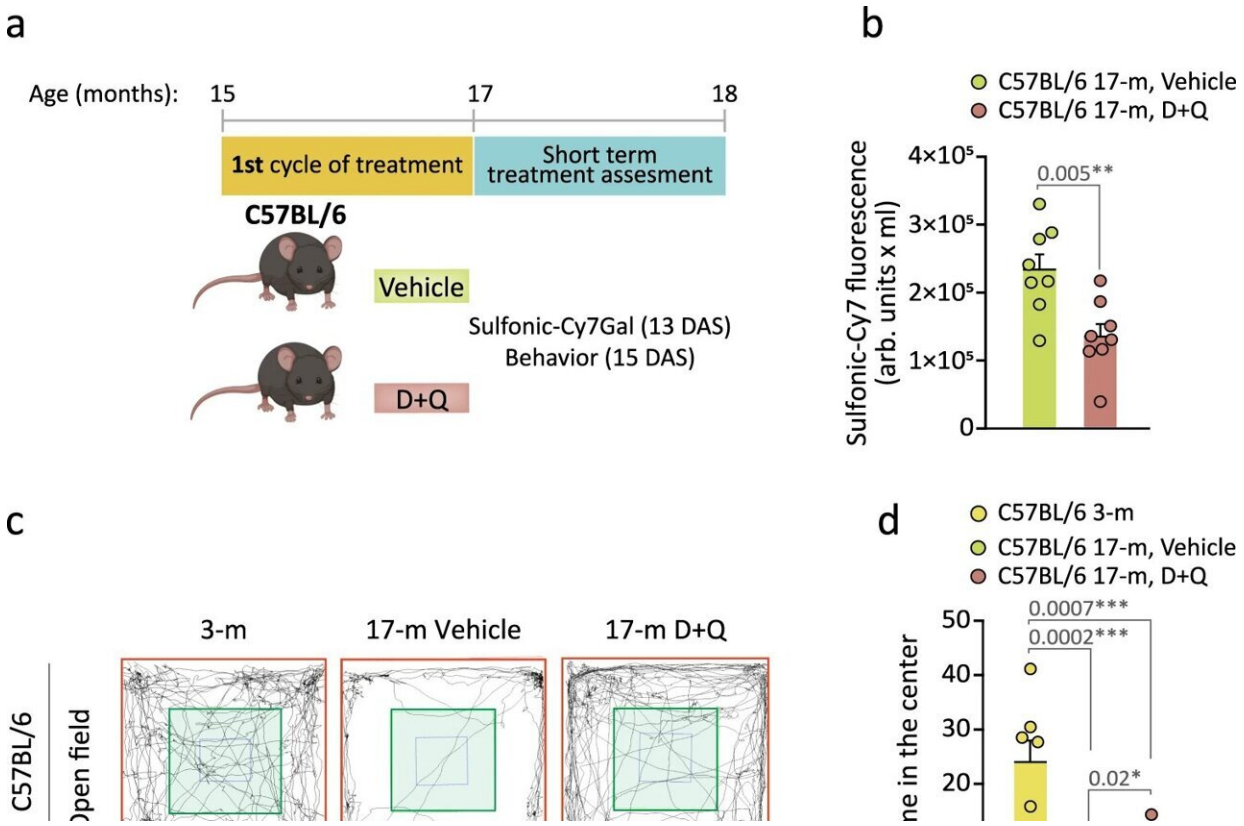
Medical Xpress

How do we age? New probe can detect senescent cells in urine

February 28 2024



Monitoring of senolytic intervention with the sulfonic-Cy7Gal probe during natural aging. **a** Schedule of the senolytic treatment and its monitoring in C57BL/6 mice. 15-m mice received the senolytic drugs D + Q or the vehicle for 5 weeks and, 13 days after senolysis (DAS), the overall β-Gal activity was assessed with sulfonic-Cy7Gal as a measure of senescence burden. Two days later, anxious behavior was examined. **b** Sulfonic-Cy7 fluorescence measurement in the urine of 17-m C57BL/6 treated with D + Q (n = 8) or vehicle (n = 8). **c** Representative map of movement in the open field test

comparing young (3-m) to old mice (17-m) that were treated or not with senolytic drugs. **d** Quantification of the percentage of the time that mice spent in the central area (green zone) of the open field, comparing mice aged 3- (n = 7) to 17-m treated with D + Q (n = 10) or vehicle (n = 8). **e**, Representative map of movement in the EPM test comparing young (3-m) to old (17-m) mice that were treated with vehicle or senolytic drugs. **f** Quantification of the percentage of time that mice spent in the open arm of the EPM, comparing mice of 3- (n = 6) and 17-m that were treated (n = 10) or not (n = 10) with D + Q. **g** Significant linear correlation between sulfonic-Cy7 fluorescence in urine and the percentage of time spent in the center of the open field in mice treated with D + Q (n = 5) or vehicle (n = 7). **h** Significant linear correlation between sulfonic-Cy7 fluorescence in urine and the percentage of time spent in the open arm of the EPM test in mice treated with D + Q (n = 6) or vehicle (n = 8). Fold change refers to sulfonic-Cy7 fluorescence levels in the urine of untreated mice in both correlation graphs. Graphs represent mean ± SEM. Unpaired two-tailed Student's t-test was used for statistical analysis of the sulfonic-Cy7Gal fluorescence readout, one-way ANOVA for the assessment of anxious behavior and multiple linear regression to determine the relationship equation between both. P-values and the number of independent biological samples (represented as dots) are shown in the graphs. Source data is provided as a Source Data file. Credit: *Nature Communications* (2024). DOI: 10.1038/s41467-024-44903-1

A team of researchers has developed a new probe to detect senescent cells in urine, which could help to monitor and better understand the processes related to aging and establish new strategies to reverse the degenerative processes associated with it.

The research is published in *Nature Communications*.

As the researchers explain, one of the hallmarks of aging is the increased frequency of senescent cells in most organs, leading to tissue dysfunction. The presence of these cells is also associated with many age-related diseases.

"The main goal of cellular senescence is to prevent the proliferation of damaged cells that can lead to cancer. However, when damage persists or during aging, senescent cells accumulate abnormally, affecting tissue function and accelerating aging."

"This is why it is important to create new systems to detect these cells easily and effectively," says Ramón Martínez Máñez, deputy director of the Inter-University Research Institute for Molecular Recognition Research and Technological Development (IDM) at the UPV and scientific director of CIBER-BBN.

When injected into mice, the probe interacts with an enzyme particularly abundant in senescent cells, producing a fluorescent compound rapidly excreted in the urine. "And depending on the intensity of the signal in the urine, we can know the burden of senescent cells in the organism," says Isabel Fariñas of the UV and deputy director of CIBERNED, and researcher Mar Orzáez of the CIPF.

In their study, they also monitored senolytic treatment with drugs that eliminate senescent cells and can rejuvenate tissues. They observed that the intensity of the signal in the urine was related to the reduction of senescence in the animals and the reduction of age-related anxiety.

"When administered, a fluorophore is released, which is ultimately excreted by the kidneys and can be measured in the urine. The intensity of the fluorophore indicates the level of cellular senescence load, and we have seen that this correlates with age-related anxiety during aging and senolytic treatment," explains Isabel Fariñas of UV and deputy director of CIBERNED.

The results obtained by the team from the Universitat Politècnica de València, Universitat de València, CIBER-BBN, CIBERNED, and the Príncipe Felipe Research Centre open up a way to better understand

aging and its effects on health. "It could help us to develop more effective ways of tackling age-related problems, as well as easy urinary treatments aimed at eliminating or reducing cellular senescence, even in humans," concludes Ramón Martínez Máñez.

More information: Sara Rojas-Vázquez et al, A renal clearable fluorogenic probe for in vivo β-galactosidase activity detection during aging and senolysis, *Nature Communications* (2024). DOI: 10.1038/s41467-024-44903-1

Provided by Universitat Politècnica de València