COMPARATIVE ANALYSIS OF COMPLETE BLOOD COUNT, SERUM CHEMISTRY AND IMMUNE PHENOTYPE BETWEEN SRG AND CD RATS

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Background: The number of cancer drugs in development has doubled over the last decade, increasing the need for well-characterized immunodeficient animal models that allow human xenograft engraftment, an important component of the drug development process. With their larger organism size, immunodeficient rats are suited for studies that require serial sampling of tissues such as blood and tumor, or for surgical procedures that are complicated by the small size of mice. The SRG is an immunodeficient rat with deletions in the recombination activating gene 2 (Rag2) and interleukin 2 receptor gamma (Il2r-g) resulting in impaired V(D)J recombination and lymphocyte maturation respectively, ensuring nearly absent functional T, B and NK cells. However, our understanding of its other immune components, such as monocytes and the complement cascade, remains limited. In this study, we compared the immune phenotype of the SRG rat with CD® (Sprague Dawley) rats, focusing on parameters such as complete blood count, complement cascade activity, and monocyte levels. Potential immunophenotypic differences between male and female SRG rats was also explored in this study.

Methods: Whole blood was collected from 20 SRG rats of each sex (n=40) with 2 CD (Sprague Dawley) rats of each sex used as control group (n=4). PBMCs were isolated and analyzed by flow cytometry for CD4 and CD8 positive T cells, B cells, NK cells and monocytes. Whole blood from 10 SRG and 10 CD rats of each sex was isolated and sent to Idexx for complete blood count and serum chemistry analysis. Complement activity was measured in serum from 3 SRG and 3 wild-type rats of each sex, using the Rat complement pathway assay kit from Hycult®Biotech and performed according to manufacturer’s instruction.

Results: While levels of circulating T, B and NK cells in SRGs were reduced compared to WT CD rats (p≤0.05), no statistically significant difference was observed in monocyte subpopulation (p>0.05). Complement activity was detected in SRG rats with an increase in measured activity compared to CD rats. There was also no significant difference in T, B, NK cells as well as monocyte levels between male and female SRGs (p>0.05).

Conclusions: This study provides further insight into the immune phenotype of the SRG rat model, confirming the expected deficiencies in T, B, and NK cells while revealing detectable monocyte levels and complement activity. These findings enhance our understanding of the SRG rat’s immune characteristics, facilitating more targeted utilization of this model in future studies.

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