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The CB17/Icr-*Prkdc*^{scid}/IcrIcoCrl Mouse:
A Fox Chase SCID® (Severe Combined Immunodeficiency) Model

The congenic CB17 SCID mouse model is commonly used in tumor biology, xenograft research, transplantation, and immunology studies.

Origin and History

SCID mice possess a genetic autosomal recessive mutation designated *Prkdc*^{scid}. This mutation was first detected in 1980 by Dr. M.J. Bosma and his associates in BALB/c-*Igh*^{b} (C.B-17/Icr) mice (a strain congenic to the BALB/c, carrying the Igh-1b allele from the C57BL/Ka strain) at the Fox Chase Cancer Center in Philadelphia, Pennsylvania. SCID mice are homozygous (C.B-17/Icr *Prkdc*$^{scid/scid}$) for the *Prkdc*^{scid} allele, which has been mapped to the centromeric end of chromosome 16. These animals are coisogenic with the normal C.B-17/Icr strain. In 1991, Charles River (CR) obtained a foundation colony of SCID mice from IFFA CREDO, a well-respected animal breeder in France that is now doing business as Charles River France. The sale of these animals by Charles River is under license agreement with the Fox Chase Cancer Center. The original breed stock received by IFFA CREDO was caesarean rederived by standard aseptic hysterectomy techniques. Their virus antibody free (VAF/Plus®) status has been maintained since that time and has been verified by Charles River. The official nomenclature for the congenic SCID mice sold by Charles River is CB17/Icr-*Prkdc*^{scid}/IcrIcoCrl.

Pathophysiology

SCID mice have severe combined immunodeficiency affecting both B and T lymphocytes. SCID mice lack functional lymphocytes because of impaired VDJ rearrangement (rearrangement of separate gene elements of the immunoglobulin and T cell antigen receptor genes). This mutation disrupts the differentiation of both B and T lymphocyte progenitor cells. The immunodeficiency in SCID mice is manifest in a number of characteristics, including lymphopenia, agammaglobulinemia, and a very high susceptibility to infection with viruses, bacteria, and other microorganisms. When housed under conventional conditions, it is not uncommon for these animals to develop life-threatening infections due to *Pneumocystis murina*, adventitious rodent viruses, or opportunistic bacteria. Such infections can jeopardize experimental studies and must be assiduously avoided during housing and experimental procedures. The same immunodeficiency, however, provides a wide tolerance to implantation of foreign tissues and tumors, thereby making the animals desirable research models.

Other than this immunodeficiency, SCID mice are normal in all other respects. They have normal numbers and function of nonlymphoid blood cells, including natural killer cells, macrophages, and granulocytes. They have lymph nodes and a thymus that are abnormally small, but present. The thymus has a rudimentary medulla without a cortex while the spleen and lymph nodes have follicles that are devoid of lymphocytes.

SCID mice are deficient in epidermal and follicular dendritic Thy-1$^{\pm}$ cells. This deficiency leads to an inability to produce antibodies to common antigens and an inability to reject allogenic grafts. Their spleen cells do not proliferate in response to T- or B-cell-specific mitogens. About 15% of SCID mice spontaneously develop thymic lymphomas.

Even though CB17/Icr-*Prkdc*^{scid}/IcrIcoCrl mice represent a genetically uniform congenic strain, there is some variability in phenotype, specifically the complete absence of mature B and T lymphocytes. A low, but variable, percentage of SCID mice are “leaky” in that they develop a few clones of functional B and T cells, thus producing detectable levels of serum IgG and IgM. The immunoglobulin levels in “leaky” mice are usually less than 1% of normal, but on rare occasions can approach normal levels. The percentage of leaky animals in young adults varies from 2-10%.

technical sheet

Breeding, Maintenance, and Shipping of SCID Mice

Due to the SCID mouse's severe immunodeficiency, their exposure to potentially pathogenic organisms must be prevented. A variety of housing systems can be used in either the research or animal breeding environment, but all such systems require sterilization of feed, bedding, water, and all cage components. The use of filter-top or individually ventilated caging systems, coupled with laminar flow work and change stations, and strict adherence to aseptic techniques for handling these animals is a common method of husbandry in the research environment. As an alternative, semi-rigid or flexible film isolators may also be used and are more commonly employed by large commercial breeders. SCID mice produced by Charles River are raised in flexible film and semi-rigid isolators using accepted aseptic methodology.

Multiple isolator colonies are maintained at Charles River and orders are filled from these multiple colonies. Animals are transferred from isolators into sterile laminar flow workstations using aseptic transfer techniques. In these work-stations the animals are packed into small isolator-like containers that have been pre-sterilized. These shipping containers (Gnoto-safe™ shippers) are the preferred means of shipping these animals. For those investigators who maintain isolator-based colonies, lightweight shipping devices that resemble small flexible film isolators can also be used for a direct transfer from isolator production colonies.

The CB17/Icr-*Prkdc*^{scid}/IcrIcoCrl mice are maintained as a true congenic strain. Each production isolator maintains a foundation colony from which all breeding animals are selected. These breeders are used to produce offspring for sale. A primary foundation colony is also maintained in a separate isolator and is used to restock the satellite foundation colonies within individual production isolators.

All foundation colonies are pedigreed. The *Prkdc*^{scid} mutation is recessive and all of the production animals and foundation colonies are homozygous recessive for the mutation. Charles River has validated an assay to accurately confirm the presence of the *Prkdc*^{scid} point mutation.

Quality Control

A comprehensive health monitoring program ensures animal health status. Immunocompetent female sentinel mice (pigmented strain, to avoid further the possibility of unnoticed accidental interbreeding) are removed from each isolator and bled for serologic screening for adventitious viruses and mycoplasma. SCID mice are removed from each isolator and undergo a complete health monitoring exclusive of serology. This includes gross pathology, histopathology as required, parasitology, and bacteriology. At each complete health monitoring the animals are also assessed for the presence on *Pneumocystis murina*. In addition, as common human-borne bacteria such as *Staphylococcus aureus* pose an ongoing risk to immunodeficient mice, microbiologic culture of each individual isolator is conducted monthly. On a regular basis, animals are removed from each production isolator and assayed for gammaglobulin levels (IgG and IgM) in order to establish the current incidence of "leakiness". Health monitoring and other quality control data is available on our website or upon request.

Charles River Laboratories maintains bibliographical as well as technical information on this strain. For additional information, please contact your Charles River Regional Sales Manager or Charles River Technical Services at 1.800.338.9680. To place an order, call our Customer Service Department at 1.800.LAB.RATS.
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