Characterization of A New Hairless SCID Mouse

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Abstract

Severe combined immunodeficient (SCID) mice are used in oncology research. However, the hair coat hinders subcutaneous cell implantation, accurate tumor measurement and also interferes with many imaging modalities. We have produced a SCID hairless outbred mouse, SHO™-*Prkdc*^{scid}*Hr*^{hr} (SHO™), by crossing a SCID mouse, Crl:HA-*Prkdc*^{scid} (outbred SCID) with an immunocompetent outbred hairless mouse, Crl:SKH1-*Hr*^{hr} (SKH1). Characterization of this new strain reveals it combines the B and T cell deficiencies of the outbred SCID mouse and the hairlessness of the SKH1 mouse. Tumor xenograft study demonstrates a higher engraftment efficiency compared to that in athymic nude mice. The hairlessness of this novel line of SCID mice provides advantages to oncology research.

Introduction

Athymic nude and SCID mice are the two most widely used mouse models in oncology research. Athymic nude mice lack T cells, but retain functional B cells, limiting the growth of some tumor lines. However they are still commonly used because the lack of a hair coat facilitates tumor implantation and assessment. SCID mice lack both B and T cells and support the growth of a broader range of tumor lines, but SCID mice have a normal hair coat which can hinder accurate tumor measurement and interfere with many imaging modalities. In order to attempt to combine the favorable attributes of both athymic nude and SCID mice, we produced a SCID hairless outbred mouse, SHO™ by crossing an outbred SCID mouse with an immunocompetent outbred hairless mouse, SKH1. Here we report the characteristics of this new model.

Materials and Methods

Animals

SHO™ was produced by crossing outbred SCID mice with hairless SKH1 mice. Homozygosity for *hr* mutation was verified by the hairless phenotype and homozygosity for the scid mutation by PCR. All animals used in these characterization studies were 6 to 8 weeks old.

Flow cytometric analysis

Cells were harvested from animals, followed by antibody staining and flow cytometric analysis.

Tumor xenograft

Human breast adenocarcinoma MDA-MB-231 cells were cultured in DMEM supplemented with 10% FBS and 2mM glutamine. SHO™ and athymic nude (Crl:NU-*Foxn1*^{nu}) mice were subcutaneously injected with 2 x 10^7 cells per mouse. Tumor volume = (length x width^2)π /6.

Histology

Skin of the left mammary fat pad and right lateral thorax from female SHO™ (n=6), SKH1 (n=6) and athymic nude (n=5) mice was compared by routine histopathologic evaluation of hematoxylin and eosin-stained sections.

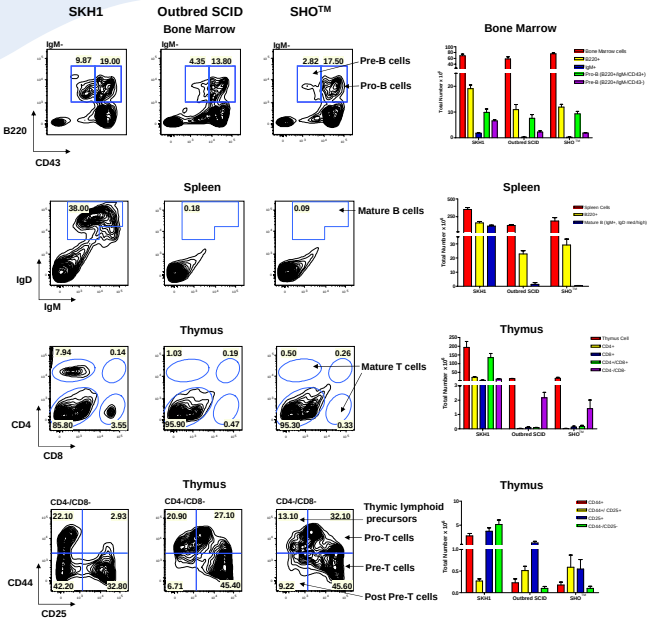
Results

Peripheral Leukocyte Count (10^3/µL) With Differential

Sex	Animal Strain	WBC	Neutrophils	Lymphocytes	Monocytes	Basophils	Eosinophils
Female	SKH1	7.53 ± 1.00	1.82 ± 0.26	4.81 ± 0.65	0.62 ± 0.12	0.23 ± 0.05	0.04 ± 0.01
	Outbred SCID	3.59 ± 0.47	1.36 ± 0.42	1.42 ± 0.21	0.54 ± 0.07	0.21 ± 0.12	0.04 ± 0.02
	SHO™	3.65 ± 0.32	2.08 ± 0.55	0.98 ± 0.23	0.45 ± 0.12	0.11 ± 0.03	0.02 ± 0.01
Male	SKH1	7.36 ± 1.68	3.23 ± 0.84	3.32 ± 0.61	0.59 ± 0.14	0.17 ± 0.06	0.06 ± 0.03
	Outbred SCID	1.23 ± 0.20	0.52 ± 0.10	0.59 ± 0.09	0.10 ± 0.01	0.01 ± 0.01	0.00 ± 0.00
	SHO™	5.97 ± 0.60	4.80 ± 0.54	0.67 ± 0.10	0.25 ± 0.05	0.18 ± 0.01	0.07 ± 0.01

Data are presented as mean ± SEM. N=3.

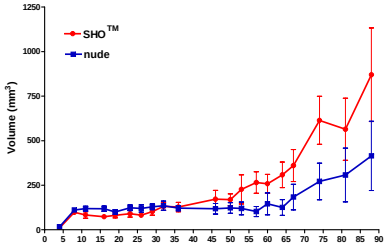
Flow Cytometric Analysis



Flow cytometric analysis suggests, like its parental SCID mouse, the SHO™ mouse lacks mature B and T cells. The differentiation of B cells was blocked in the transition from Pro-B to Pre-B; while the development of T cells was retarded at Pro-T and Pre-T stages.

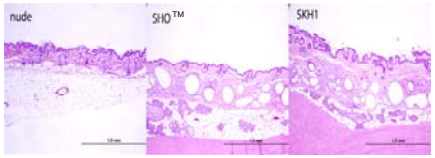
Total subset cells are presented as mean ± SEM. N=6.

In Vivo Tumor Growth of Human Breast Adenocarcinoma MDA-MB-231



Tumor volume is presented as mean ± SEM. N=10.

Skin Histopathology



Skin histology (right lateral thorax) of the SHO™ resembles the parental SKH1 stock. The SHO™ and SKH1 have significantly more mammary development than the nude.

Conclusion

We have produced a new mouse model, SHO™ by crossing an outbred SCID with an immunocompetent outbred hairless mouse, SKH1. Our studies demonstrate the new model combines the immune deficiency of the SCID mouse with the hairlessness of the SKH-1 mouse. SHO™ mice have higher tumor engraftment efficiency than athymic nude mice.

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