Immunodeficient Mice

FROM CHARLES RIVER EUROPE

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Common Name	NSG	NRG	NOD SCID	Fox Chase SCID® Beige	SCID	B6 *Rag*1	Inbred Nude	Outbred Nude
Full Nomenclature	NOD.Cg-*Prkdc*^{scid} *Il2rg*^{tm1Wjl}/SzJ	NOD.Cg-*Rag1*^{tm1Mom}*Il2rg*^{tm1Wjl}/SzJ	NOD.CB17-*Prkdc*^{scid}/J NOD.CB17-*Prkdc*^{scid}/NcrCrl	CB17.Cg-*Prkdc*^{scid}*Lyst*$^{bg-J}$/Crl	**BALB/c SCID** CBySmn.CB17-*Prkdc*^{scid}/J* **Fox Chase SCID®** CB17/Icr-*Prkdc*^{scid}/IcrIcoCrl **SHO® Mouse: SCID Hairless Outbred** Crl:SHO-*Prkdc*^{scid} *Hr*^{hr}	B6.129S7-*Rag1*^{tm1Mom}/J	**BALB/c Nude Crl** CAnN.Cg-*Foxn1*^{nu}/Crl **BALB/c Nude J** CAnN.Cg-*Foxn1*^{nu}/J	**Athymic Nude** Crl:NU(NCr)-*Foxn1*^{nu} **CD-1® Nude** Crl:CD1-*Foxn1*^{nu} **NMRI Nude** Crl:NMRI-*Foxn1*^{nu} **NU/NU** Crl:NU-*Foxn1*^{nu} **Swiss Nude** Crl:NU(Ico)-*Foxn1*^{nu}
Mature B cells	Absent	Absent	Absent	Absent	Absent	Absent	Present	Present
Mature T cells	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Dendritic cells	Defective	Defective	Defective	Present	Present	Present	Present	Present
Macrophages	Defective	Defective	Defective	Present	Present	Present	Present	Present
Natural killer cells	Absent	Absent	Defective	Defective	Present	Present	Present	Present
Hemolytic complement	Absent	Absent	Absent	Present	Present	Present	Present	Present
Leakiness	Very Low	Absent	Low	Low	Low	Absent	N/A	N/A
Radiation tolerance	Low	High	Low	Low	Low	High	High	High
Spontaneous tumour incidence (type)	Low	Low	High (thymic lymphoma)	High (thymic lymphoma)	High (thymic lymphoma)	Low	Low	Low
Features and research applications	• Engrafts the widest range of solid and hematological cancers, including ALL and AML • Most sensitive host for cancer stem cells when compared to NOD SCID or nude mice • Longer lifespan than NOD SCID; supports long-term engraftment studies and capabilities; >89 weeks median survival	• Tolerant of ionizing radiation and DNA damaging chemotherapeutics while NOD background maintains compatibility with human tissues • Long-term multilineage hematopoietic stem cell repopulation similar to NSG mice • Engrafts human PBMC without irradiation similar to NSG • Engrafts a wide range of solid and hematological cancers	• Higher take-rates for slowgrowing cancer cell lines than SCID or Nude models • Xenotransplantation of some solid human tumours • Adoptive transfer from strains on NOD background enables study of cell function and track cell movement	• Engrafts hematopoietic cancer cell lines • Suitable for therapeutic antibody testing due to functional complement	• Engrafts hematopoietic cancer cell lines, some primary cells • Allows allogeneic and xenogeneic cancer cell lines & tissues • Improvements in engraftment efficiency over nude models for some cancer lines	• Most commonly used genetic background • Adoptive transfer from strains on B6 background permits to study cell function and track cell movement • Radiation resistant, providing an alternative to SCID mutants	• Engraftment of human & mouse tumour cell lines • Easy assessment of subcutaneous tumour growth due to lack of fur	• Engraftment of human & mouse tumour cell lines • Easy assessment of subcutaneous tumour growth due to lack of fur
Considerations	• No thymic lymphomas – can be used for long and short-term experiments • Sensitive to irradiation	• No thymic lymphomas – can be used for long-term experiments • Higher dose of irradiation to obtain human HSC engraftment is advised	• Develops thymic lymphomas by 8–9 months - best used in short term experiments • Poor radiation tolerance • 36 weeks median survival	• BEIGE mutation leads to defective NK cells • Provides alternative to NOD SCID	• NK activity limits engraftment • Poor radiation tolerance • Innate immunity intact	• Innate immunity intact • Poor host for primary cells • NK cell activity limits engraftment	• Innate immunity intact • Little engraftment of hematopoietic cancer cells • Not suitable for primary cells	• Innate immunity intact • Little engraftment of hematopoietic cancer cells • Not suitable for primary cells
Degree of immunodeficiency	Most immunodeficient							Least immunodeficient

Gene names and functions

Foxn1
forkhead box N1, formerly Hfh11
The *Foxn1*^{nu} mutation is commonly known as nude. Homozygous mutants lack a thymus and therefore are T-cell deficient; they respond very poorly to thymus-dependent antigens, are unable to reject allogeneic and xenogeneic grafts, and have greatly increased susceptibility to infection.

Rag1
recombination activating gene 1
Rag1 is essential for the V(D)J gene rearrangements that generate functional antigen receptors in T and B cells; homozygous *Rag1*^{tm1Mom} mutants have no mature, functional T and B cells. The *Rag1*^{tm1Mom} mutation on the NOD background renders NOD mice diabetes-free. Aging NOD.129S7(B6)-*Rag1*^{tm1Mom}/J mice develop B-cell lymphomas at a high-frequency.

Il2rg
interleukin 2 receptor, gamma chain
Il2rg is indispensable for IL2, IL4, IL7, IL9, IL15, and IL21 high-affinity binding and signaling; in mice, it is also thought to play a key role in mediating susceptibility to thymic lymphomas. Thus, NOD.Cg-*Prkdc*^{scid} *Il2rg*^{tm1Wjl}/SzJ mice do not develop thymic lymphomas characteristic of aging NOD.CB17-*Prkdc*^{scid}/SzJ mice. Most importantly, *Il2rg* deficiency blocks the development of NK cells and causes other defects in innate immunity.

Prf1
perforin 1 (pore-forming protein)
Prf1 is a critical component of the lytic pathway by which NK and CD8+ lymphocytes kill targeted cells.

Prkdc
protein kinase, DNA-activated, catalytic polypeptide
The *scid* mutation in the *Prkdc* gene stands for severe combined immunodeficient. *Prkdc* is instrumental in repairing double-stranded DNA breaks and in recombining the variable (V), diversity (D), and joining (J) segments of immunoglobulin and T-cell receptor genes. Homozygous mutants have no mature T and B cells, cannot mount cell mediated and humoral adaptive immune responses, do not reject allogeneic and xenogeneic grafts, and are useful cancer research models. The *scid* mutation renders NOD mice diabetes-free and thereby makes them useful for adoptive transfer of diabetes by T cells. (Note: the NOD.NON-*Thy*^{1a}/1Lt (004483) strain provides an allotypically-marked T cell population and develops diabetes at the same rate and frequency as does the standard NOD/LtJ (*Thy*^{1a}) strain. Thus, it is useful as a T-cell donor source.)

Leakiness definition as applied to Prkdc*^{scid} *mice
Leakiness refers to a tendency (on certain backgrounds) for mice to produce some functional B and T cells as they age.

Animal Model Evaluation Programme
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Additional Models
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The Jackson Laboratory

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