BIOMEDICAL & VETERINARY SCIENCES

GRADUATE PROGRAM

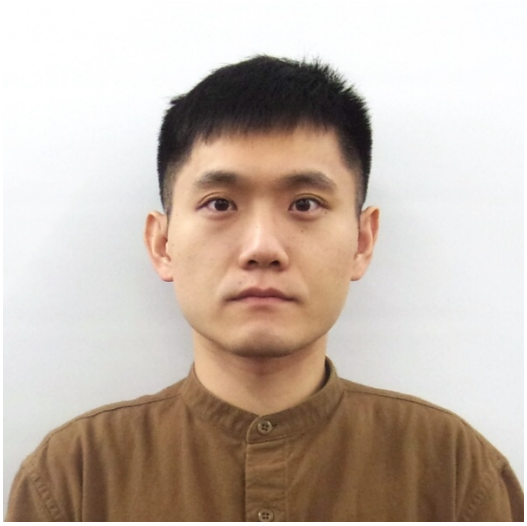
ANNOUNCES

The Doctor of Philosophy Seminar and Examination of

Zhuang Wang

"Investigation of microRNAs in lupus-prone lpr mice"

Friday, May 5th, 2023
11:30AM
Vet Med Classroom 121



Bio

Zhuang did his B.S. in Agriculture in China and participated in research in a bacteria-borne infectious disease lab lead by Dr. Mingchun Liu. With an interest in Immunology and the will to explore the mystery in epigenetics factors, he joined the lab of Dr. Ansar Ahmed to pursue a PhD in the field of Immunology after graduation. His research in Ahmed lab focused on the expression and function of microRNAs in the pathogenesis of autoimmune disease, SLE, by genetic modification. Meanwhile, the methylation change under lupus background is investigated utilizing different lupus-prone mouse models.

Funded by

Alliance for Lupus Research
VCOM One Health
VMCVM Internal Research Competition
VMCVM Office of Research and Graduate Studies

Lay Language Abstract

Systemic lupus erythematosus (SLE) is an autoimmune disease that causes damage to multiple organs. Same with other autoimmune diseases, the exacerbated immune reaction to self-antigen and auto-reactive adaptive immune cells were described in SLE. Currently, the treatment of lupus mainly uses immunosuppressive drugs to inhibit the global immune reaction. Thus, innovative curing drug is desperately needed for SLE patients. MicroRNAs (miRNAs) are small RNAs that inhibit the expression of genes by binding to mRNAs in a complimentary manner. Since the discovery of the first microRNA, the pivotal role of microRNAs in immunity and autoimmunity has been vigorously investigated. Our lab firstly described a set of miRNAs that are commonly upregulated in three murine lupus models. Among these miRNAs, miR-183, miR-96, and miR-182 belong to the miR-183-96-182 cluster (miR-183C).

The aim of the study in this dissertation focused on illuminating the dysregulation pattern of miRNAs in different cell sources in the murine lupus model and the role of miR-183C in the pathogenesis of SLE. We found that miRNAs are similarly dysregulated in peripheral blood mononuclear cells and splenic lymphocytes of MRL/lpr mice. Then we conditionally knocked out the miR-183C in B6/lpr mice and investigated the effect of miR-183C loss on the pathogenesis of autoimmunity. Importantly, we found that the deletion of miR-183C led to a reduced production level of autoantibodies and ameliorated the deposition of immune complexes in the kidney. Moreover, the production of proinflammatory cytokines of splenic lymphocytes was regulated by miR-183C as well. Besides miR-183C, I also investigated the effect of early growth response 2 (EGR2), a transcription factor, on the expression of a set of lupus-related miRNAs and the methylation changes at the genome location of these miRNAs.

In summary, miR-183C can be a potential therapeutic target for lupus treatment. Clinical human studies are needed to better clarify the effectiveness and efficiency.

Publications

Wang Z, Dai R, Ansar Ahmed S. MicroRNA-183/96/182 cluster in immunity and autoimmunity. Frontiers in Immunology. 2023 Feb 20;14:1134634. doi: 10.3389/fimmu.2023.1134634.

Wang Z, Heid B, Lu R, Sachdeva M, Edwards MR, Ren J, Cecere TE, Khan D, Jeboda T, Kirsch DG, Reilly CM, Dai R, Ahmed SA. Deletion of microRNA-183-96-182 Cluster in Lymphocytes Suppresses Anti-DsDNA Autoantibody Production and IgG Deposition in the Kidneys in C57BL/6-Faslpr/lpr Mice. Frontiers in Genetics. 2022 Jul 7;13:840060. doi: 10.3389/fgene.2022.840060.

Cabana-Puig X, Mu Q, Lu R, Swartwout B, Abdelhamid L, Zhu J, Prakash M, Cecere TE, Wang Z, Callaway S, Sun S, Reilly CM, Ansar Ahmed S, Luo XM. Lactobacillus spp. act in synergy to attenuate splenomegaly and lymphadenopathy in lupus-prone MRL/lpr mice. Frontiers in Immunology. 2022 Jul 28;13:923754. doi: 10.3389/fimmu.2022.923754.

Dai R, Wang Z, Heid B, Eden K, Reilly CM, Ansar Ahmed S. EGR2 Deletion Suppresses Anti-DsDNA Autoantibody and IL-17 Production in Autoimmune-Prone B6/lpr Mice: A Differential Immune Regulatory Role of EGR2 in B6/lpr Versus Normal B6 Mice. Frontiers in Immunology 2022 Jun 15;13:917866. doi: 10.3389/fimmu.2022.917866.

Cabana-Puig X, Bond JM, Wang Z, Dai R, Lu R, Lin A, Oakes V, Rizzo A, Swartwout B, Abdelhamid L, Mao J, Prakash M, Sangmeister C, Cheung N, Cowan C, Reilly CM, Sun S, Ansar Ahmed S, Luo XM. Phenotypic Drift in Lupus-Prone MRL/lpr Mice: Potential Roles of MicroRNAs and Gut Microbiota. Immunohorizons. 2022 Jan 17;6(1):36-46. doi: 10.4049/immunohorizons.2100082.

Dai R, Wang Z, Ansar Ahmed S. Epigenetic Contribution and Genomic Imprinting Dlk1-Dio3 miRNAs in Systemic Lupus Erythematosus. Genes (Basel). 2021 May 1;12(5):680. doi: 10.3390/genes12050680.

Wang Z, Heid B, Dai R, Ansar Ahmed S. Similar dysregulation of lupus-associated miRNAs in peripheral blood mononuclear cells and splenic lymphocytes in MRL/lpr mice. Lupus Science Medicine. 2018 Nov 5;5(1):e000290. doi: 10.1136/lupus-2018-000290.

Presentations

BMVS Seminar. miR-182 is largely dispensable for adaptive immunity: lack of correlation between expression and function. 2017

29th VMCVM Annual Research Symposium, Poster Presentation "Similar dysregulation of lupus-associated miRNAs in peripheral blood mononuclear cells and splenic lymphocytes in MRL/lpr mice". 2018

17th Congress of the International Union of Immunological Societies (IUIS), Poster Presentation (presented by Dr.Rujuan Dai) "Conditional depletion of microRNA-183-96-182 cluster in lymphocytes suppresses autoantibody production in Lpr lupus mice ". 2019

30th VMRCVM Annual Research Symposium, Poster Presentation "Conditional depletion of microRNA-183-96-182 cluster in lymphocytes suppresses inflammatory cytokine and autoantibody production in Lpr lupus mice." 2019

BMVS Seminar. In vivo depletion of microRNA-183-96-182 cluster alleviates autoimmunity. 2019

Via Research Recognition Day – Virginia Campus. Depletion of microRNA-183-96-182 cluster in lymphocytes suppresses anti-dsDNA autoantibody production and IgG in kidney in C57BL/6Faslpr/lpr mice. 2021

31th Annual BMVS Graduate Research Symposium. Depletion of microRNA-183-96-182 miRNA cluster in lymphocytes suppresses anti-dsDNA autoantibody production and IgG deposition in kidney in C57BL/6-Faslpr/lpr mice. 2021

Via Research Recognition Day – Virginia Campus. EGR2 is critical for the upregulation of the genomic imprinting DLK1-DIO3 miRNAs in murine lupus-prone B6/lpr mice. 2022

Examination Graduate Committee

Major Advisor/Chair:

S. Ansar Ahmed, BVSc,Ph.D.
Associate Dean of Research and Graduate Studies
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