CHARLES RIVER
LABORATORIES

REDERIVATION

Rederivation by embryo transfer or cesarean section is the principle method of removing adventitious agents from laboratory stocks and strains. Charles River's Chairman and Founder, Dr. Henry L. Foster, pioneered the technique of large-scale rederivation of commercial laboratory rodents by cesarean section. While still the principle method of removing viruses, bacteria, and parasites from large production colonies, this procedure has limitations. Therefore, when working with client projects, Transgenic Services performs embryo transfer to achieve the same result in genetically-modified animals. The embryo transfer procedure involves aseptic collection of embryos and surgical transfer to VAF™ pseudopregnant recipient females. All rederivation projects are maintained in the biosecurity of semi-rigid or flexible film isolators, protecting the health status of the newly-rederived VAF™ colony.

Standard Rederivation Procedure
To initiate mouse embryo collection for rederivation, we require two proven breeder males, less than 6 months old, and approximately 10 females, 3-4 weeks old. Superovulation protocols synchronize the estrous cycle of embryo donors, increase the number of oocytes ovulated, and facilitate timed matings. Exogenous doses of hormones that in their effect mimic follicle stimulating hormone (FSH) and luteinizing hormone (LH) are routinely used on mice to increase the number of oocytes ovulated. Timed matings determine when to collect 1.5 day old mouse embryos.

For rat embryo collection, we require four proven breeder males, less than 6 months of age, and 10-15 females between 10 and 12 weeks of age. We use an impedance measuring device and vaginal cytology to determine when female rats are in estrus. Although conventional superovulation protocols are less effective in rats than in mice, we perform rat superovulation to synchronize the estrous cycle under certain circumstances. Females in estrus are mated, and plug checks are performed the following morning. Embryo donors are euthanized at the appropriate time and 4.5 day old rat embryos are collected.

Collected embryos are transferred into the oviduct or uterine horn of pseudopregnant recipient females. After rederived pups are born and weaned, the recipient females are submitted for health monitoring to confirm the success of the procedure. All rederivation services include comprehensive health monitoring of recipient females.

At the completion of standard rederivation, at least 3 rederived breeding pairs with complete health reports will be available. These animals can ship immediately to any institution in the world. Alternatively, animals can be used to initiate a breeding program at Charles River. We offer a wide variety of services including colony maintenance, genetic testing, and model characterization to further develop genetically-altered rodent strains.

Embryo Transfer
Embryo collection and transfer techniques minimize the risk of transmitting agents that could infect the uterus and/or placenta, including *Pasteurella pneumotropica* and *Mycoplasma pulmonis*.

The zona pellucida covering the preimplantation-stage embryo offers a natural barrier against pathogens and resists repeated washing in antibiotic and proteolytic solutions. Rederivation by embryo transfer decreases the risk of a foster mother rejecting pups. Additionally, this method eliminates the need for precise timing of cesarean surgery, a common obstacle with transgenic and knockout lines in which gestation length often varies. Charles River performs hundreds of embryo transfer rederivations each year at our Wilmington, MA facility. In addition, we collect hundreds of thousands of preimplantation-stage embryos annually, and reconstitute many stocks and strains by embryo transfer. These activities fall under the supervision of board-certified veterinarians, laboratory professionals, and animal surgeons.

Visit www.criver.com/info/quotes for project estimates.

Rapid Rederivation

Rapid Rederivation for mice and rats significantly reduces the cost and time associated with the rederivation procedure. To initiate a project, we require two proven breeder males and approximately 10 prepubescent females (mice) or four proven breeder males and 10-15 females at 10-12 weeks of age (rats). Males are bred with superovulated females for collection of preimplantation-stage embryos. Collected embryos are transferred into the oviduct or uterine horn of pseudopregnant recipient females. Recipient females are maintained in a sterile isolator for two weeks post-embryo transfer. For each line, Charles River returns at least two visibly-pregnant females to the client. For added security, the pre-rederived colony is maintained for seven days after the shipment. Rapid rederivation projects are completed in about four weeks. We cannot guarantee that visibly-pregnant females will produce litters, nor can we guarantee the zygosity of the rederived offspring. Since rapid rederivation does not include health monitoring of the embryo transfer recipients, we cannot guarantee the health status of the rederived litters.

Routinely Performed on Recipient Females Upon Completion of Standard Rederivation

Viral Agents		Bacterial Agents	Parasites	Pathology
Mouse	Rat	**Cecum cult:** Pseudomonas spp. Ps. aeruginosa Salmonella spp. **Colon cult:** Citrobacter spp. C. rodentium K. oxytoca K. pneumoniae Ps. aeruginosa **Nasal aspirate:** B. bronchiseptica C. kutscheri K. oxytoca K. pneumoniae Mycoplasma pulmonis** Pasteurella spp. P. multocida P. pneumotropica Pseudomonas spp. Ps. aeruginosa Staph. aureus Strep. pneumoniae Beta Strep. - Group B Beta Strep. - Group G Beta Strep. spp. Fecal pellets: Helicobacter spp.**	Ectoparasites Helminths Protozoa	Gross pathology only with histopathology of any observed lesions Lungs: RRV Screen ***
CARB ECTRO ECUN EDIM HANT K LCMV MAV 1&2 MCMV MHV MPUL MPV-1 MPV-2 MTLV* MVM NS-1 POLY PVM REO SEND TMEV	CARB ECUN H-1 HANT LCMV MAV 1&2 MPUL NS-1 PVM REO RMV RPV KRV SDAV SEND TMEV			

* IFA is the primary test, no alternative test available
** PCR Assay
*** Rats only

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