Humanized mouse line expressing the human WT or CX3CR1I249/ M280 polymorphic variant (HHMI/USTA)

This mouse model expresses the human version of the receptor CX3CR1 harboring the sequence I249/M280 and can be used to study neuroinflammatory processes related to microglia-neuron communication in neurodegenerative diseases.

Fractalkine is a unique chemokine present on neuronal membranes and capable of being released as a soluble protein. Fractalkine exerts its functions by binding the receptor CX3CR1 on microglial cells. Mice lacking fractalkine or its receptor exhibit severe brain pathology in models of multiple sclerosis and in models of mild systemic inflammation induced by the major component of gram negative bacteria lipopolysaccharide. In humans, two single nucleotide polymorphisms result in amino acid substitutions: at position 249 of the protein (Valine to Isoleucin) and at position 280 (Threonine to Methionine). The variant CX3CR1 I249/M280 is present in about 25-30% of the population and exerts a dominant effect that leads to reduced adhesive properties. CX3CR1 I249/M280 is associated with reduced risk of atherosclerosis, and increased susceptibility to age related macular degeneration. To study the function of the human receptor, the researcher has generated knock-in mice expressing the variant CX3CR1I249/M280 sequence under the control of the mouse CX3CR1 regulatory elements to define the role of the human CX3CR1 variant in neuroinflammation.

Technology ID

LIT01-29

Category

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Life Sciences/Materials/Mouse Models

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