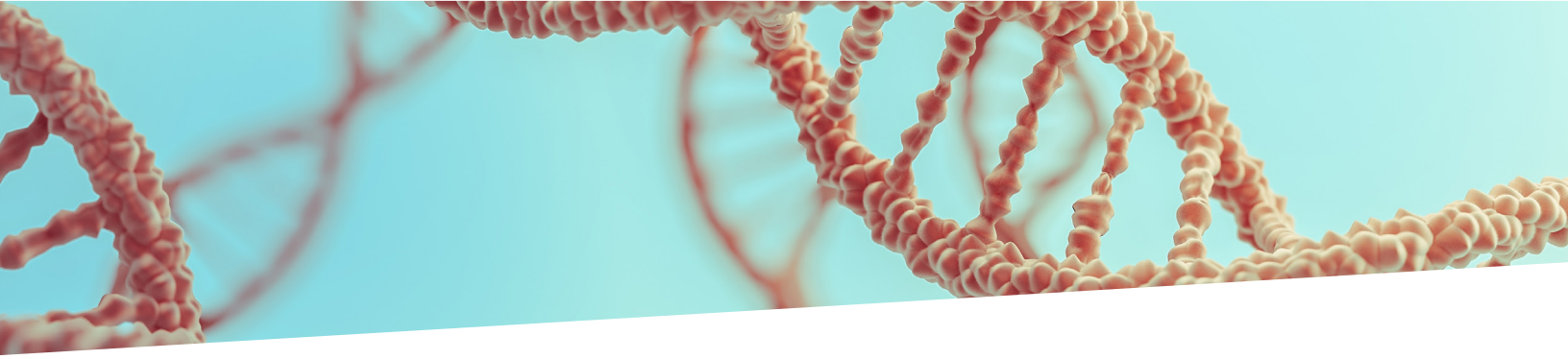
inotiv
analyze. answer. advance.

Genetic integrity assurance program

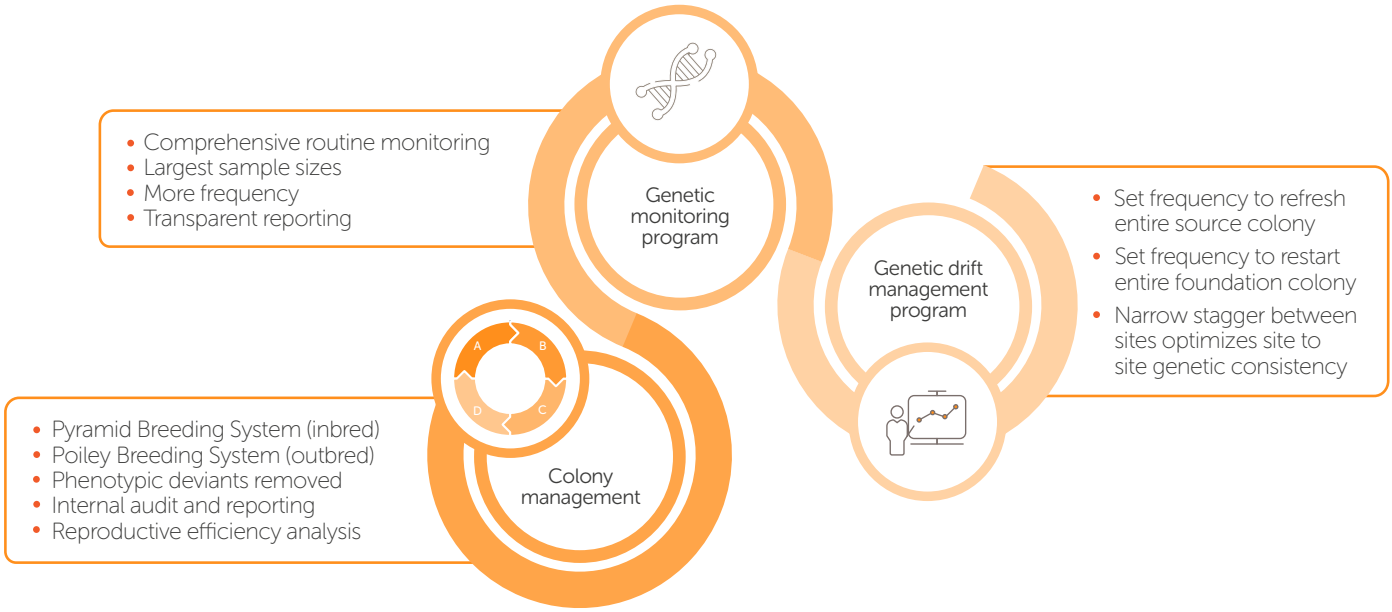
Maintaining the genetic integrity of your research models is essential to minimize variability and improve reproducibility in your research experiments. At Inotiv, we manage our models under the Genetic Integrity Assurance Program, which represents the most comprehensive and transparent program in the industry.

It's important to fully understand how a laboratory animal vendor ensures genetic integrity to maintain quality control. **Learn more about how our three-tiered strategy supports high quality standards in our rodent models.**

inotivco.com



Inotiv's three-tiered strategy



- **Genetic monitoring program:** Benefit from our extensive genetic monitoring program and gain a transparent view of our operations
- **Genetic drift management program:** Trust in a more consistent model as we address the natural mechanism of cumulative genetic drift with a routine colony refreshing program
- **Robust colony management:** Rely on our industry-standard breeding schemes along with robust operational procedures and internal quality auditing to minimize the genetic divergence of your models

Genetic Monitoring

UNDERSTANDING THE ESSENTIALS:

Genetic monitoring is an essential part of maintaining the genetic integrity of animal models. Genetic monitoring programs are employed for the detection of genetic contamination or bottlenecking, but are not designed to detect genetic drift due to spontaneous mutations. Several methods of genetic monitoring are available, including biochemical markers, phenotypic analysis, and, more recently, microsatellite DNA and single nucleotide polymorphism (SNP) analysis. While each method has its advantages, Inotiv uses SNP analysis because of the combination of speed, efficiency and accuracy at detecting genetic contamination.

MONITORING FOR CONSISTENCY:

Inotiv regularly monitors production indices that are specific to each model (i.e., detailed production records, pedigrees, and cage cards) to ensure operational consistency in breeding our models. Technicians are also trained to identify and report phenotypic deviants.

SNP ANALYSIS:

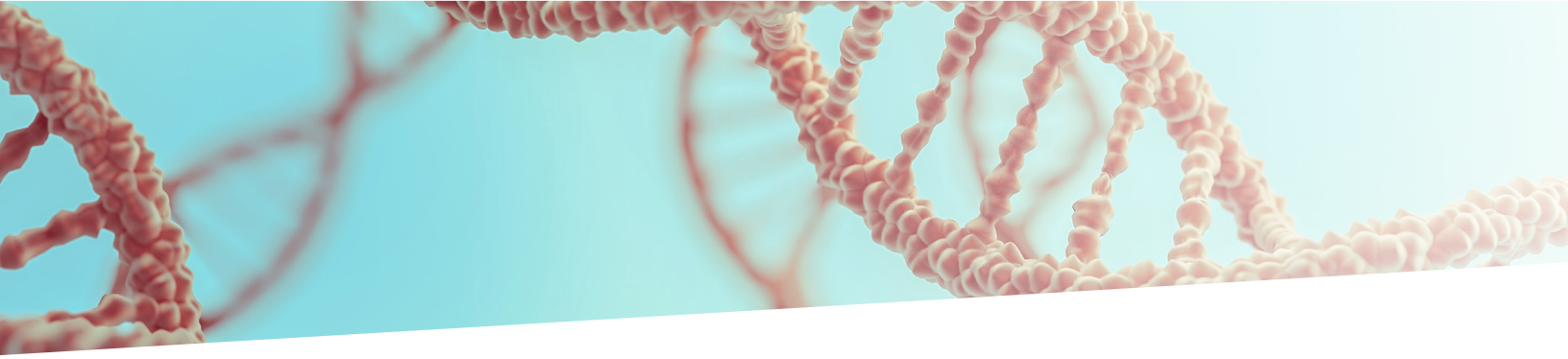
Testing is performed at Infinity BiologiX (formerly Bionomics Research Technology Center at Rutgers University), a world renowned genomics laboratory, which uses high-throughput liquid handling robot technology to evaluate the genetic integrity of Inotiv's rat and mouse colonies globally.

TESTING INBRED MODELS:

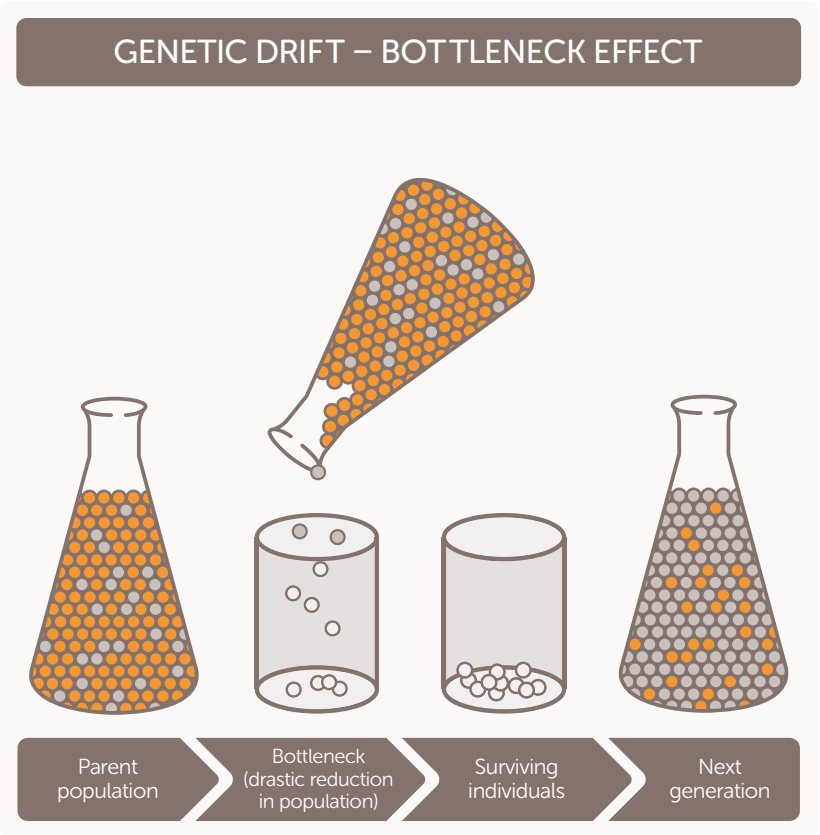
Using a custom panel of 48 single nucleotide polymorphism (SNP) markers, all new barrier-bred foundation colony (FC) cages are tested quarterly. All isolator bred foundation colonies are tested annually (five inbred isolator cages per FC).

TESTING OUTBRED MODELS:

Using a custom panel of 96 single nucleotide polymorphism (SNP) markers, colonies are tested from select models annually. These models include Hsd:Sprague Dawley® SD®, Hsd:RH *Foxn1*^{mu}, HsdBlu:LE, RccHan®:WIST, Hsd:ICR(CD-1®), and Hsd:Athymic nude-*Foxn1*^{nu}.



Genetic drift management

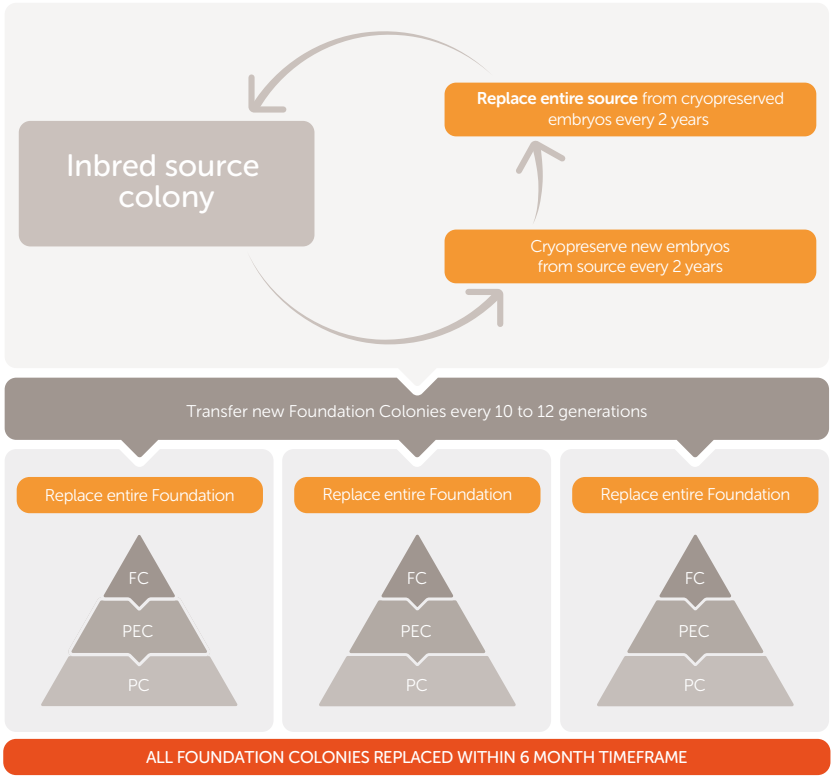


UNDERSTANDING THE ESSENTIALS:

Genetic drift describes fluctuations in the numbers of gene variants in a population that can be caused by various mechanisms, such as spontaneous mutation, bottlenecking, and migration. Many of these genetic alterations are in regions of non-coding DNA.

A smaller but significant change could occur in protein-coding regions of the genome and potentially could alter the gene expression, which may lead to a change in the gene function and/or phenotype.

Genetic drift management at Inotiv

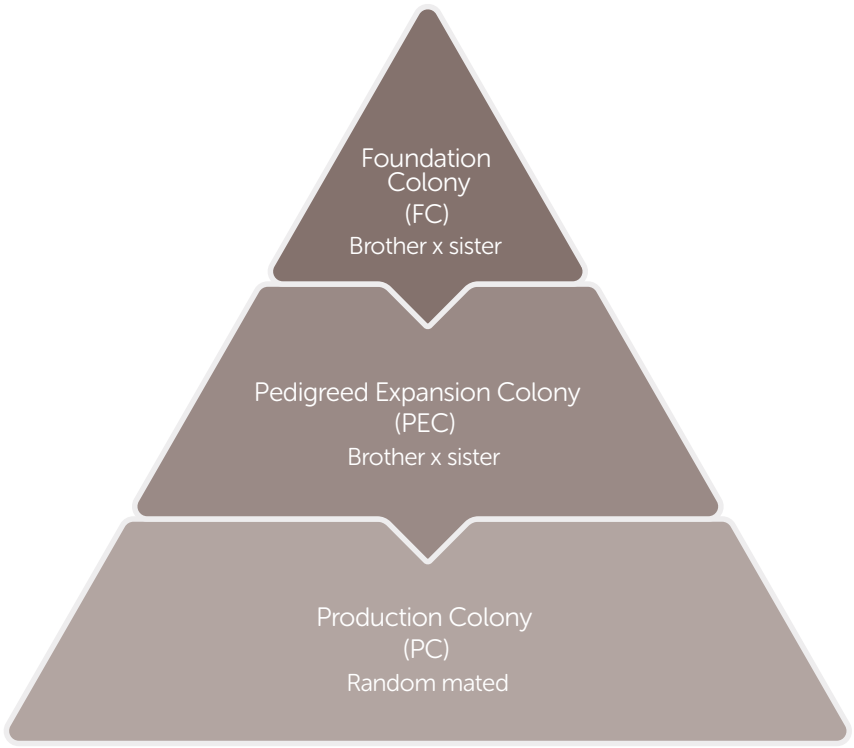


UNDERSTANDING THE ESSENTIALS:

Inotiv uses a colony refreshing program with cryopreserved embryos from a single source.

Here, a single source colony is used to replace all foundation colony breeders every 10 to 12 generations in our C57BL/6NHsd, BALB/cAnNHsd, C57BL/6JOlaHsd and BALB/cOlaHsd inbred mouse models. Embryos are cryopreserved from the Source Colony every 10 to 12 generations and used to completely replace the Source Colony 10 to 12 generations later, just prior to the next round of foundation colony replacements.

Breeding Schemes



BREEDING INBRED STRAINS

To reduce the potential for spontaneous mutations becoming fixed in an inbred colony, Inotiv breeds inbred strains using a pyramid mating system. The structure of inbred colonies consists of three groups: the Foundation Colony (FC), Pedigreed Expansion Colony (PEC) and the Production Colony (PC). Breeders for the FC only come from the FC while breeders for the PEC only come from the FC. Breeders for the PC can come from the FC and the PEC but never from the PC.

This breeding methodology reduces the chance of cumulative genetic drift because spontaneous mutations are more likely to occur on the larger PC where they would be eliminated within one generation.

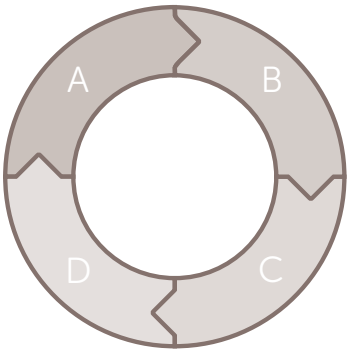
Breeding Schemes (continued)

BREEDING OUTBRED STOCKS

In contrast to inbred strains, outbred stocks must be bred to maintain maximum heterogeneity. Inotiv employs a Poiley[1] rotational breeding system in barrier-bred rodent models to ensure that only unrelated animals are mated together. This system reduces the inbreeding coefficient within each colony and limits cumulative genetic drift by preventing genetic bottlenecks.

(1) Poiley, S.M. (1960). A systematic method for breeder rotation for inbred laboratory animal colonies.

Proc Anim Care Pan 10, 159–166.



Sections

Female (Dam)	Male (Sire)	Offspring
A	B	C
B	C	D
C	D	A
D	A	B

EXAMPLE OF A 4-SECTION POILEY ROTATIONAL BREEDING SYSTEM:

Females from Section A are mated to males from Section B. Their offspring are assigned to Section C. Females from Section B are mated to males from Section C. Their offspring are assigned to Section D, etc. By using the Poiley Rotational Breeding System, each generation of animals are rotated throughout different sections in the colony to ensure a low inbreeding coefficient.

inotiv

analyze. answer. advance.

For more information email
RMSinfo@inotivco.com