Data input form: MouseAGE Database

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Preferred acknowledgement:

Summarise supporting data attached:

SAMP8 (senescence accelerated prone mouse 8) is a commercially available mouse obtained by phenotype selection, widely used in studies of aging focussed on brain changes of inflammation, cognitive loss and other traits of early Alzheimer-like neurodegeneration. The control strain is SAMR1 (senescence resistant prone mouse 1). Strains were obtained by Takeda's group in the 1970s.

Information and selected references are included.

Ageing / disease:

Accelerated senescence / Alzheimer (traits)

Model: SAMP8

Clinically relevant? (Yes or No): Yes

Explanation of why clinically relevant or not:

This mouse strain models early pathological phases of age-related dementia and Alzheimer, without showing amyloid plaques. It has been used and characterized for behaviour and tissue alterations by several laboratories.

Characteristics, timing of appearance of phenotype and phenotypic tests used (attach supporting data when unpublished if available):

Strains were established through phenotypic selection from a common genetic pool of AKR/J mice (Takeda, 1999). The phenotype of pathological brain aging is fully developed at 5 months, showing cognitive loss measured by standardized test of learning and memory and a range of cerebral alterations. Namely: (i) reduced synaptic plasticity with impaired long-term potentiation LTP) and lower activation of plasticity pathways; (ii) increased levels of hyperphosphorylated tau (p-tau) with tau-related enzyme disorder; (iii) higher accumulation of amyloid b peptides (Ab) which would be

caused by an abnormally elevated synthesis of Ab protein precursor (AbPP) (in addition to disturbances in the blood-brain barrier); (iv) oxidative stress, (v) increased inflammation, and (vi) altered epigenetic markers. However it is not a good model for Behavioral and Psychological symptoms of dementia (BPSD)-like behaviors. Specifically, these mice show lower anxiety than controls.
See selected references below for strain characteristics (Akiguchi et al., 2017; Griñán-Ferré et al., 2018) and protective studies (Pérez-Cañamás et al., 2016; Palomera-Ávalos et al., 2017; Corpas et al., 2017).
Furthermore, astrocyte and neuron cultures derived from SAMP8 embryos maintain senescence and neurodegeneration markers and are suitable cell systems for frailty studies (Díez-Vives et al., 2009; García-Matas et al., 2015; Cristòfol et al., 2012).

If applicable, Intervention(s) performed (type, dose, route of administration, frequency):

The model develops in natural conditions. Experimental interventions to study treatments are practicable.

Phenotype post-treatment (include null or negative results and attach supporting data separately):

A number of treatments demonstrated active protection, with partial or total reversion of the age-related phenotype.

References (list below):

Strain

Takeda T. Senescence-accelerated mouse (SAM): a biogerontological resource in aging research. Neurobiol Aging. 1999;20(2):105-10. Review. PMID: 10537019

Akiguchi I, Pallàs M, Budka H, Akiyama H, Ueno M, Han J, Yagi H, Nishikawa T, Chiba Y, Sugiyama H, Takahashi R, Unno K, Higuchi K, Hosokawa M. SAMP8 mice as a neuropathological model of accelerated brain aging and dementia: Toshio Takeda's legacy and future directions. Neuropathology. 2017;37(4):293-305. doi: 10.1111/neup.12373. Review. PMID: 28261874

Griñán-Ferré C, Corpas R, Puigoriol-Illamola D, Palomera-Ávalos V, Sanfeliu C, Pallàs M. Understanding epigenetics in the neurodegeneration of Alzheimer's disease: SAMP8 mouse model. J Alzeimers Dis, 2018;62(3):943-963. doi: 10.3233/JAD-170664. Review. PMID: 29562529

Studies

Pérez-Cañamás A, Sarroca S, Melero-Jerez C, Porquet D, Sansa J, Knafo S, Esteban JA, Sanfeliu C, Ledesma MD. A diet enriched with plant sterols prevents the memory impairment induced by

cholesterol loss in senescence-accelerated mice. Neurobiol Aging. 2016;48:1-12. doi: 10.1016/j.neurobiolaging.2016.08.009. PMID: 27622776

Palomera-Avalos V, Griñán-Ferré C, Puigoriol-Illamola D, Camins A, Sanfeliu C, Canudas AM, Pallàs M. Resveratrol Protects SAMP8 Brain Under Metabolic Stress: Focus on Mitochondrial Function and Wnt Pathway. Mol Neurobiol. 2017;54(3):1661-1676. doi: 10.1007/s12035-016-9770-0. PMID: 26873850

Corpas R, Hernández-Pinto AM, Porquet D, Hernández-Sánchez C, Bosch F, Ortega-Aznar A, Comellas F, de la Rosa EJ, Sanfeliu C. Proinsulin protects against age-related cognitive loss through anti-inflammatory convergent pathways. Neuropharmacology. 2017;123:221-232. doi: 10.1016/j.neuropharm.2017.06.014. PMID: 28624504

IN VITRO

Díez-Vives C, Gay M, García-Matas S, Comellas F, Carrascal M, Abian J, Ortega-Aznar A, Cristòfol R, Sanfeliu C. Proteomic study of neuron and astrocyte cultures from senescence-accelerated mouse SAMP8 reveals degenerative changes. J Neurochem. 2009;111(4):945-55. doi: 10.1111/j.1471-4159.2009.06374.x. PMID: 19735447

García-Matas S, Paul RK, Molina-Martínez P, Palacios H, Gutierrez VM, Corpas R, Pallas M, Cristòfol R, de Cabo R, Sanfeliu C. In vitro caloric restriction induces protective genes and functional rejuvenation in senescent SAMP8 astrocytes. Aging Cell. 2015;14(3):334-44. doi: 10.1111/acel.12259. PMID: 25711920

Cristòfol R, Porquet D, Corpas R, Coto-Montes A, Serret J, Camins A, Pallàs M, Sanfeliu C. Neurons from senescence-accelerated SAMP8 mice are protected against frailty by the sirtuin 1 promoting agents melatonin and resveratrol. J Pineal Res. 2012 Apr;52(3):271-81. doi: 10.1111/j.1600-079X.2011.00939.x. PMID: 22085194