Liudmila Kulik, PhD **CURRICULUM VITAE**

Assistant Professor of Medicine, Division of Rheumatology, University of Colorado School of Medicine
Address: 1775 Aurora Ct., Mail Stop B115, Aurora, CO 80045
Phone: 303.724.7593
Email: liudmila.kulik@ucdenver.edu

Education

1987	MD, Biochemistry	Belarus State University, Minsk, Belarus
1994	PhD, Bioorganic chemistry	Institute of Bioorganic Chemistry, Moscow, Russia

Academic appointments

1994-1995	Junior Scientist	Institute of Bioorganic Chemistry, Moscow, Russia
1995-1997	Scientist	Institute of Bioorganic Chemistry, Minsk, Belarus
1997-2001	Postdoctoral Fellow	Institute of Molecular Biology, Academia Sinica, Taiwan
2001-2007	Postdoctoral Fellow	Colorado University Health Scientist Center, Denver
2007-2015	Instructor Medicine	University of Colorado School of Medicine, Aurora, CO
2015-present	Assistant Professor	University of Colorado School of Medicine, Aurora, CO

Inventions, intellectual property and patents held or pending

Patent number	Filling date	Status	Title
US 2011/0014270 A1	1/20/2011	Issued	Prevention and Treatment of Ischemia-Reperfusion Injury and Related Conditions
US 2015/0306254 A1	8/16/2013	Issued	Compositions and methods for detecting complement activation
PCT/US2015/034270	10/4/2014	Pending	MAP44 polypeptides and constructs based on natural antibodies and uses thereof
US 2016/0083463	7/23/2015	Issued	Targeting constructs based on natural antibodies and uses there of
981590	2/17/2015	Issued	Antibodies to the C3d fragment of complement component 3

Review and referee work

TEACHING ACTIVITIES

Grant support

Current

R01 AR051749 (Co-investigator) NIH/NIAMS	04/03/15 – 03/31/20	$220.000

Complement in the Pathogenesis of Autoimmune Arthritis
The major goals of this project are to determine the in vivo role of the lectin and alternative pathways of complement, as well as a novel effector pathway-mediated amplification loop, in the development of joint inflammation and injury in the collagen antibody-induced arthritis model of human rheumatoid arthritis; and to experimentally manipulate the functions of these pathways in order to understand the mechanism and effects on the modulation of tissue injury

ADMEX HLRS-KLK SPA (Holers)	5/7/18-6/30/20	$337,044
MIRX/AWD	Co-investigator	

The major goals of this project are based on previously obtained monoclonal antibody to C3d to generate inhibitors blocking B cells activation and preventing self immunological responses in the body.

PREVIOUS

R01 DK102912 (Tomlinson)	07/01/15–03/31/19	$74,044
NIH	Co-investigator	

Antibodies and Complement in Ischemia Reperfusion Injury and Regeneration
The major goals of this project are to study the natural antibodies and complement on the development of liver injury post-transplantation and the subsequent regeneration of the tissue. Understanding the relative roles of these components of the immune response has potential for the development of therapeutics that will greatly improve outcome for small for size liver graft recipients, as well as patients undergoing liver resection.

257141 (Holers)	02/01/13 – 05/16/16	$190,407
Alliance for Lupus Research	Co-investigator	

The CR2:C3d Receptor: Ligand Interaction as a Therapeutic Target in Lupus
The goal of this project is to study the (NZBxNZW)F1 model of human lupus erythematosus and determine the effects of blocking the interaction of human complement receptor type 2 (CR2/CD21) with its complement C3 fragment ligand designated C3d. Unique monoclonal antibodies that recognize the protein:protein interface have been developed and will be utilized in the studies.

Disease Targeted Inn. Research (Haskins)	07/01/14 – 06/30/15	$185,185
Rheumatology Research Foundation	Co-investigator	

Pathogenic T cells in a Mouse Model of Rheumatoid Arthritis
The goals of this project are to characterize and pursue the cloning of pathogenic CD4 T cells in the draining lymph nodes and synovium of mice undergoing models of human arthritis, including collagen induced arthritis and anti-collagen antibody-induced arthritis. The pathogenicity of these CD4 T cells will be evaluated in vitro by characterizing cytokine production and in vivo by cell transfer approaches.

R21 AI105717 (Holers)	02/01/13 – 01/31/15	$193,489
NIH/NIAIDS	Co-investigator	

Disconnecting CR2/CD21 from its C3d Ligand to Ameliorate Lupus
The goal of this project is to study the MRL/lpr model of human lupus erythematosus and evaluate the effects of blocking function of human complement receptor type 2 (CR2/CD21) and its ability to interact with its complement C3 fragment ligand designated C3d.

1403 (Holers)	07/01/14 – 06/30/15	$100,000

Arnold and Mable Beckman Foundation Co-investigator

Inhibition of Complement Factor H Related Protein De-Regulatory Activity as a Therapeutic Strategy in Age-Related Macular Degeneration: Proof of Concept in a Murine Model

The major goals of this program were to determine the effects of inhibiting a complement de-regulator in a murine model of AMD and assess whether clinical improvement could follow that therapeutic strategy.

MUSC12-062 (Roher) 07/01/12 – 06/30/13 $35,000
Medical University of South Carolina Co-investigator

Utilization of Natural IgM Molecules for the Recognition of Oxidative Stress Markers and Non-Invasive Imaging in Advanced Age-Related Macular Degeneration. The major goals of this program were to utilize a previously developed set of natural antibody hybridomas to determine which ones were reactive with neo-epitopes that arose through the process of cells stress responses. These would subsequently be utilized for imaging studies.

Bibliography

Selected Peer-reviewed Publications (of 40 total):

1. Goetz L, Laskowski J, Renner B, Pickering MC, **Kulik** L, Klawitter J, Stites E, Christians U, van der Vlag J, Ravichandran K, Holers VM, Thurman JM. Complement factor H protects mice from ischemic acute kidney injury but is not critical for controlling complement activation by glomerular IgM. Eur J Immunol. 2018;48(5):791-802. PMID:29389016.
2. He YG, Pappworth IY, Rossbach A, Paulin J, Mavimba T, Hayes C, **Kulik** L, Holers VM, Knight AM, Marchbank KJ. A novel C3d-containing oligomeric vaccine provides insight into the viability of testing human C3d-based vaccines in mice. Immunobiology. 2018,223:125-134. PMID:29017821
3. Narang A, Qiao F, Atkinson C, Zhu H, Yang X, **Kulik** L, Holers VM, Tomlinson S. Natural IgM antibodies that bind neoepitopes exposed as a result of spinal cord injury , drive secondary injury by activating complement. J Neuroinflammation. 2017, 14:120.. PMID 28629465.
4. Holers VM, Tomlinson S, **Kulik** L, Atkinson C, Rohrer B, Banda N, Thurman JM. New therapeutic and diagnostic opportunities for injured tissue-specific targeting of complement inhibitors and imaging modalities. Semin Immunol. 2016, 28:260-7. Review. PMID:27282113
5. Panzer SE, Laskowski J, Renner B, **Kulik** L, Ljubanovic D, Huber KM, Zhong W, Pickering MC, Holers VM, Thurman JM IgM exacerbates glomerular disease progression in complement-induced glomerulopathy Kidney Int. 2015; 88:528-37. PMID:25945405.
6. Atkinson C, Qiao F, Yang X, Zhu P, Reaves N, **Kulik** L, Goddard M, Holers VM, Tomlinson S. Targeting pathogenic postischemic self-recognition by natural IgM to protect against posttransplantation cardiac reperfusion injury. Circulation. 2015,131:1171-80. PMID:25825397.
7. **Kulik** L, Hewitt FB, Willis VC, Rodriguez R, Tomlinson S, Holers VM. A new mouse anti-mouse complement receptor type 2 and 1 (CR2/CR1) monoclonal antibody as a tool to study receptor involvement in chronic models of immune responses and disease. Mol Immunol. 2015,63(2):479-88. PMID: 25457881.
8. Neher MD, Rich MC, Keene CN, Weckbach S, Bolden AL, Losacco JT, Patane J, Flierl MA, **Kulik** L, Holers VM, Stahel PF. Deficiency of complement receptors CR2/CR1 in $Cr2^{-/-}$ mice reduces the extent of secondary brain damage after closed head injury. J Neuroinflammation. 2014 11:95. 1742-2094; PMCID:PMC4050415
9. Joseph K, **Kulik** L., Coughlin B., Kunchithapautham K., Bandyopadhyay M., Thiel S., Thielens N.M., Holers V.M., Rohrer B. Oxidative stress sensitizes retinal pigmented epithelial (RPE) cells to complement-

mediated injury in a natural antibody-, lectin pathway-, and phospholipid epitope-dependent manner. J. Biol Chem., 2013, 288:12753-12765. PMCID:PMC3642321
10. Fuquay R., Renner B., **Kulik** L., McCullough J.W., Amura C., Strassheim D., Pelanda R., Torres R., Thurman J.M. Renal ischemia-reperfusion injury amplifies the humoral immune response. J Am Soc Nephrol., 2013, 24:1063-1072. PMCID:PMC 3699821
11. Thurman J.M., **Kulik** L, Orth H., Wong M., Renner B., Sargsyan S.A., Mitchell L.M., Hourcade D.E., Hannan J.P., Kovacs J.M., Coughlin B., Woodell A.S., Pickering M.C., Rohrer B., Holers V.M. Detection of complement activation using monoclonal antibodies against C3d. J Clin Invest., 2013, 123:2218-2230. PMCID:PMC3635726
12. Strassheim D., Renner B., Panzer S., Fuquay R., **Kulik** L., Ljubanović D., Holers V.M., Thurman J.M. IgM contributes to glomerular injury in FSGS. J Am Soc Nephrol., 2013, 24:393-406. PMCID:PMC 3582199.
13. Weckbach S., Neher M., Losacco J., Bolden A., **Kulik L**., Flierl M., Bell S., Holers VM., Stahel P. Challenging the role of adaptive immunity in neurotrauma: Rag1-/- mice lacking mature B and T cells do not show neuroprotection after closed head injury. J Neurotrauma., 2012, 29:1223-1242. PMCID:PMC 3325549
14. Elvington A, Atkinson C, **Kulik** L, Zhu H, Yu J, Kindy MS, Holers VM, Tomlinson S. Pathogenic Natural antibodies propagate cerebral injury following ischemic stroke in mice. J. Immunol. 2012, 188:1460-1468. PMCID: PMC3262954
15. Willis VC, Gizinski AM, Banda NK, Causey CP, Knuckley B, Cordova KN, Luo Y, Levitt B, Glogowska M, Chandra P, **Kulik** L, Robinson WH, Arend WP, Thompson PR, Holers VM. N-α-benzoyl-N5-(2-chloro-1-iminoethyl)-L-ornithine amide, a protein arginine deiminase inhibitor, reduces the severity of murine collagen-induced arthritis., J Immunol. 2011 Apr 1;186(7):4396-404. PMCID: PMC3085980
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17. Renner B, Strassheim D, Amura CR, **Kulik** L, Ljubanovic D, Glogowska MJ, Takahashi K, Carroll MC, Holers VM, Thurman JM. B cell subsets contribute to renal injury and renal protection after ischemia/reperfusion. J Immunol. 2010, 185:4393-400. PMCID: PMC3133676
18. **Kulik L**, Fleming SD, Moratz C, Reuter JW, Novikov A, Chen K, Andrews KA, Markaryan A, Quigg RJ, Silverman GJ, Tsokos GC, Holers VM. Pathogenic natural antibodies recognizing annexin IV are required to develop intestinal ischemia-reperfusion injury. J Immunol. 2009; 182:5363-73. PMCID: PMC2820395
19. Twohig JP, Pappworth IY, Sivasankar B, **Kulik L**, Bull M, Holers VM, Wang EC, Marchbank KJ. Defective B cell ontogeny and humoral immune response in mice prematurely expressing human complement receptor 2 (CR2, CD21) is similar to that seen in aging wild type mice. Mol Immunol. 2009;46:2002-13. PMCID: PMC2706330
20. Pappworth IY, **Kulik L**, Haluszczak C, Reuter JW, Holers VM, Marchbank KJ. Increased B cell deletion and significantly reduced auto-antibody titre due to premature expression of human complement receptor 2 (CR2, CD21). Mol Immunol. 2009 Mar;46(6):1042-9. PMCID: PMC2657831
21. Ho J, Moir S, **Kulik L**, Malaspina A, Donoghue ET, Miller NJ, Wang W, Chun TW, Fauci AS, Holers VM. Role for CD21 in the establishment of an extracellular HIV reservoir in lymphoid tissues. J Immunol. 2007; 178:6968-74.
22. Twohig J, **Kulik L**, Haluszczak C, Reuter J, Rossbach A, Bull M, Holers VM, Marchbank KJ. Defective B cell ontogeny and immune response in human complement receptor 2 (CR2, CD21) transgenic mice is partially recovered in the absence of C3. Mol Immunol. 2007, 44: 3434-44.
23. **Kulik L**., Marchbank, K.J., Lyubchenko T., Kuhn K.A., Liubchenko G, Haluszczak C., Gipson M.G., Boackle S.A, and Holers V.M. Intrinsic B cell hypo-responsiveness in mice prematurely expressing human CR2/CD21 during B cell development. Eur J Immunol. 2007, 37:623 -33.
24. Holers V.M., and **Kulik L**. Complement receptor 2, natural antibodies and innate immunity: Inter-relationships in B cell selection and activation.Mol Immunol. 2007, 44:64-72. Review.
25. Kuhn K.A., **Kulik L**., Tomooka B., Braschler K.J., Arend W.P., Robinson W.H., and Holers V.M. Antibodies against citrullinated proteins enhance tissue injury in experimental autoimmune arthritis. J Clin Invest. 2006; 116:961-73.

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27. Marchbank, K.J., **Kulik L**., Gipson M.G., Morgan B.P., Holers V.M. Expression of human complement receptor type 2 (CD21) in mice during early B cell development results in a reduction in mature B cells and hypogammaglobulinemia. J Immunol. 2002; 169:3526-35.
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29. Lai YG, Gelfanov V, Gelfanova V**, Kulik L**, Chu CL, Jeng SW, Liao NS. IL-15 promotes survival but not effector function differentiation of CD8+ TCRalphabeta+ intestinal intraepithelial lymphocytes. J Immunol. 1999, 163:5843-50. PMID:10570268.
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31. Davydov V, **Kulik** LN, Kisel' MA. [Entrapment of antibiotics in liposomes containing phosphatidylethanol]. Antibiot Khimioter. 1996;41(5):25-9. Russian. PMID:9054313.
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33. **Kulik** LN, Ivanov VS, Chikin LD, Berkova NP, Kozhich AT, Gabriélian AE, Ivanov VT. [Modeling antigenic determinants of the hepatitis A virus using synthetic peptides]. Bioorg Khim. 1994 Jul;20(7):709-19. Russian. PMID:7527634.
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Abstracts (peer-reviewed; *denotes oral presentation)

Banda N.K., Ramirez J.R., Yang Y., Khan N., Wang G., Simberg D., **Kulik L**., Tomlinson S., V. Michael Holers V.M. Natural antibodies enhances inflammation and their local targeting by recombinant single chain antibody fused complement inhibitors attenuate arthritis in mice. XXVII International Complement workshop 2018.
Kulik L., Laskowski J., Thurman J.M., Holers V.M. Treatment of MRL/*lpr* mice with a mAb blocking binding of C3d to its receptors decreases anti-DNA antibodies and proteinuria: therapeutic proof of concept in a murine model of systemic lupus erythematosus. XXVI International Complement Workshop.2016.
Kulik L., Laskowski J., Thurman J.M., Holers V.M. Treatment of MRL/*lpr* Mice with a mAb Blocking Binding of C3d to Its Receptors Decreases Anti-DNA Autoantibodies and Proteinuria: Support for Targeting the CR2:C3d Interaction as a Therapeutic Strategy in SLE. Lupus 21th century. 2016.
Kulik L., Laskowski J., Thurman J.M., Holers V.M.Amelioration of Disease in the MRL/*lpr* Model of Lupus by Treatment with an Anti-C3d Monoclonal Antibody That Blocks C3d:CR2 Ligand:Receptor Interactions 8th International Conference on Complement Therapeutics, 2015.
Holers V.M., **Kulik L**., Thurman J.M., Laskowski J., Hewitt F.B., Rodriguez R. The CR2:C3d receptor:ligand interaction as a therapeutic target in lupus.15th Annual *Forum for Discovery* 2015.
Qiao F, Zhang L., Yang X., Hua Y., Narang A., **Kulik L**., V. Holers V.M., Tomlinson S. Role of pathogenic natural antibodies and complement in a murine model of spinal cord injury. American Association of Immunologists Annual Meeting. 2013.
Kulik L., Thurman J.M., Hannan J.P., Tomlinson S., Holers V.M. Novel mouse anti-mouse monoclonal antibodies that block either the ligand or receptor member of the CR2-C3d interaction pair impair antigen-specific humoral immune responses to model antigens XXIV International Complement Workshop.2012.

***Kulik L.**, Fleming S.D., Moratz C., Quigg R.J., Silverman G.J, Tsokos G.C., Holers V.M. Pathogenic Natural Antibodies Recognizing Annexin IV Are Required to Develop Intestinal Ischemia-Reperfusion Injury. XXII International Complement Workshop. 2008.

***Kulik L**, Hannan J.P., Huber B.T., Holers V.M. Treatment with a Highly Inhibitory Monoclonal Antibody Directed to the C3d Ligand Binding Site on Human CR2/CD21 Suppresses Antigen-Specific Immune Responses In Vivo XXII International Complement Workshop.2008.

Kulik L., S. D. Fleming, C.Moratz, G. C. Tsokos, V. M. Holers Selected for epitopes on intestinal epithelial cells monoclonal antibodies obtained from unmanipulated *Cr2+/+* or *Cr-/-* mice induce ischemia reperfusion injury. XXI International Complement Workshop.2006.

Atkinson C., **Kulik L**., Zhu H., Yu J., Kindy M.S., Holers V.M., Tomlinson S. Pathogenic natural IgM antibodies recognizing different antigens mediate injury following ischemic stroke in Rag1-/- mice. XXI International Complement Workshop.2006.

Kuhn K.A., **Kulik L**, Braschler K.J., Arend W.P., Holers V.M. Antibodies to citrulline-modified proteins enhance Tissue Injury in Inflammatory Arthritis. Experimental Biology. 2005.

Kulik L, Marchbank J.D , Haluszczak C., Morgan B.P., Holers V.M. Premature expression of complement receptor type 2 (CR2/CD21) on pro-B cells in the bone marrow induces partial B cell deletion and results in defective peripheral immune responses by remaining cells. XX International Complement Workshop. 2004.

Kulik L., Malaspina A., Donoghue E.T., Miller N., Chun T.-W., Fauci A.S., Holers V.M., Moir S. Complement receptors CR2 and CR1 are essential for HIV loading on murine lymph node cells. XX International Congress of Immunology. 2004.

Kuhn K.A, **Kulik L**., Marchbank K.J., Holers V.M. Premature Expression of Human Complement Receptor 2 (hCR2) During B cell Development Suppresses Autoimmunity. XX International Complement Workshop. 2004.

Kuhn KA, Arend WP, **Kulik L**, Braschler KJ, Holers VM. Development of an anti-cyclic citrullinated peptide-antibody response in collagen-induced arthritis. American College of Rheumatology Annual Meeting. 2004.

Kuhn KA, **Kulik L**, Holers VM. Suppression of Autoimmunity by Premature B cell Expression of an InnateImmune System Receptor. American Association of Immunologists Annual Meeting. 2003.

Kulik L., Fleming S.D., Tsokos G.C., Holers V.M. Absence of complement receptors CR1 and CR2 causes changes in the natural antibody repertoire to intestinal and thymic autoantigens in mice. XIIII International Congress of Immunology. 2002.

Marchbank K.J., **Kulik L.,** Gipson M.G., B. Morgan B.P.,Holers V.M. Expression of Human Complement Receptor Type 2 (CR2/CD21) in Mice During Early B Cell Development Results in a Reduction Mature B Cells and Hypogammaglobulinemia. XIXth International Complement Workshop.2002.

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