

Advances in Mouse Models of Lupus

Yijun Lan *

Youjiang Medical University for Nationalities, Baise, Guangxi, China

* Corresponding author Email: 1204045885@qq.com

Abstract: Systemic lupus erythematosus (SLE) is a typical autoimmune disease with complex clinical manifestations and involvement of organs and tissues of multiple systems throughout the body, but its pathogenesis is still unclear, therefore, the establishment of a suitable animal model of lupus is of great significance in exploring the etiology, pathogenesis and treatment of SLE. Constructing a lupus mouse model is a good tool for studying SLE. In this review, we will introduce the methods of establishing different kinds of lupus mouse models and their characteristics, and discuss the advantages and disadvantages of various models, with a view to providing researchers with references in the process of exploring the pathogenesis of lupus, and in the development of targeted interventions and therapeutic drugs.

Keywords: SLE; Mouse; Animal Model; Pristane; NZB; NZW; cGVHD.

1. Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease, which often occurs in young women. This disease involves many organs and tissues of the whole body. The disease has a variety of phenotypes, and the clinical manifestations of the patients are different, from mild skin and mucous membrane to multiple organs and central nervous system involvement. But the pathogenesis of lupus is still unclear. Genetic, immune, endocrine and environmental factors are all involved in SLE among many experimental animals. Mice, as the first choice for scientific research, have the advantages of easy feeding, high reproduction rate, high genetic homozygosity and small differences among individuals. The abnormal immune mechanisms of systemic lupus erythematosus include immune complex formation, autoantibody formation and immune-mediated tissue damage. The formation of immune complexes and autoantibodies can lead to tissue damage, such as skin, lymph nodes, cardiovascular system, lungs, kidneys and joints. In addition, SLE may also involve central (CNS) and peripheral (PNS) nervous systems and some mental symptoms. Autoantibodies in systemic lupus erythematosus include antinuclear antibodies (ANA), anti-double-stranded DNA antibodies, anti-SSA antibodies, anti-SSB antibodies and anti-Sm antibodies. They have varying degrees of sensitivity and specificity, and some can also be seen in other autoimmune disease [1]. The diagnosis of SLE is based on a series of signs, symptoms and laboratory tests. The American Society of Rheumatology (ACR) first formulated the classification standard of SLE in 1971 and revised it twice in 1982 and 1997. Systemic lupus erythematosus International Cooperative Clinic (SLICC) further revised the 1997 ACR standard in 2012, which includes glomerulonephritis confirmed by biopsy and patients with positive antinuclear or anti-ds-DNA antibodies can be directly classified as SLE even if they lack any other criteria. This played a role in verifying the success of building a SLE mouse model. In addition, there is no effective treatment for systemic lupus erythematosus, so SLE animal model plays a vital role in exploring the pathogenesis and effective treatment of systemic lupus erythematosus. In the past few decades, many scholars at home and abroad have established a variety of SLE mouse models, which can be

divided into spontaneous lupus model and induced lupus model. This article will introduce the existing SLE mouse models from the methods of establishing the model and the manifestation of the disease.

2. Spontaneous Lupus Model in Mice

2.1. NZB x NZW F1 Mouse Model

In 1959, Bielschowsky et al found that immunologically abnormal spontaneous autoimmune diseases appeared in NZB strain mice. Holmes and Burnet found in 1963 that 4-5-month-old NZB mice spontaneously showed positive antiglobulin test (Coombs). The following year, Norins and Holmes found that antinuclear factor (ANF) may be present in the serum of some NZB mice. As they get older, most mice show severe splenomegaly and lymphadenopathy. Studies in NZW mice have shown that these mice occasionally show weak positive reactions to the Coombs test, but they may also develop autoimmune kidney disease. Both NZB and NZW mice showed skin, liver, lymphoid tissue and kidney lesions, which were similar to those of human systemic lupus erythematosus[2].

The NZBxNZWF1 mouse model was produced by hybridizing female NZW with male New Zealand black (NZB). The female NZB/WF1 represents the SLE phenotype characterized by the production of anti-ds-DNA antibodies and immune complex-mediated glomerulonephritis[3]. And these F1 mice also showed high titers of antinuclear antibodies, B cell hyperactivity, IgG immune complex and other characteristics, and eventually developed renal failure, which is a better lupus mouse model than NZB. A study comparing NZBxNZW's F1 cubs found that the disease progressed faster in females, which is in line with the fact that human systemic lupus erythematosus is more common in women. In the process of exploring the causes of faster onset in female NZBxNZWF1 mice, many scholars believe that sex hormones play an important role, while a large number of animal studies have shown that androgens play a protective role, while estrogen accelerates the progression of the disease.

The disease progression of NZBxNZWF1 includes: at 1 month old, antinuclear antibodies may be detected in female NZB/WF1 mice and increase with age; after 4 months, an increase in antinuclear antibody titer may be found in mice;

at 6-9 months old, deposited immune complexes can be found in the glomeruli of NZB/WF1 mice. Then at the age of 9-12 months, these female NZBxNZWF1 mice may die of renal failure. [4]

Because NZBxNZWF1 mice can spontaneously develop autoimmune diseases similar to human systemic lupus erythematosus, NZB/WF1 model is generally considered to be the best natural model of human autoimmune diseases.

2.2. NZB x SWR F1 Mouse Model

Because of the low incidence of autoimmune glomerulonephritis in NZB mice, it is difficult to be directly used as a SLE model. Different from NZB mice, SWR mice rarely have autoimmune diseases, but one of the characteristics of SWR mice is that diabetes insipidus such as polydipsia and polyuria occurs with the increase of age. So when NZB mice cross with normal SWR mice, almost 100% of female F1 hybrids (SNF1) develop fatal glomerulonephritis. In addition to early immune complex-mediated glomerulonephritis, SNF may also show anti-DNA (most of which are IgG2b) and anti-ANA. Female patients with immune glomerulonephritis will die about 10-12 months after birth[5].

The development of autoimmune diseases is a multi-step, multi-gene process. Some differences in hybridization with NZBxNZW (B/WF) make NZBxSWR (SNF) hybridization more suitable for genetic analysis of autoimmune diseases. In the NZBxNZW model, the parents themselves have problems with the immune system, resulting in glomerulonephritis. In the NZBxSWR model, the SWR parental mice of SNF1 do not have autoimmune diseases and autoantibodies, so NZBxSWR blotting is suitable for determining the role of normal non-autoimmune strains in the development of lupus nephritis.

2.3. NZM Mouse Model

This strain retains the strongest susceptible site of NZB/WF1, which plays an important role in the study of the pathogenesis of systemic lupus erythematosus regulated by polygenes. NZM2328 and NZM2410 mouse models are important tools to study the pathogenesis of systemic lupus erythematosus. The discovery of their different characteristics and susceptibility sites will help us to better understand the nature of this complex disease.

New Zealand hybrid (NZM) mouse is a newly inbred strain obtained by selective inbreeding of the hybrid offspring of NZB and NZW mice. According to the occurrence of glomerulonephritis and the difference of specific strains of disease expression in mice, 12 of 27 new NZM strains were selected for analysis. Two strains used in SLE model were called NZM2410 and NZM2328.

NZM2328 female mice spontaneously develop severe albuminuria and lupus nephritis, leading to early death. Although male NZM2328 mice have deposits of ANA, anti-ds-DNA antibodies and immune complexes, they do not have severe proteinuria and early death, and have gender bias, which is consistent with the characteristics of human SLE[6]. Glomerulonephritis (GN) in NZM2328 mice can be divided into two stages: acute nephritis and chronic glomerulonephritis. Acute GN is characterized by active proliferative GN, including signs of Mesangial hyperplasia and glomerular cell proliferation. By contrast, chronic GN is characterized by fibrotic changes. NZM2328 males develop acute GN at the age of 12 months, rather than end-stage renal

failure[7].

Compared with other models, the main manifestation of NZM2410 mice is that it can develop into severe early-onset lupus-like disease in both female and male mice[8]. And the main advantage of this strain is that it retains the strongest NZB/WF1 susceptible site. In order to explore the susceptibility sites of NZM2410, Morel and Mohan et al found that NZM2410xC57BL/6F1 was backcrossed to analyze the whole genome of the susceptibility to systemic lupus erythematosus (SLE) in NZM2410, and three homologous lines were obtained, namely, B6.NZMc1 carrying Sle1, B6.NZMc4 carrying Sle2 and B6.NZMc7 carrying Sle3. B6.Sle1 showed high titers of IgG antinuclear autoantibodies but did not have any severe glomerulonephritis. B6.Sle2 leads to the enhancement of B cell response to in vitro stimulation and in vivo antigen attack. It has been found that B6.Sle2 should help amplify the ongoing autoimmune response by lowering the B cell signal threshold. B6.Sle3 can develop into severe lupus nephritis[9]. The discovery of three susceptible sites in NZM2410 mice plays an important role in studying the pathogenesis of systemic lupus erythematosus regulated by polygenes.

2.4. NZB x SJL F1 Mouse Model

Sex-dependent thymic abnormalities and SLE-like autoimmune symptoms in NSF1 mice can be regulated by estrogen and DHT castration and treatment, so NSF1 model has the function of studying the role of sex hormones in the pathogenesis of SLE.

SJL mice were bred by inbreeding after crossing three kinds of Swiss mice with James Lambert in 1955. Male SJL mice are prone to autoimmune encephalitis, which can be used in the study of multiple sclerosis[10]. In 1980, studies by Dumont and Robert showed that F1 progenies (NSF1) of healthy NZB mice without autoimmune expression for 3 months and healthy SJL mice aged 12 months would have thymic abnormalities according to age and sex. In female F1 mice, obvious thymic abnormalities occur during aging, which is characterized by the accumulation of mature T and B cells in the thymus. In contrast, the thymus of male NSF1 mice showed almost normal age-related degeneration, and there was no significant change in the proportion of lymphocyte subsets. In addition, female NSF1 mice have a shorter life span than male NSF1 mice, and show a variety of autoimmune symptoms of systemic lupus erythematosus-like syndrome such as antinuclear antibodies, anti-ds-DNA antibodies and circulating immune complex deposition in the early stage of life. It's the same as abnormal thymus. Proteinuria also increased with age in female F1 mice, but not in male mice. In the reverse SJLxNZB mouse hybridization, similar phenomena were only observed in female offspring, indicating that this sex dependence phenomenon mainly depends on hormone effects[11]. Studies have shown that androgen has an inhibitory effect on these SLE-like symptoms.

2.5. MRL/lpr Mouse Model

MRL/lpr mice may have sex-biased SLE-like symptoms, glomerulonephritis and autoantibody production. It can also provide important clues for further understanding the susceptibility sites of MRL/lpr mice and the role of lpr gene in autoimmune diseases. These findings will help to better use the MRL/lpr mouse model to study the pathogenesis and

treatment of autoimmune diseases such as systemic lupus erythematosus. In addition.

MRL/lpr mice were first established by Murphy and Roths in 1976 and were produced by complex mating of four strains: LG/J, AKR/J, C3H/HeDi and C57BL/6J. Spontaneous autosomal recessive mutations occurred in the 12th generation and were divided into two sublimes, one of which was MRL/MpJ-Fas^{lpr} (MRL/lpr) strain with loss of lymphoproliferative gene (lpr) mutation, and the other was MRL/MpJ^{lpr/Fas} (MRL+/+) strain. There is no lymphadenopathy in this subline. From the age of 8 weeks, all MRL/lpr mice develop massive systemic lymph node enlargement, and by the age of 16-18 weeks, their weight is more than 100 times that of normal mice. The extent of lymph node enlargement in males is smaller than that in females. And MRL/lpr mice will develop autoantibodies such as anti-dsDNA and ANA, as well as autoimmune diseases such as lupus nephritis, polyarteritis, arthritis and sialitis[12]. The severity and incidence of the disease are the same as those of human SLE, showing gender bias against women. Compared with the control strain MRL+/+, the autosomal defect of Fas antigen led to the accumulation of CD4-CD8- double negative T cells in the lymph nodes and spleen of MRL/lpr mice. Since normal Fas is considered to be important in programmed cell death and apoptosis, it is considered that lpr-related defects in Fas will interfere with normal apoptosis. MRL/lpr mice began to develop from 3 months old and developed severe glomerulonephritis (early and late) at 6-7 months. Lpr mutation accelerated the autoimmune phenomenon of MRL/lpr mice[13].

In order to explore the susceptibility sites in MRL/lpr mouse model, Murphy and Roths et al compared four mouse strains with different genes and studied the effects of autosomal mutant gene lpr on the development of various autoantibodies and immune complexes of glomerulonephritis. The existence of lpr gene not only enhanced the production of autoantibodies in MRL/MpJ strains with autoimmunity, but also induced the other three strains of mice to form various autoantibodies, but there was no obvious tendency of autoimmune diseases. These results suggest that MRL mice have an autoreaction tendency independent of lpr gene. In order to determine whether other mice with lpr gene can also express autoantibodies, the anti-DNA antibody response of B6lpr/lpr mice was studied. The mice of this strain produced anti-DNA antibodies, and the antibody level of female animals was significantly higher than that of males. These results suggest that lpr gene can stimulate the production of autoantibodies in mice other than MRL strain, and does not need the abnormality specific to this background to enhance self-response[14].

40-90% of patients have neuropsychiatric (NP) manifestations, neuropsychiatric lupus erythematosus (NPSLE) is a common manifestation of systemic lupus erythematosus. with symptoms ranging from anxiety, depression and cognitive impairment to mental illness, collectively referred to as neuropsychiatric lupus erythematosus or central nervous system lupus erythematosus, which is still the leading cause of death in SLE. Compared with other models, MRL/lpr mice showed early NP manifestations and were widely used in lupus-related NP studies. The NP of MRL/lpr mice showed gender bias. 5-week-old female mice showed obvious depressive symptoms, while male mice only observed such symptoms at 18 weeks old, which was similar to human SLE[15,16].

2.6. BXSB Mouse Model

BXSB mice may have many symptoms similar to human systemic lupus erythematosus, such as autoantibodies, circulating immune complexes, severe glomerulonephritis and so on. this strain of mice is characterized by male dominant diseases due to Y gene from male SB/le mice and different sex bias related to sex hormones in NSF1 mice. The Yaa gene expressed in BXSB mice can accelerate the autoimmune response depending on the background of lupus gene.

In 1977, Murphy of Jackson Laboratory in Bar Harbor, Maine, developed an inbred strain of mice that spontaneously suffered from SLE-like syndrome, which was a recombinant inbred strain of BXSB mice formed by the hybridization of female C57BL/6 and male SB/Le. This is a mouse characterized by a male dominant disease. Similar to NZB × WF1 mice, BXSB mice also have symptoms similar to human systemic lupus erythematosus, such as B cell hyperactivity, autoantibodies, circulating immune complex, abnormal complement, extensive thymic cortical atrophy and severe IC glomerulonephritis with retrovirus gp70 glomerulonephritis. The Y gene from male SB/le mice is called the autoimmune accelerator (Yaa) associated with Y chromosome. Therefore, the onset of autoimmune diseases in male BXSB mice is earlier and more severe[17]. By contrast, male BXSB mice that lack the Yaa gene (called BXSB-Yaa-) do not develop autoimmune diseases because their Y chromosomes come from C57BL/6J. Unlike other models affected by sex hormones, castrated male and female BXSB mice, the results showed that orchietomy did not delay the development of autoimmune diseases in male BXSB mice, and ovariectomy did not aggravate the progression of female mice. The mutation of BXSB mice is different from that of MRL/lpr mice. The abnormality of lpr mutation is related to the ability of Fas antigen to mediate apoptosis, but Yaa gene itself can not induce significant autoimmune response in mice without obvious SLE background. This suggests that the role of Yaa gene may require the existence of abnormal autosomal genome in lupus susceptible mice[18]. Members of the Toll-like receptor family can act as pathogen sensors and participate in local autoimmune responses. In BXSB mice, there was a correlation between glomerular injury and TLR expression. In particular, the overexpression of TLR8 is related to the progression of glomerulonephritis[19,20].

2.7. BXD2 Mouse Model

The BXD2 mouse strain is one of about 80 BXD recombinant inbred (RI) mouse strains. Dr. Benjamin obtained it through more than 20 generations of inbred C57BL/6J (B6) and DBA/2J (D2) strains. Adult BXD2 mice spontaneously develop into systemic autoimmune diseases, including increased serum titers of glomerulonephritis (GN), rheumatoid factor (RF) and anti-DNA antibodies, as well as monocyte infiltration, synovial hyperplasia and cartilage erosion. The results show that BXD2 mice can be used to determine the immune pathogenesis and genetic segregation of lupus erythematosus and erosive arthritis[21].

2.8. Lupus Mouse Model Induced by Pristane

Pristane is an isoprene-like alkane. It is mainly extracted from shark liver. In 1995, Satoh et al first used pristane to induce symptoms similar to human systemic lupus erythematosus in BALB/c mice, and established a pristane-induced lupus mouse model (PIL model)[22]. Ascites rich in

monoclonal antibodies was produced in BALB/c, SJL/J and C57BL/6 mice after intraperitoneal injection of pristane. A few months after injection of pristane, SLE specific autoantibodies appeared, including anti-dsDNA antibody, anti-Sm antibody, anti-RNP antibody (antiRNP) and so on. Severe glomerulonephritis was also induced by intraperitoneal injection of pristane mice, which was characterized by albuminuria, Mesangial hyperplasia and glomerular immune complex deposition. The severity of glomerulonephritis gradually increased with the time of pristane injection[23].The mechanism of autoantigen formation induced by Pristane remains to be clarified. It is speculated that the cytotoxicity of pristane induces programmed cell death, triggering immune and tissue damage, leading to autoimmune diseases similar to systemic lupus erythematosus[24].The preparation of Pristane-induced lupus mouse model is simple and widely susceptible to lupus autoantibodies. This method has become the most commonly used method to induce lupus model.

2.9. Drug-induced Lupus Mouse Model

Compared with the pristane-induced lupus mouse model, the time of autoimmune symptoms was shorter, but the similar symptoms disappeared after drug withdrawal. In 1988, Hess found that patients treated with certain drugs showed immune responses and antibodies were observed in sera. These characteristics were similar to systemic lupus erythematosus, but there were usually no SLE-related complications. Patients recovered completely after discontinuation of pathogenic drugs[25].Drugs related to drug-induced lupus include procainamide, hydrazine, quinidine and chlorpromazine. Some studies have shown that the pathogenesis of autoimmunity induced by drugs with heterogeneous chemical structure and function is that non-bilayer phospholipid arrangement (NPA) liposomes induced by drugs such as chlorpromazine or procainamide lead to autoimmune diseases similar to human lupus erythematosus in BALB/c mice, while producing specific anti-NPAIgM and IgG antibodies[26].To establish a mouse model of drug-induced lupus erythematosus, the drug should be mixed with liposome and injected into the mouse body at first, then injected into the spleen on the 1st and 15th day, and then injected intraperitoneally from the 30th day, once a week for one month. Anti-NPA antibody could be found in serum about 15 days after the first injection. Anti-NPA antibodies are biomarkers of lupus-like diseases in mice similar to human lupus erythematosus. They appear together with anticardiolipin antibodies, antihistone antibodies and lupus anticoagulant antibodies[27].Studies have shown that these non-bilayer phospholipid liposomes have immunogenicity, which provides a possibility that NPA may induce non-membrane phospholipid autoantibodies, leading to the occurrence of autoimmune diseases.

2.10.Lupus Mouse Model Induced by Graft-versus-host Disease (GVHD)

Chronic graft-versus-host disease (cGVHD) is a major late complication after allotransplantation. Compared with acute GVHD, which can better reflect apoptosis and necrosis, cGVHD is mainly a process of inflammation and fibrosis. Clinically, cGVHD is characterized by continuous T and B cell activation and autoantibody production, which may lead to renal lesions similar to lupus symptoms[30].After hybridization of two different strains of mice, spleen cells of

parental female mice were injected intravenously into F1 mice twice a week to induce chronic graft-versus-host disease. F1 mice can develop an autoimmune disease similar to human SLE, which is characterized by autoantibody production, immune complex deposition and proteinuria. The lupus mouse model induced by this method can be used to further explore the pathogenesis of SLE.

3. Summary

In the past few decades, some experts have established a variety of SLE mouse models with similar symptoms to human SLE disease. These lupus mouse models play an important role in human cognition of systemic lupus erythematosus, and can also be used in clinical testing and evaluation of lupus drugs. In recent years, some humanized mouse models began to emerge. with the deepening of research, lupus mouse model which is more similar to human SLE disease may appear in the future, which is more helpful for the treatment of systemic lupus erythematosus disease.

References

- [1] ZUCCHI D, ELEFANTE E, SCHILIRÒ D, et al. One year in review 2022: systemic lupus erythematosus[J/OL]. *Clinical and Experimental Rheumatology*, 2022, 40(1): 4-14.
- [2] BAGAVANT H, MICHROWSKA A, DESHMUKH U S. The NZB/W F1 mouse model for Sjögren's syndrome: A historical perspective and lessons learned[J/OL]. *Autoimmunity Reviews*, 2020, 19(12): 102686.
- [3] YOUNES S T, SHOWMAKER K, JOHNSON A C, et al. Single cell RNA sequencing reveals ferritin as a key mediator of autoimmune pre-disposition in a mouse model of systemic lupus erythematosus[J/OL]. *Scientific Reports*, 2021, 11(1): 24245.
- [4] GILL R F, MATHIEU P A, LASH L H, et al. Naturally occurring autoimmune disease in (NZB X NZW) F1 mice is correlated with suppression of MZ B cell development due to aberrant B Cell Receptor (BCR) signaling, which is exacerbated by exposure to inorganic mercury[J/OL]. *Toxicological Sciences: An Official Journal of the Society of Toxicology*, 2023, 197(2): 211-221.
- [5] HALKOM A, WU H, LU Q. Contribution of mouse models in our understanding of lupus[J/OL]. *International Reviews of Immunology*, 2020, 39(4): 174-187.
- [6] CUNNINGHAM M A, RICHARD M L, WIRTH J R, et al. Novel mechanism for estrogen receptor alpha modulation of murine lupus[J/OL]. *Journal of Autoimmunity*, 2019, 97: 59-69.
- [7] CHU S Y, PONG E, BONZON C, et al. Inhibition of B cell activation following in vivo co-engagement of B cell antigen receptor and Fcγ receptor IIb in non-autoimmune-prone and SLE-prone mice[J/OL]. *Journal of Translational Autoimmunity*, 2021, 4: 100075.
- [8] WIRTH J R, MOLANO I, RUIZ P, et al. TLR7 Agonism Accelerates Disease and Causes a Fatal Myeloproliferative Disorder in NZM 2410 Lupus Mice[J/OL]. *Frontiers in Immunology*, 2019, 10: 3054.
- [9] FLORES R, ZHANG P, WU W, et al. Siglec genes confer resistance to systemic lupus erythematosus in humans and mice[J/OL]. *Cellular & Molecular Immunology*, 2019, 16(2): 154-164.
- [10] DAVIS M J, MARTIN R E, PINHEIRO G M, et al. Inbred SJL mice recapitulate human resistance to *Cryptococcus* infection due to differential immune activation[J/OL]. *mBio*, 2023, 14(5): e0212323.

- [11] DOU D R, ZHAO Y, BELK J A, et al. Xist ribonucleoproteins promote female sex-biased autoimmunity[J/OL]. *Cell*, 2024, 187 (3): 733-749.e16.
- [12] CHEN X C, WU D, WU H L, et al. Metformin improves renal injury of MRL/lpr lupus-prone mice via the AMPK/STAT3 pathway [J/OL]. *Lupus Science & Medicine*, 2022, 9(1): e000611.
- [13] CHEN K, DENG Y, SHANG S, et al. Complement factor B inhibitor LNP023 improves lupus nephritis in MRL/lpr mice[J/OL]. *Biomedicine & Pharmacotherapy = Biomedecine & Pharmacotherapie*, 2022, 153: 113433.
- [14] NAMBA T, ICHII O, NAKAMURA T, et al. Compartmentalization of interleukin 36 subfamily according to inducible and constitutive expression in the kidneys of a murine autoimmune nephritis model[J/OL]. *Cell and Tissue Research*, 2021, 386(1): 59-77.
- [15] HAN X, XU T, DING C, et al. Neuronal NR4A1 deficiency drives complement-coordinated synaptic stripping by microglia in a mouse model of lupus[J/OL]. *Signal Transduction and Targeted Therapy*, 2022, 7(1): 50.
- [16] TOMALLA V, SCHMEISSER M J, WEINMANN-MENKE J. Mouse models, antibodies, and neuroimaging: Current knowledge and future perspectives in neuropsychiatric systemic lupus erythematosus (NPSLE)[J/OL]. *Frontiers in Psychiatry*, 2023, 14: 1078607.
- [17] ALMIZRAQ R J, FRIAS BOLIGAN K, LORIAMINI M, et al. (NZW × BXSB) F1 male mice: An unusual, severe and fatal mouse model of lupus erythematosus[J/OL]. *Frontiers in Immunology*, 2022, 13: 977698.
- [18] NAMBA T, ICHII O, NAKAMURA T, et al. Altered morpho-functional features of bones in autoimmune disease-prone BXSB/MpJ- Yaa mice[J/OL]. *Experimental Biology and Medicine (Maywood, N.J.)*, 2019, 244(5): 333-343.
- [19] YUAN X, DAI B, YANG L, et al. Emodin ameliorates renal injury in BXSB mice by modulating TNF- α /ICAM-1[J/OL]. *Bioscience Reports*, 2020, 40(9): BSR20202551.
- [20] SAITOH S I, SAITOH Y M, KONTANI K, et al. ADP-ribosylation factor-like 8b is required for the development of mouse models of systemic lupus erythematosus[J/OL]. *International Immunology*, 2019, 31(4): 225-237.
- [21] HONG H, ALDURAIBI F, PONDER D, et al. Host Genetics But Not Commensal Microbiota Determines the Initial Development of Systemic Autoimmune Disease in BXD2 Mice [J/OL]. *Arthritis & Rheumatology (Hoboken, N.J.)*, 2022, 74(4): 634-640.
- [22] CHEN J, LIAO S, ZHOU H, et al. Humanized Mouse Models of Systemic Lupus Erythematosus: Opportunities and Challenges[J/OL]. *Frontiers in Immunology*, 2021, 12: 816956.
- [23] MIAO N, WANG Z, WANG Q, et al. Oxidized mitochondrial DNA induces gasdermin D oligomerization in systemic lupus erythematosus[J/OL]. *Nature Communications*, 2023, 14(1): 872.
- [24] YANG F, HE Y, ZHAI Z, et al. Programmed Cell Death Pathways in the Pathogenesis of Systemic Lupus Erythematosus [J/OL]. *Journal of Immunology Research*, 2019, 2019: 3638562.
- [25] SOLHJOO M, GOYAL A, CHAUHAN K. Drug-Induced Lupus Erythematosus[M/OL]//StatPearls. Treasure Island (FL): StatPearls Publishing, 2024[2024-03-16].
- [26] RESÉNDIZ-MORA A, LANDA C, SÁNCHEZ-BARBOSA S, et al. Lupresan, a new drug that prevents or reverts the formation of nonbilayer phospholipid arrangements that trigger a murine lupus resembling human lupus[J/OL]. *Biochemical and Biophysical Research Communications*, 2019, 509(1): 275-280.
- [27] RESÉNDIZ-MORA A, WONG-BAEZA C, NEVÁREZ-LECHUGA I, et al. Interleukin 4 deficiency limits the development of a lupus-like disease in mice triggered by phospholipids in a non-bilayer arrangement[J/OL]. *Scandinavian Journal of Immunology*, 2021, 93(3): e13002.
- [28] ZHANG J, WANG X, WANG R, et al. Rapamycin Treatment Alleviates Chronic GVHD-Induced Lupus Nephritis in Mice by Recovering IL-2 Production and Regulatory T Cells While Inhibiting Effector T Cells Activation[J/OL]. *Biomedicines*, 2023, 11(3): 949.