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Advanced Autism Spectrum Disorder Research

Translational Disease Models and Behavioral Phenotyping Assays

Inotiv offers disease models and assays that are optimized to deliver translationally relevant data to guide autism spectrum disorders (ASD) research. Powered by our legacy companies, such as Envigo, Bolder BioPATH, and Histotox Labs, our models and services can help propel the discovery and development of therapies for ASD.

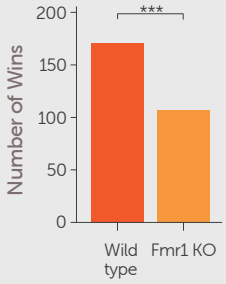
Genetically Engineered Rat Models

Inotiv offers genetically engineered rat models of ASD. Our models, originally created at SAGE Labs, Inc., provide researchers preclinical tools for investigating the role of genetic mutations and environmental factors in the etiology of ASD.

- CHD8 knockout rat
- Cntnap2 knockout rat
- Fmr1 knockout rat
- Gabrb3 knockout rat
- MeCP2 knockout rat
- Met knockout rat
- mGluR5 knockout rat
- Nrxn1 knockout rat
- Nlgn3 knockout rat
- Rbfox1 knockout rat

Figure 1 Fmr1 Knockout Male Rats Display Subordinance to Wild Type Cage Mates

Male hemizygous fragile X mental retardation 1 gene knockout (Fmr1 KO) rats were tested for dominance against wild type cage mates in the tube test of social dominance. Fmr1 KO rats (orange bar) had fewer wins compared to the wild type animals (red bar). *Data from Saxena, K. et al. (2018) Proc. Bio. Sci. 285:20180294.*

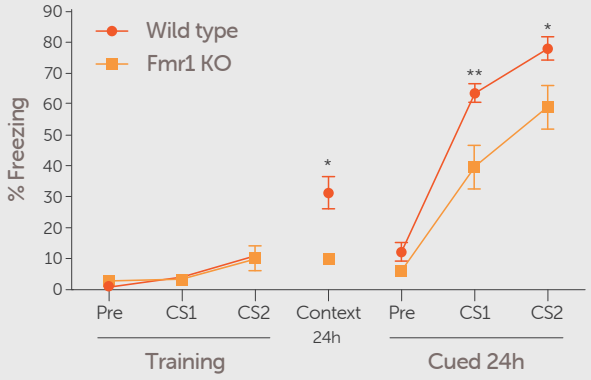


Behavioral Assays

Modeling ASD in rodents is difficult as the clinical presentation of this disorder is variable and includes a wide range of behaviors. Utilize the neuroscientists at Inotiv to assess the behavioral phenotype of your ASD model. Our assays have been validated on commonly used mouse models of ASD; however, we are able to validate these assays in your model of interest.

- Light/dark box test
- Open field assay
- Morris water maze
- Contextual/cued fear conditioning
- Nestlet shredding/nest building
- Marble burying
- Elevated plus maze

Figure 2 Fmr1 Knockout Mice Have Impaired Associative Fear Memory



Fmr1 KO mice were tested for associative fear memory with a contextual/cued fear memory behavioral assay. Compared to wild type mice (red line), knockout mice (orange line) showed reduced freezing during the testing phase to both the context and conditioned stimulus that was paired with an aversive stimulus.

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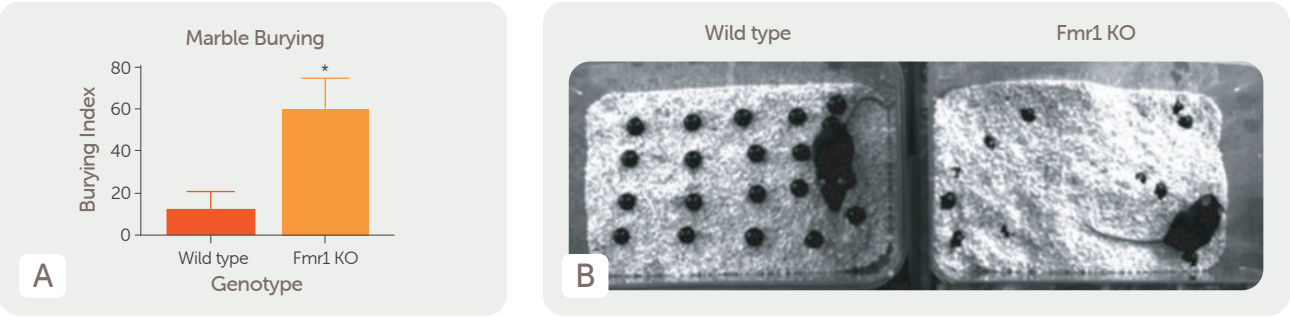
Behavioral Assays, continued

Figure 3 **Fmr1 Knockout Mice Exhibit Increased Perseverative Behavior**



A) Fmr1 KO mice (orange bar) display enhanced marble burying compared to wild type (red bar) mice, indicating increased perseverative behavior.
B) Representative cages showing marble burying of wild type (left image) and Fmr1 KO (right image) mice.

Histopathological Assessment

Inotiv offers a full range of immunohistochemistry, histopathology, and image analysis/digital pathology services for evaluation of ASD-related markers in neural tissue from your animal model. Our expertise includes, but is not limited to:

- Paraffin and frozen sections
- Brightfield and fluorescence microscopy
- New antibody protocol optimization
- Custom antibody panels
- Antibody validation
- Project specific R&D
- Automated quantification of IHC including nuclear, membrane, cytoplasm, and CD markers

We can also help with other aspects of your project, providing customized services to meet your requirements.

Additional Services for ASD Research

Inotiv's capabilities extend beyond models and behavioral testing. Other services include GLP and non-GLP *in vivo* and *in vitro* assays that can be customized to provide solutions for your research program.

- Stereotaxic surgery
- Tissue harvesting
- Oxidative stress enzymology
- Cytokine analysis with ELISA and Luminex® Assays
- CBC/clinical chemistry analysis
- Mass spectrometry proteomics
- Primary neural cell culturing
- Human stem cell and brain organoid culturing
- Confocal & electron microscopy

Contact us at inotivco.com/contact to discuss how our models and services can support your ASD research.