RESEARCH PROJECTS

I. Hepatitis E Seroprevalence Study in *canis lupis familiaris* and Associations to Human Owners. Sporadic, acute Hepatitis E is emerging more frequently in humans in the developed world, even in Texas. HEV may be more abundant in humans and other animals than we realize. One U.S. human seroprevalence survey found HEV IgG rates of 21%. Many theorize a zoonotic nature of transmission as antibodies have been detected in a wide range of mammals. For instance, a recent study found 40% HEV prevalence in laboratory rabbits. Current thinking from USDA and CDC places suspicion on feral pigs. **This collaborative project** is designed to study the prevalence of HEV in East Texas and the role of domestic doges in emerging of this zoonotic disease.

II. **Liposomal antibiotics in Infection Therapy**

Liposomes are emerging as a preferred drug carrier to combat antibiotic resistant strains due to their ability to fuse with the prokaryotic cell membrane as the endpoint of their carrier function. In this project, we investigate the efficacy of this alternate method on microbial adhesion, which is accepted as a prerequisite to *P. aeruginosa* colonization and infection. Using A549 pulmonary epithelial cells, we quantify *P. aeruginosa* adhesions to host cells using fluorescence microscopy and colony forming unit assay. **The ultimate goal** is to safely eliminate bacterial infections caused by organism resistant to conventional drugs. **Our hypothesis** for this line of research is that the use of liposomal antibiotics as opposed to conventional methods will augment the existing antibiotics ability to efficiently inhibit the adherence of *P. aeruginosa* to human lung cells and therefore decrease susceptibility to infection.

III. **Therapeutics for Pulmonary Inflammatory disease**- We are investigating the efficacy of both free and liposomal erythromycin in reducing inflammation in human alveolar cells. Using human A549 cells, we model inflammation and the immunomodulatory effects of erythromycin. We use an ELISA to determine exact concentrations of various mediators of inflammation including IL-8 and TNFα. **Our ultimate goal** is to understand the inflammatory process set forth by structural cells of the lungs in an effort to provide more options for relieving inflammation in the pulmonary system.

IV. Cellular Mechanism of Pulmonary edema- *Pseudomonas aeruginosa* frequently infects patients with cystic fibrosis and immunocompromised individuals. One of the first steps in pulmonary injury is the loss of epithelium integrity; which is followed by inflammation and edema. Previous reports from our lab indicate that *P. aeruginosa* elastase (PE) activates host cells' signal transduction pathways that, in part, contribute to tight junction disruption. The exact mechanism of epithelial disruption, however, is not yet fully understood. **We investigate** the role of cell receptors and signaling cascades in PE-induced modification of Tight Junction organization and epithelial barrier integrity. An *in vitro* model of human pulmonary epithelial cell (Calu-3) grown on tissue culture inserts are utilized in this project.

V. **Plasminogen Activator inhibitor (PAI-1) activity as a biomarker and target for therapeutic intervention.** Pleural loculation or scarring in the pleural space is now difficult to treat and is associated with poor outcomes. As a member of a research team at UTHSCT, we identified PAI-1 activity as a biomarker and target for therapeutic intervention. **Our ultimate goal** is to identify a novel PAI-1-targeted intrapleural fibrinolytic therapeutic, which we will advance to IND-enabling work in anticipation of near-term clinical trial testing to provide better, safer treatment for patients with pleural loculation.

PEER REVIEWED PUBLICATIONS (44)

Students' publications are in Italics

1. Andrey A. Komissarov, Galina Florova, Ali O Azghani, Ann Buchanan, Jake Boren, Timothy Craig Allen, Najib M. Rahman, Kathleen Koenig, Mignote Chamiso, Sophia Karandashova, James Henry, Steven Idell. 2016. **Dose dependency of outcomes of intrapleural fibrinolytic therapy in new rabbit empyema models.** Am J Physiol - Lung Cell Mol Physiol. 311, 2, p. 389-399.

2. Komissarov AA, Florova G, **Azghani** AO, Buchanan A, Bradley WM, Schaefer C, Koenig K, Idell S. The time course of resolution of adhesions during fibrinolytic therapy in tetracycline-induced pleural injury in rabbits. Am J Physiol Lung Cell Mol Physiol. **2015**

3. Florova G, **Azghani** A, Karandashova S, Schaefer C, Koenig K, Stewart-Evans K, Declerck PJ, Idell S, Komissarov AA. Targeting of plasminogen activator inhibitor 1 improves fibrinolytic therapy for tetracycline-induced pleural injury in rabbits. Am J Respir Cell Mol Biol. **2015** Apr;52(4):429-37

4. **Ali Azghani**, Kourtney Neal, Steven Idell, Rodolfo Amaro, Jason W. Baker, Abdelwahab Omri, and Usha R. Pendurthi. **2014**. Mechanism of Fibroblasts Inflammatory Response to *Pseudomonas aeruginosa* Elastase. Microbiology, 160, 547-555.

5. Andrey A. Komissarov, Galina Florova, **Ali Azghani**, Sophia Karandashova, Anna K. Kurdowska, and Steven Idell. **2013**. Active α-macroglobulin is a reservoir for urokinase after fibrinolytic therapy in rabbits with tetracycline-induced pleural injury and in human pleural fluids. A J. Physiol, Lung Cell and Molecular Physiol. (305): L682-L692.

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9. **Azghani, Ali**. **2010**. The Central Dogma of Molecular Biology and the New Clinical Research Order. The Monitor, 24(1): 25-28.

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11. *Halwani M, Hebert S, Suntres ZE, Lafrenie RM, **Azghani AO**, Omri A. **2009**. Bismuththiol incorporation enhances biological activities of liposomal tobramycin against bacterial biofilm and quorum sensing molecules production by Pseudomonas aeruginosa. Int J Pharm. 21;373(1-2): 141-6.*

12. *Halwani, M, B. Yebio1, Z. E. Suntres, M. Alipour, **A. O. Azghani**, and A. Omri1, **2008**.Co-encapsulation of gallium with gentamicin in liposomes enhances antimicrobial activity of*

gentamicin against Pseudomonas aeruginosa. Journal of Antimicrobial Chemotherapy 62(6): 1291-7.

13. *Halwani, M, Shanna Blomme , Zacharias E. Suntres, Misagh Alipour, **Ali O. Azghani**, Aseem Kumar, Abdelwahab Omri**. 2008**. Liposomal Bismuth-Ethanedithiol Formulation Enhances Antimicrobial Activity of Tobramycin. International Journal of Pharmaceutics, 2008, 358(1-2): 254-63.*

14. Idell S, **Azghani A,** Chen S, Koenig K, Mazar A, Kodandapani L, Bdeir K, Cines D, Kulikovskaya I, Allen T. **2007**. Intrapleural low-molecular-weight urokinase or tissue plasminogen activator versus single-chain urokinase in tetracycline-induced pleural loculation in rabbits. Exp Lung Res. 33(8): 419-40.

15. *Yarlagadda, B, N. Subramanian, and **A. Azghani**. **2007**. Artificial Neural Network-Based Estimation for Pseudomonas aeruginosa Experiments. IEEE Proceedings, 1-4244, 133-137.*

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17. Steven Idell, Timothy Allen, Shande Chen, Kathy Koenig, Andrew Mazar and **Ali Azghani**. **2007**. Intrapleural activation, processing, efficacy, and evolving tetracycline-induced pleural injury in rabbits. Am J Physiol Lung Cell Mol Physiol. 292: 25-32.

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28. *Ashraf I. Zahra, Steven Idell, **Ali Azghani**, Mamdouh Sallam, Hosny el Sallab. 2004, Inflammation and Infection in Cardiothoracic Patients. The Medical Journal of Teaching Hospitals & Institutes, Egypt, 2004, 61, 19-45.*

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MANUSCRIPTS SUBMITTED or in PREPARATION

1. Galina Florova, **Ali Azghani,** Sophia Karandashova, Chris Schaefer, Serge Yarovoi, Paul J. Declerck, Douglas Cines, Steven Idell, and Andrey A. Komissarov. 2006**.The rate of fibrinolysis determines the selection of the mechanism for targeting plasminogen activator inhibitor 1 in tetracycline-induced pleural injury in rabbits**. Submitted to J. Biol. Chem., July 2016.

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2. Omar Castillo, Beatriz Calvo, Halima Farooq, and **Ali Azghani.** *Pseudomonas aeruginosa* elastase modifies tight junction proteins via an EGFR dependent pathway. Microbiology

3. Bidisha Pal and **Ali Azghani**. *Pseudomonas aeruginosa* Elastase Disturbs Actin Filament Dynamics via the RhoA- Mediated Signaling. Am J Resp Cell Mol Biol.

4. Majed A. Majrashi, Moyad Alhariri , **Ali O Azghani** , Mohammad A. Khiyami, Ali H. Bahkaly , Essam J. Alyamani, and Majed A. Halwani.. Increasing gentamicin encapsulation load enhaces efficacy of liposomal formulations against pathogens.

BOOK CHAPTERS

1. **Azghani, A.O**. and Curtis Clark. **2011.** Bacterial Infection Process: An overview. Infection and Immunity. Transworld Research Network

2. Alipour M, Zacharias E. Suntres, **Ali O. Azghani**, and Abdlewahab Omri. **2008**. Pulmonary infection in Cystic Fibrosis: Role of quorum-sensing. Recent Development in Signal Transduction Research, 2008, Editors; CV Ramana, Richard I. Enelow and Aseem Kumar.

3. Omri, M.L Anderson, C. Mugabe, Z. Suntres, M. R. Mozafari, and **A. Azghani**. **2007.** Artificial implants–new developments and associated problems in nanomaterials and nanosystems for biomedical applications, Springer, Volume editor: M. Reza Mozafari

4. **Azghani, A.O.** and Rodolfo Amaro. **2003.** Molecular basis of Pseudomonas inflammation and new therapeutic interventions in cystic fibrosis. Infection & Immunity 1:387-403; Transworld Research Network.

5. Hector, J., **Azghani, A.O**., and Johnson, A.R. **1993.** Genetic regulations of elastase in *P. aeruginosa*, pp. 145-162. In "Microbial Pathogenesis and Immunity," edited by M. Campa et al, Plenum Press, New York.

RECENT ABSTRACTS / PRESENTATIONS

1. Andrew Griffin, Andrea Grzybowski, William Sorensen, Sharon Phillips, and Ali Azghani. 2016 Seroprevalence of Canine HEV in Smith County, Texas. TriBeta Regional Conference 2016,

2. Galina Florova, Andrey A. Komissarov, **Ali O. Azghani**, Ann Buchanan, Jake Boren, Chris Schaefer, Kathleen Koenig, and Steven Idell. Validation of a Novel Rabbit *S. pneumoniae* Model of Empyema and Responses to Intrapleural Fibrinolytic Therapy with tPA or scuPA. ATS 2016.

3. Galina Florova, **Ali O. Azghani**, Sophia Karandashova, Chris Schaefer, Serge V. Yarovoi, Paul J. Declerck, Douglas B. Cines, Steven Idell, and Andrey A. Komissarov. The slow rate of fibrinolyisis limits inhibitor selection when targeting plasminogen activator inhibitor 1 to enhance intrapleural fibrinolytic therapy. ATS 2016.

4. Bidisha Pal and **Ali Azghani**. Mechanism of Pseudomonas Elastase- Induced Cytoskeleton Remodeling. American Society for Microbiology, Texas Branch. April 2015

5. Steven Idell, **Ali Azghani**, Chris Schaefer, Andrey A. Komissarov, William Bradley,Kahtleen Koenig, Ann Buchanan, Galina Florova. Remodeling of Tetracycline-Induced Pleural Injury in Rabbits after Intrapleural Fibrinolytic Therapy. International meeting of American Thoracic Society, May 2015.

6. Galina Florova, **Ali Azghani**, Chris Schaefer, Serge Yarovoi, Sophia Karandashova,Douglas B. Cines, Steven Idell, Andrey A. Komissarov. A Nearly 100-Fold Decrease in the Rate of the Reaction Between Urokinase and Plasminogen Activator Inhibitor 1 Does Not Improve the Outcome of Fibrinolytic Therapy of Tetracycline Induced Pleural Injury in Rabbits. International meeting of American Thoracic Society, May 2015**.**

NON-PEER REVIEWED PUBLICATIONS

Azghani, Ali O, **2004**. Professional Achievements of Dr. Robert Fuerst. ASM news 70 (8): 376.

Azghani, Ali O, **2003.** Pharmacogenomics and Anti-infective Drugs Discovery. Newsletter, Association of Clinical Research Professional, North Texas Chapter, 6 (1): 2.

Azghani, Ali O, **2002**. Gene Therapy. Newsletter, Association of Clinical Research Professional, North Texas Chapter, 5(2): 2.

INTERNAL AND EXTERNAL GRANT- Current (4)

Proposals funded

1. **UTT,** Internal Research Support Program (IRSP), **Azghani,** $3,700.0,

2. **UTT,** Collaborative grant, Academic Innovation and Student Success (CRIA), **Azghani** and Sorenson, $5,000.00.

3. **LSAMP** Undergraduate Student Research, $4,500.00.
4. TriBeta Undergraduate Research Grant ($400.00), Spencer Shastid.

5. **UTT** Co-curricular Travel Grants ($1,500) for student presentations at:

    a) ASM, Texas for research students at Dr. Azghani's lab

    b) TriBeta Regional conference, OK, for Biology Honor Society members

Pending Proposals

2017-18 Fulbright US Scholar Program PI, Prevalence of multiple drug resistant bacteria in Baku, Azerbaijan.

2016- 2021 NIH, Co- Investigator, Delivery of PAI-1-targeted intrapleural fibrinolytic therapy for empyema, PI: Andrey Komissarov, UTHSC.

INVITED SEMINARS

I. International (4)

2016 Khazar University, Azerbaijan, My 9 -13, 2016. Emerging Antibiotic Resistant Bacteria.

2012 East Mediterranean University, Cyprus (EMU). Mechanism of Epithelial Barrier Disruption by *Pseudomonas aeruginosa* and its Consequences. Dec 18, 2012

2012 EMU. Strategies for Team-Based Scientific Teaching. Dec. 19, 2012

2009 Laurentian University, Department of Chemistry and Biochemistry, Montreal, Canada. Mechanism of ERK 1/2 Activation in Pseudomonal Infection"

1993 International Congress of Physiology and Pharmacology, University of Tabriz, Iran