

# Analysis of social interactions in a genetic model of Lamb-Shaffer syndrome autism spectrum disorders

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Many neurodevelopmental disorders associated with deficiencies in social interaction, language difficulties and repetitive behaviours are grouped under the name of autism spectrum disorders (ASD). Although the genetic causes of ASD are complex, one of the genes that have been associated with ASD is *Sox5*. In humans, heterozygous genetic alterations comprising *Sox5* cause Lamb-Shaffer syndrome (OMIM #616803). *Sox5* encodes a transcription factor with important functions in the control of neurogenesis (Li et al., 2022) and in the specification of projection neurons of the cerebral cortex (Lai et al., 2008). Moreover, it has been described that the CA2 region of the hippocampus is fundamental in social behaviour in mice, a region where we have previously shown that *Sox5* is expressed (Fernandez-Lamo et al., 2019; Hitti & Siegelbaum, 2014). Using conditional *Sox5* mutant mice specific for the CA2 region (*Amigo2-cre/Sox5<sup>fl/fl</sup>;Sox5<sup>Amigo2</sup>*) we have determined that robust lack of *Sox5* expression causes PCP4 level decrease in more than half of the pyramidal neurons in CA2. Furthermore, using an extensive battery of behavioural assays we have determined that *Sox5<sup>Amigo2</sup>* mutant mice: i) exhibit normal basic reflexes, weight, locomotion abilities, and anxiety levels; ii) exhibit a good performance in Morris water maze test; iii) present normal social preference and iv) both males and female lose social recognition memory. Preliminary data also suggest possible alterations in the expression of neuronal activity marker cFos in the CA2 region of *Sox5<sup>Amigo2</sup>* mice after performing social interaction tasks. Thus, we propose that *Sox5<sup>Amigo2</sup>* mice could provide a new model of ASD, based on cellular and functional alterations of the CA2 region of the hippocampus, that serves to understand the hippocampal component in the pathophysiology of ASD in Lamb-Shaffer syndrome and for the testing of new therapeutic strategies.

**Keywords (max.3):** *Sox5*, Lamb-Shaffer, ASD