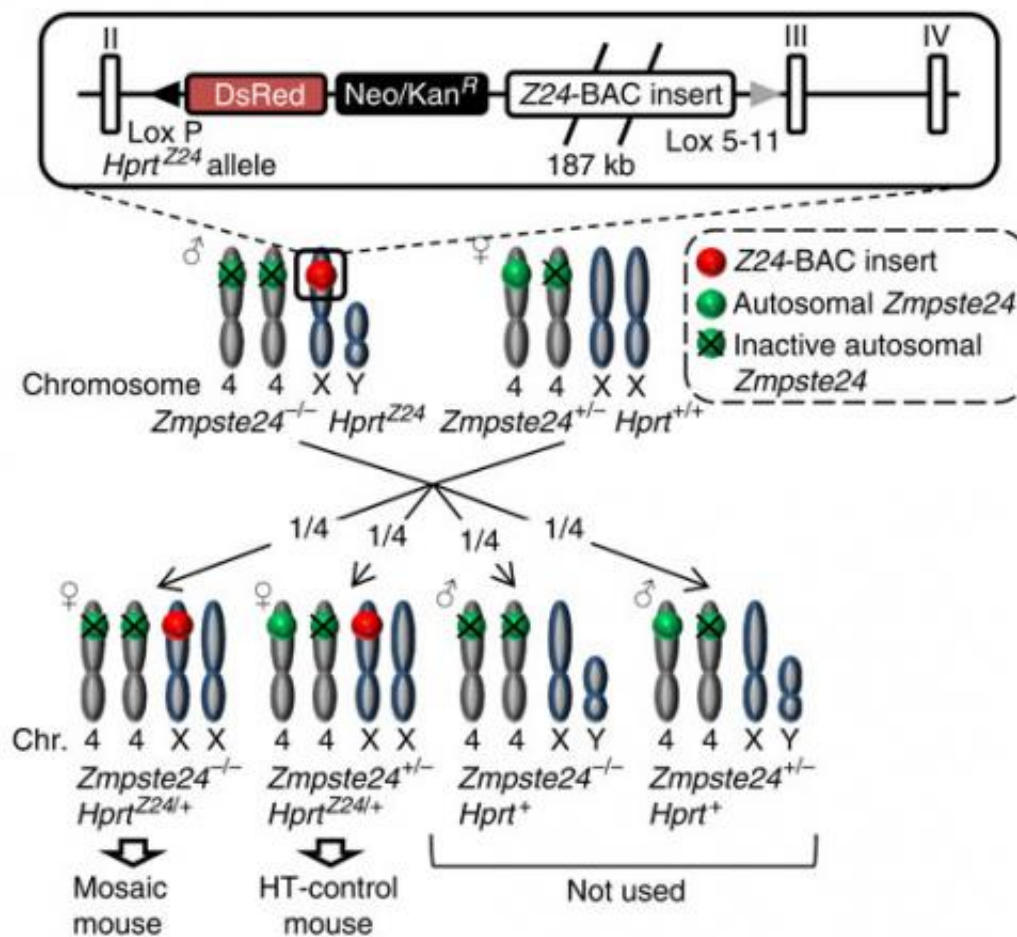


Prelamin A protein causes accelerated ageing disorders and also prevents the spread of cancer cells

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Absence of progeroid phenotype in ZMPSTE24 mosaic mice. (a) Breeding scheme. ZMPSTE24/HprtZ24 male mice were bred with ZMPSTE24^b/Hprt^b/b female mice to yield female offspring that were either ZMPSTE24/HprtZ24/b (mosaic) or ZMPSTE24^b/HprtZ24/b (HTcontrol). DOI: 10.1038/ncomms3268

Researchers have found that a protein responsible for accelerated aging disorders can dramatically slow down the spread of cancers.

The team revealed that prelamin A, responsible for accelerated ageing in a condition called progeria, can prevent the progression of malignant or cancerous tumours. They achieved this by using mosaic mouse models, genetically modified [mice](#) bearing the [protein](#) prelamin A in half of their cells.

Ageing and cancer are intimately related processes, but their links are complex. The risk of developing tumours increases with age, but some of the mechanisms favouring ageing can also slow down the appearance and development of cancer. The results from this study represent an advance in the understanding of the underlying [biological mechanisms](#) that link age and [cancer development](#), as well as possible new [drug targets](#) in the future.

"Mice with prelamin A in all their cells [age](#) more quickly and do not live longer than 4-5 months, which extremely hampers the study of cancer, as there is no time for the disease to fully develop," indicates Jorge de la Rosa, first author from Instituto de Medicina Oncológica y Molecular de Asturias.

Researchers previously developed mice that have an underactive ZMPSTE24 gene that mimic the ageing disorder progeria to test for possible treatments. This causes the protein prelamin A to accumulate and in turn results in progeria. To better study the association of ageing and cancer development, the team developed a mosaic model where ZMPSTE24 was underactive in half of the cells and working normally in the other half of the cells.

"Mosaic mice, however, live as long as normal mice, up to two to three years, and they keep 50% of cells with prelamin A in all their tissues

throughout [lifespan](#), which has permitted us to study the effect of this protein on cancer," comments Juan Cadiñanos, lead author from the Instituto de Medicina Oncológica y Molecular de Asturias.

The team found that the mosaic mice were completely healthy, without any of the physical deformities shown by mice with prelamin A-induced progeria: reduced size and weight, loss of fat, infertility and premature death. This suggests that it might not be necessary to correct the defects in all the cells of patients with progeria, but only some. These results provide hope for a successful treatment of patients with [progeria](#) in the future.

The team studied the development of tumours such as skin, lung and mouth cancers in the mosaic mice. Although the mosaic mice developed the same number of tumours as normal mice, they had fewer cancerous or malignant tumours - tumours cells that can break through the biological barriers that confine them and spread to other tissues in the body. They could also check the anti-invasive effect of prelamin A on human oral, lung and breast cancer cells.

Accumulation of prelamin A in [cells](#) appears not to stop or reduce the initiation and development of tumour growth, but greatly reduces the capacity of the tumour to become cancerous and spread to other parts of the body. The role prelamin A has to prevent the invasion of cancer suggests that ZMPSTE24 could be an attractive new target for cancer therapy.

"Our results are extremely exciting and offer great potential for the development of new therapies against both cancer and accelerated ageing disorders," says Dr Allan Bradley, author from the Wellcome Trust Sanger Institute. "These mouse models are invaluable for understanding the origins of disease and also to inspire new treatments against these debilitating conditions."

More information: de la Rosa, J. et al. Prelamin A causes progeria through cell-extrinsic mechanisms and prevents cancer invasion? *Nature Communications* 2013. [DOI: 10.1038/ncomms3268](https://doi.org/10.1038/ncomms3268)

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