



THE UNIVERSITY *of* EDINBURGH

Edinburgh Research Explorer

A primate resource for autism research

Citation for published version:

Osterweil, E 2019, 'A primate resource for autism research', *Science translational medicine*.
<https://doi.org/10.1126/scitranslmed.aay3571>

Digital Object Identifier (DOI):

[10.1126/scitranslmed.aay3571](https://doi.org/10.1126/scitranslmed.aay3571)

Link:

[Link to publication record in Edinburgh Research Explorer](#)

Document Version:

Peer reviewed version

Published In:

Science translational medicine

General rights

Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy

The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact openaccess@ed.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.



Editor's Choice Summary

Issue date: (we will complete)

DOI: 10.1126/scitranslmed.axyXXXX (we will complete)

Volume: (we will complete)

E-locator: (we will complete)

Overline: Autism Spectrum Disorder

Title: A primate resource for autism research

One-sentence summary: A macaque model of *SHANK3* mutation exhibits neurological phenotypes similar to patients with autism and Phelan-McDermid Syndrome (PMS).

Your name: Emily K. Osterweil

Your affiliation:

Centre for Discovery Brain Sciences, Simons Initiative for the Developing Brain

University of Edinburgh, Edinburgh, UK EH8 9XD

Emily.osterweil@ed.ac.uk

Text of summary

The prevalence of autism in the US and UK population is greater than 1%, yet there are currently no available therapeutics that target the underlying pathology. The rise of rodent models targeting identified risk genes for autism has generated a renewed interest in the search for a pharmacological therapy. However, the spectrum of behavioural disturbances associated with autism have been difficult to model in rodents that display clear differences in cognitive and social strategies. Additionally, the development of biomarkers using resting-state functional MRI has been difficult to adapt to preclinical rodent models. To tackle these problems, Zhou et al. have created a primate model of autism by introducing germline mutations in the *SHANK3* gene of macaques (*Macaca fascicularis*) using CRISPR-Cas9 genetic editing. Mutations in *SHANK3* are frequently associated with the development of autism and the neurodevelopmental disorder Phelan-McDermid Syndrome (PMS). Using a battery of behavioural tests, the authors show that macaques with *SHANK3* mutations exhibit multiple behavioural phenotypes reminiscent of patients with autism or PMS. These include severe sleep disturbances, increased stereotypic behaviour, impaired social interaction, and reduced vocalization. In addition, video-based eye tracking revealed alterations in pupillary reflex and gaze fixation that are seen in children that develop autism. Together, the results suggest the *SHANK3* mutant macaque model will be a valuable resource for modelling the disruptions in complex brain function seen in autism. Moreover, examination of *SHANK3* mutants using resting-state functional MRI revealed alterations in global and local brain connectivity that may be useful as a preclinical biomarker.

The development of primate models such as the *SHANK3* mutant macaque is an advance that may improve the predictive value of autism models. Now researchers can use this model to test the impact of potential therapeutic strategies on more complex behavioural symptoms and identify treatment-sensitive biomarkers that can be used for clinical trials. The main limitation of the study is a relatively small sample size that is likely due to the cost of creating and housing primate models. Although further studies are needed to determine the true advantages of using this macaque model, it is likely that primate models will accelerate autism research and enable the identification of more effective therapeutic strategies.

Highlighted Article

Zhou Y, Sharma J, Ke Q, Landman R, Yuan J, Chen H, Hayden DS, Fisher JW 3rd, Jiang M, Menegas W, Aida T, Yan T, Zou Y, Xu D, Parmar S, Hyman JB, Fanucci-Kiss A, Meisner O, Wang D, Huang Y, Li Y, Bai Y, Ji W, Lai X, Li W, Huang L, Lu Z, Wang L, Anteraper SA, Sur M, Zhou H, Xiang AP, Desimone R, Feng G, Yang S. Atypical behaviour and connectivity in *SHANK3*-mutant macaques. *Nature*. Jun;570(7761):326-331. doi: 10.1038/s41586-019-1278-0. (2019).

URL of citation

<https://www.nature.com/articles/s41586-019-1278-0>