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The Crl:SHO-*Prkdc*^{scid}*Hr*^{hr} Mouse:

A Double-Homozygous SCID Hairless Outbred Model

The Crl:SHO-*Prkdc*^{scid}*Hr*^{hr} is a hairless SCID mouse (patent pending[1]). In 2007, Charles River Research Models began a breeding project to develop a hairless SCID mouse model by crossing the Crl:HA-*Prkdc*^{scid} and Crl:SKH1-*Hr*^{hr} stocks. The resulting mouse is the double-homozygous SCID hairless outbred (SHO™).

Engraftment efficiency of human tumors is higher in SCID mice than in more commonly used nude mice due to the deficiency of not only T cells, but also B cells. However, the use of SCID mice in oncology research is hindered by their hair coat, which makes tumor measurement and *in vivo* imaging difficult. Charles River has developed a hairless SCID mouse model, Crl:SHO-*Prkdc*^{scid}*Hr*^{hr}, which preserves the immunodeficient features of the Crl:HA-*Prkdc*^{scid} mouse and is hairless. Below is a summary of human tumor xenograft and immunophenotyping studies conducted using this new model.[2]

Xenograft Study Using the SHO™ Mouse

Charles River Discovery Services obtained the human prostate adenocarcinoma cell line PC-3 from American Type Culture Collection (ATCC; catalog number: CRL-1435). It was cultured in DMEM supplemented with fetal bovine serum and glutamine.

Fifteen Crl:SHO-*Prkdc*^{scid}*Hr*^{hr} and fifteen Crl:HA-*Prkdc*^{scid} male mice were injected subcutaneously with $5x10^6$ cells in 0.1 ml HBSS. Mass measurements and animal body weights were performed twice a week throughout the course of the study. Clinical observations were performed daily.

In vivo Tumor Growth of the Human Prostate Cell Line PC-3

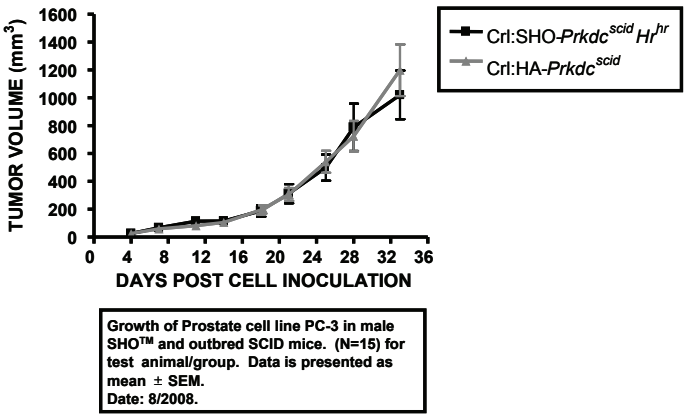

Figure 1: Tumor growth comparison of Crl:SHO-*Prkdc*^{scid}*Hr*^{hr} and Crl:HA-*Prkdc*^{scid} male mice injected with the human prostate adenocarcinoma cell line PC-3. Data is presented as mean ± standard error.

As shown in Figure 1, the tumor growth rates in Crl:SHO-*Prkdc*^{scid}*Hr*^{hr} and Crl:HA-*Prkdc*^{scid} are similar, demonstrating that the Crl:SHO-*Prkdc*^{scid}*Hr*^{hr} model is a viable alternative to the Crl:HA-*Prkdc*^{scid} model without the hair coat complications. In past studies, the PC-3 cell line, when injected in Nu/Nu mice, has exhibited a moderate ulceration rate. No ulcerations were observed in the Crl:SHO-*Prkdc*^{scid}*Hr*^{hr} model. Assessment of additional cell lines in this model is underway.

Immunophenotyping Assessment of the SHO™ Mouse

Three male and three female Crl:SHO-*Prkdc*^{scid}*Hr*^{hr} mice, 6 to 8 weeks of age, were used for immunologic characterization. Thymus, spleen, lymph nodes and bone marrow from each animal were harvested and disassociated into single cell suspensions. Cells were stained with fluorochrome-conjugated B and T cell surface markers and analyzed using flow cytometry. As shown in Figure 2A and 2C, like the Crl:HA-*Prkdc*^{scid}, Crl:SHO-*Prkdc*^{scid}*Hr*^{hr} mice lack mature B cells (IgM positive, IgD medium or high) and mature T cells (CD4 single positive or CD8 single positive). Further investigation suggests the differentiation of B cells in both Crl:SHO-*Prkdc*^{scid}*Hr*^{hr} and Crl:HA-*Prkdc*^{scid} is blocked in the transition from Pro-B (B220 positive & CD43 positive) to Pre-B (B220 positive & CD43 negative) (Figure 2B); while the development of T cells is retarded at Pro-T and Pre-T stages (Figure 2D). These confirm that the SHO mouse has similar immunodeficiencies to the Crl:HA-*Prkdc*^{scid} mouse.

Flow Cytometric Analysis

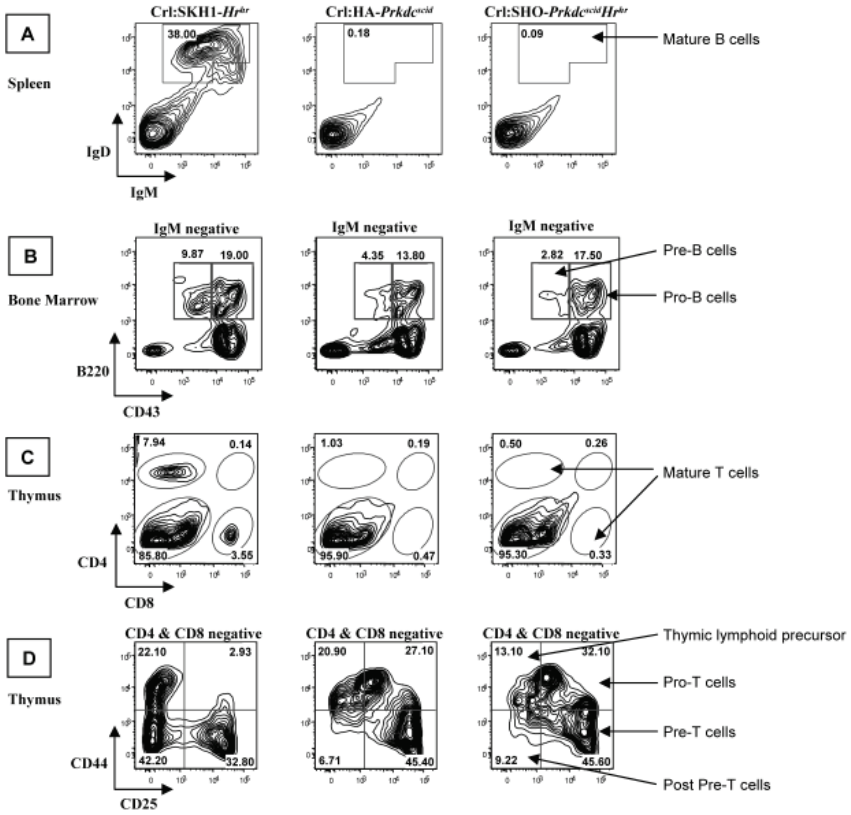

Figure 2: Representative result of flow cytometric analysis of antibodies-stained cells.

[1] A patent is pending on the SHO™ mouse that includes a portfolio of animals with similar characteristics.
[2] Studies were conducted by Discovery Services, Charles River.