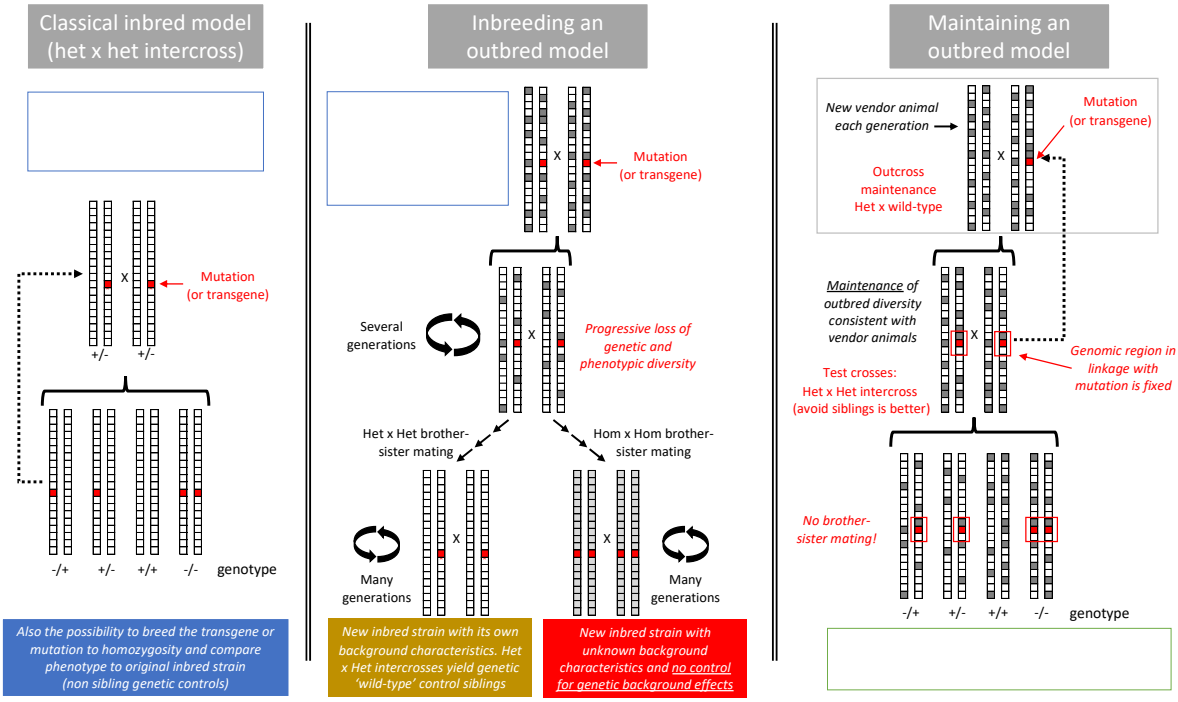
An MCW guide to maintaining outbred colonies

The Medical College of Wisconsin (MCW) takes care to maintain the genetic diversity of mutant and transgenic models generated in genetically outbred strains such as Long Evans to minimize genetic drift and maintain genetic diversity and strain phenotypes to be consistent with vendor-produced animals as much as possible.

Breeding strategies for rodent models

The diagram below compares breeding strategies for mutant and transgenic models produced in inbred and outbred rodent strains (left panel); the potential pitfalls of inbreeding an outbred model (middle panel); and the advantages of using an outcross strategy to maintain genetic diversity (right panel). The latter strategy uses a combination of outcross maintenance breeders to maintain genetic diversity and to produce heterozygous animals which are then intercrossed to generate experimental animals with the desired genotypes.

This overall breeding strategy helps to maintain the original outbred genetic nature of these models and is recommended for all laboratories who establish their own breeding colonies to avoid genetic drift and contrasting phenotypic variability across the autism research community.



Breeding strategies for autism related strains

Strategies for each autism related strain are shown below. Mutations in LE-*Cntnap2* and LE-*Nrxn1* strains are viable as homozygotes, though phenotypes are not yet characterized.

Mutations in LE-*Dyrk1a*, LE-*Grin2b*, LE-*Arid1b*, and LE-*Chd8* are lethal in a homozygous state. The timing of this lethality is currently unknown, but homozygous offspring are not found after ~P10 when we have collected tissue for genotyping.

The mutation in the LE-*Fmr1* model is X-linked like humans. We breed heterozygous females with wildtype males in our outcross stage such that a 50:50 ratio of wild-type and hemizygous mutant males are born. Viable homozygous LE-*Fmr1* females can be generated by intercrosses though, again, subsequent brother-sister mating is avoided to prevent inbreeding.