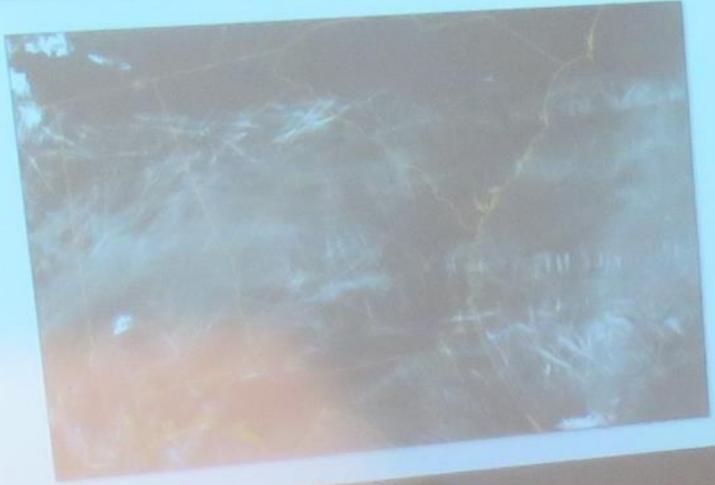


# Trainee Research Day

November 4, 2019







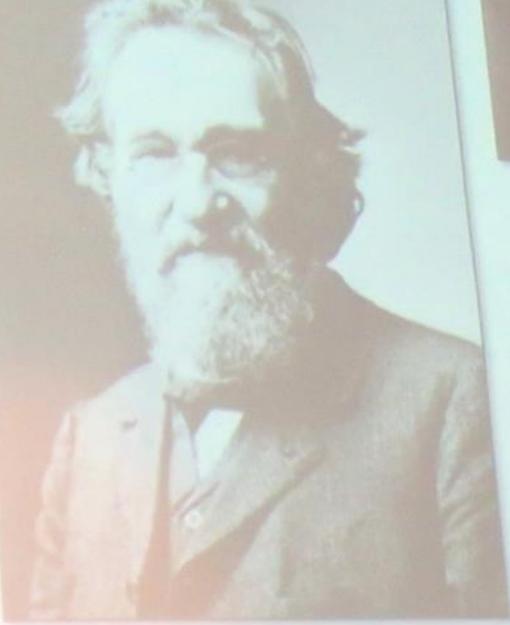
EXIT

Insight Care  
Innovative Science





Louis Pasteur



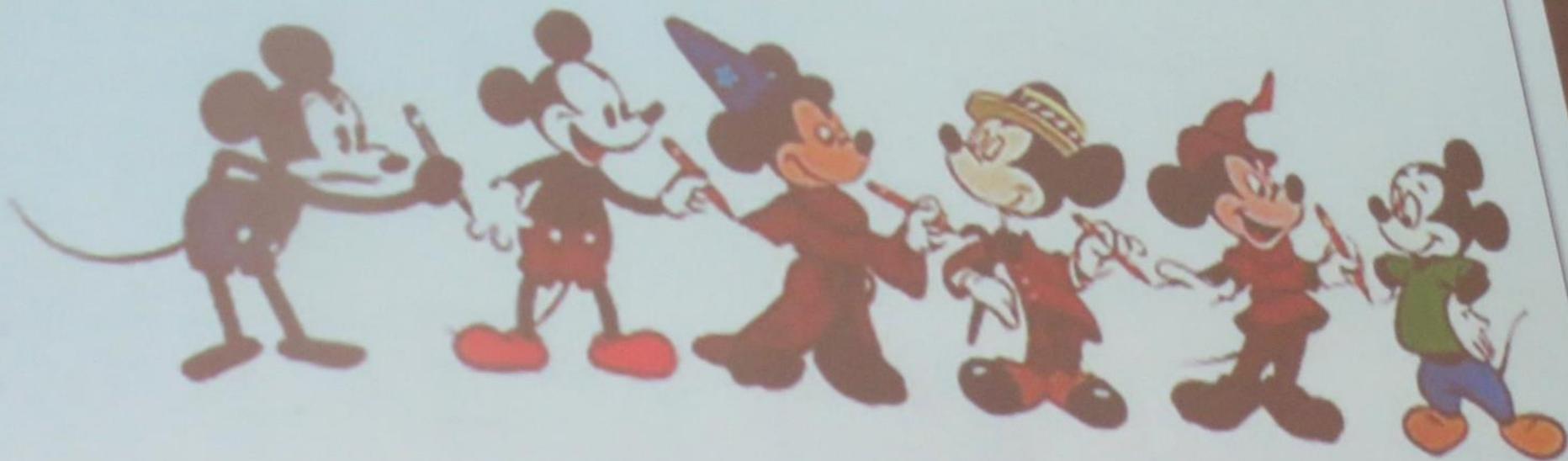
Charles Darwin



- Science is not about belief, but about skepticism
- Science starts from a body of accepted knowledge
- Science uncovers probabilities, not truths
- **Science is a social process**
- Science changes the world



# The Evolution of Mickey Mouse



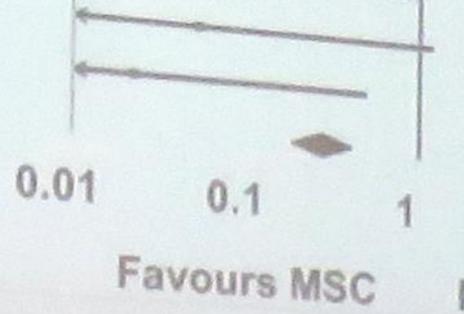
et al. 2015

**TOTAL**

$R = 33\%$

Test for overall effect:  $Z=6.27, p<0.00001$

3 / 10      10 / 10  
234 / 504    337 / 446



Tunneling  
Nanotubes

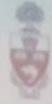


MSC



... of thrombosis: the roles of  
... of cardiovascular disease  
Si Yang, Daniel MacKeigan, Miguel Nerves, and Heyu Ni

St. Michael's  
Inspired Care.  
Inspiring Science.



Physiology  
UNIVERSITY OF TORONTO



Canadian  
Blood  
Services



CIHR IRSC  
Canadian Institutes of Health Research / Institut de recherche en santé publique

St. Michael's  
Inspired Care. Inspiring Science.

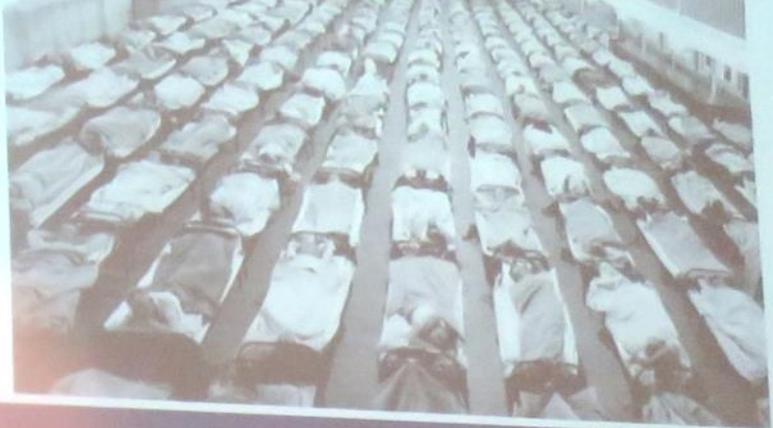


St. Michael's  
Inspired Care.  
Inspiring Science.





Last 12 Weeks:  
**RECALLS BLACK DEATH**  
**"Flu" Five Times Deadlier Than World War.**  
LONDON, Dec. 18.—Canadian Press, via Reuters.—The Times' medical correspondent says that it seems reasonable to believe that about 8,000,000 persons perished from influenza pneumonia during the past 12 weeks. It has been estimated that the war caused the death of 20,000,000 persons in four and a half years.



St. Michael's  
Inspired Care. Inspiring Science. | Keenan Research Centre for Biomedical Science



St. Michael's  
Inspired Care.  
Inspiring Science.



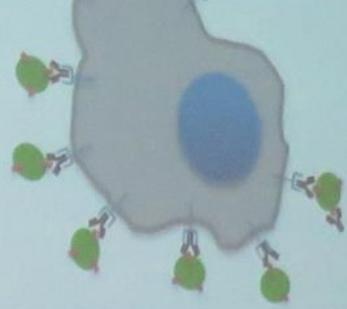


Michael's





Destruction in phagocytic system (spleen, liver)

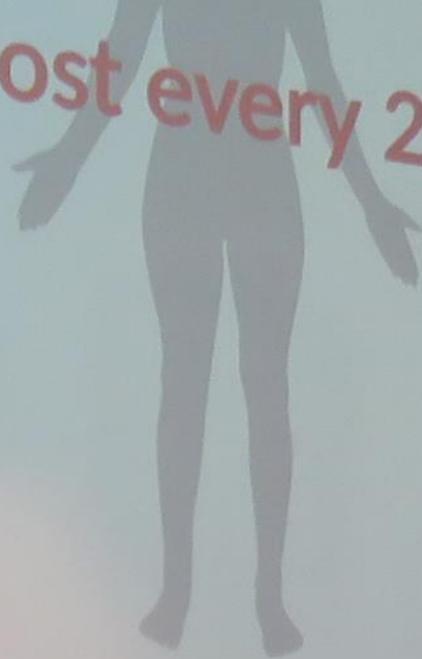


2

St. Michael's  
Inspired Care.  
Inspiring Science.



1 life lost every 2 hours





(8.9)  
Observational

Trained personnel  
present in live OR

complexities of live OR  
Bias & Missed Events

St. Michael's  
Inspired Care.  
Inspiring Science.



20g/day  
Oats, barley,  
psyllium, pulses,  
eggplant, okra,  
temperate climate  
fruit



4 Plant Sterols  
2g/day  
Plant sterol  
margarine/oil/  
supplements

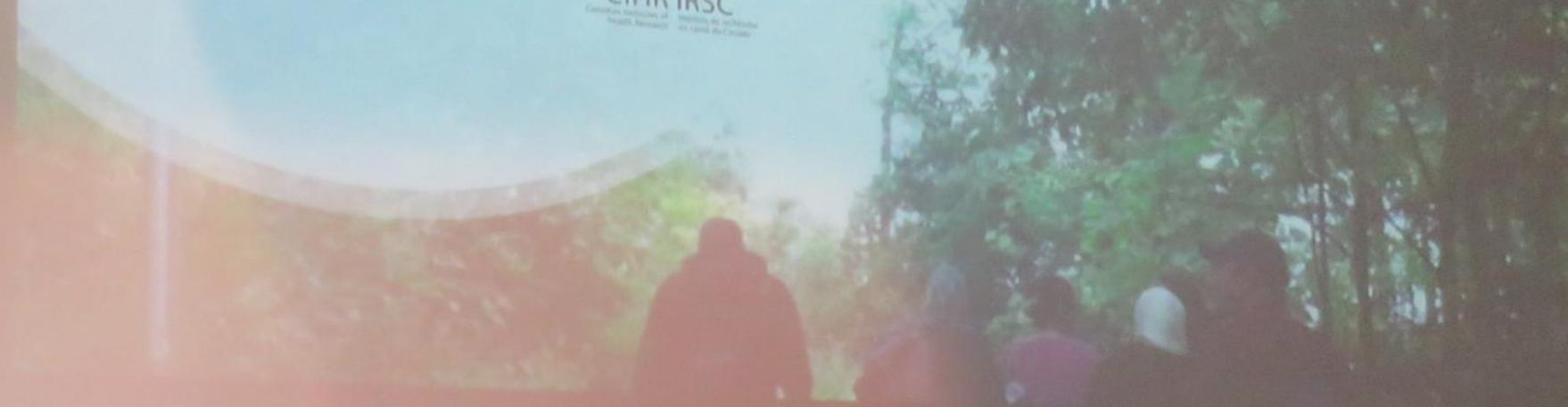


Chiavaroli L et al., Progresses in CVD, 2018  
Jenkins DJ et al. Curr Opin Lipidol, 2000  
Jenkins DJ et al., CMAJ, 2010





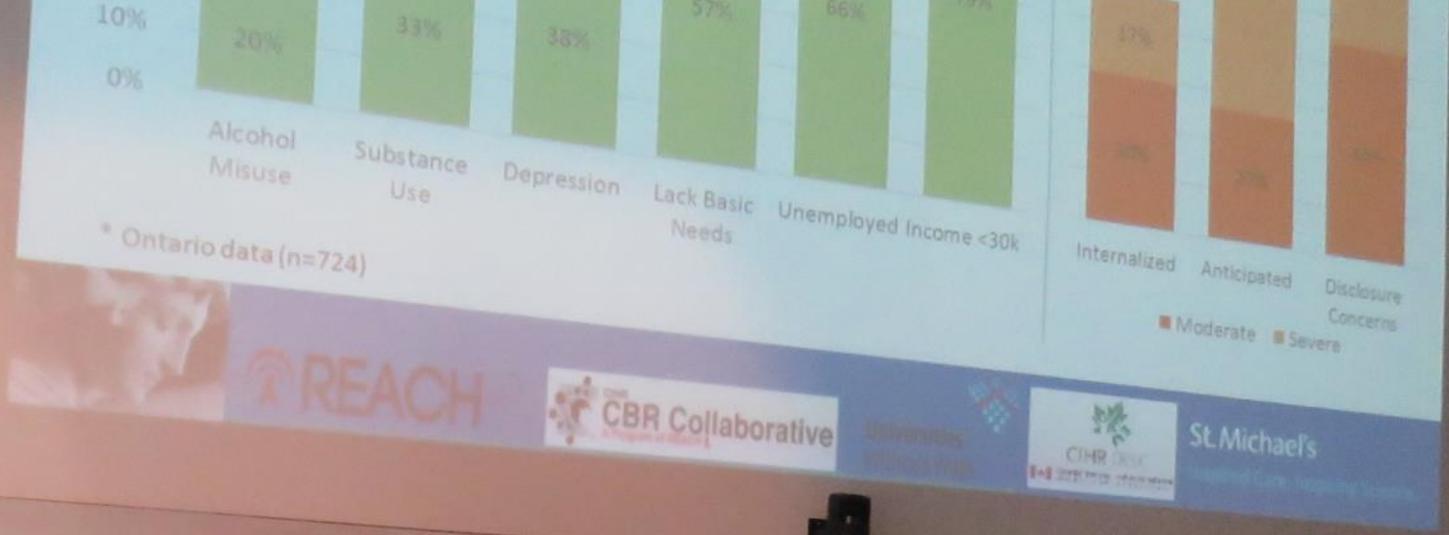
St. Michael's  
University of British Columbia  
Faculty of Health Sciences



**St. Michael's**  
Inspired Care.  
Inspiring Science.







St. Michael's  
 Inspired Care.  
 Inspiring Science.



# First Steps to Nanomedicine: Assessing Interactions between Polystyrene Nanoparticles and Albumin Proteins

Yahara Ceballos, David Gomez

Ph.D. Student, Department of Nanotechnology



**Motivation:** Nanomedicine uses smaller objects or structures within the body for diagnosis and treatment. However, the high surface area to volume ratio of nanoparticles can lead to unintended interactions, such as adsorption of proteins, which affects their function. It is important to understand these interactions to ensure nanomedicine can be used safely.

**Background:** Nanoparticles have been used in drug delivery, imaging, and diagnostics. However, their small size and high surface area can lead to unintended interactions with proteins. This study aims to understand the interactions between polystyrene nanoparticles and albumin proteins.

**Methods:** Surface Plasmon Resonance (SPR) and Dynamic Light Scattering (DLS) were used to study the interactions between polystyrene nanoparticles and albumin proteins. SPR measures the change in refractive index at the sensor surface, which is proportional to the mass of the adsorbed protein. DLS measures the size of the nanoparticles in solution.

**Results:** SPR and DLS results show that albumin proteins adsorb onto the surface of polystyrene nanoparticles. The adsorption is dependent on the size of the nanoparticles and the concentration of the protein. DLS results show that the size of the nanoparticles increases after protein adsorption.

**Conclusions:** The results of this study show that albumin proteins adsorb onto the surface of polystyrene nanoparticles. This adsorption is dependent on the size of the nanoparticles and the concentration of the protein. This study provides a first step towards understanding the interactions between nanoparticles and proteins, which is essential for the development of nanomedicine.

**Figure 1:** Schematic diagram of a human body showing the location of nanoparticles and proteins. The diagram shows a human figure with a green circle representing a nanoparticle and a red circle representing a protein. Arrows indicate the interaction between the nanoparticle and the protein.



# RECONSTRUCTION OF THE LUNG WITH LUNG BUD ORGANOID ON THE GELFOAM SPONGE

Thimika Thandabalingam B.Sc.<sup>1,2</sup>, Pyungrak Kim B.Sc.<sup>1</sup>, Yu Onedera M.D., Ph.D.<sup>1</sup>, Miyoja Jerkic M.D., Ph.D.<sup>1</sup>, Haibo Zhang M.D., Ph.D.<sup>1,2,3</sup>  
<sup>1</sup>Department of Abdominal and Critical Care Medicine, University of Toronto, Toronto  
<sup>2</sup>Department of Medical Biophysics, University of Toronto, Toronto  
<sup>3</sup>Michael G. DeGroote Center for Research Innovation & Michael G. DeGroote Institute of Health Sciences, University of Western Ontario, London

Support Can. Inspiring Science

## Introduction

To restore respiratory function by the reconstruction of the alveolar architecture, the precise structure of the distal lung organoid-like structure is essential for alveolar tissue. It could be a suitable case for pluripotent stem cells to regenerate with its appropriate structure. Pluripotent stem cells (PSCs) are reprogrammed to the embryonic state and differentiated into specialized cell types, including lung progenitor cells, which can generate lung bud organoids in vitro. Lung bud organoids (LBOs) will provide a platform for studying lung development and disease.

## Methods

Human embryonic stem (hES) cells were cultured in the presence of pluripotency factors (Oct4, Sox2, Klf4, and c-Myc) to generate hES cells. These cells were then differentiated into lung bud organoids (LBOs) using a defined medium.

## Results Cont'd

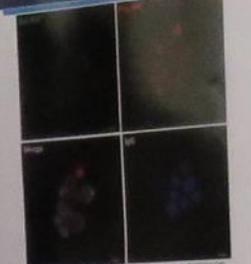


Figure 2 LBOs cultured on the defined medium (DM) medium support the formation of LBOs on GelFoam sponges. (Top) Fluorescence microscopy images of LBOs cultured on GelFoam sponges. (Bottom) Fluorescence microscopy images of LBOs cultured on GelFoam sponges with IPSCs.



Figure 3 Histological analysis of lung tissue. (Left) Control lung tissue. (Right) Lung tissue cultured on GelFoam sponges.



Figure 4 Alveolar surface area and lung volume reduction. (Top) Bar graph showing lung volume reduction. (Bottom) Bar graph showing alveolar surface area.

## Results Cont'd



Figure 4 Lung bud organoids (LBOs) on GelFoam sponges.

## Conclusions and Future Directions

- Conclusions**
- The GelFoam sponge can support LBO growth and development into MSCs.
  - A rat model of emphysema has been developed.
  - Delivery of the GelFoam sponge has been determined feasible in emphysemic rats.
- Next Steps**
- Cells cultured on the GelFoam sponge will be characterized quantitatively.
  - Feasibility of delivering cellularized GelFoam sponges into emphysemic rats will be assessed.

## Significance

The GelFoam sponge, in combination with iPSC-derived LBOs, may promote alveolar reconstruction in emphysema patients.

## References

- Shih PL, et al. Lung volume reduction for emphysema. *Lancet Respir Med.* 2017;5(2):147-156.
- Barkauskas CE, et al. Type 2 alveolar cells are stem cells in adult lung. *J. Clin. Invest.* 2013;123(7):3025-3036.
- Chen YW, et al. A three-dimensional model of human lung development and disease from pluripotent stem cells. *Nat Cell Biol.* 2017;19(9):542-549.

## Acknowledgements

iPSCs were provided by Smoek Laboratory (Columbia University, NY) upon agreement with Dr. Sumita d'Souza at the Icahn School of Medicine in Mount Sinai, NY.



# Systematic review of the impact of chronic tetracycline class antibiotics on antimicrobial resistance in host normal flora

Robinson Truong<sup>1</sup>, Vincent Tang<sup>2</sup>, Troy Greenan<sup>3</sup> & Cornell H.S. Tan<sup>1,2,3\*</sup>  
<sup>1</sup>Division of Infectious Diseases, St. Michael's Hospital  
<sup>2</sup>Centre for Urban Health Solutions, St. Michael's Hospital, <sup>3</sup>Division of Infectious Diseases, University of Toronto  
<sup>4</sup>Division of Infectious Diseases and Department of Medicine, University of British Columbia  
 Contact: Robinson.Truong@unlifehealth.ca

Keenan Research Summer Student Program

## Results

Figure 1. PRISMA Flow Chart

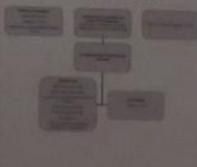


Table 1. Criteria for Assessing Risk of Bias

Study	1	2	3	4	5
Study 1	Low	Low	Low	Low	Low
Study 2	Low	Low	Low	Low	Low
Study 3	Low	Low	Low	Low	Low
Study 4	Low	Low	Low	Low	Low
Study 5	Low	Low	Low	Low	Low

Table 2. Assessment of Risk of Bias of Included Studies

Study	1	2	3	4	5
Study 1	Low	Low	Low	Low	Low
Study 2	Low	Low	Low	Low	Low
Study 3	Low	Low	Low	Low	Low
Study 4	Low	Low	Low	Low	Low
Study 5	Low	Low	Low	Low	Low

Table 3. Impact of Tetracyclines on Minimum Inhibitory Concentration

Study	1	2	3	4	5
Study 1	Low	Low	Low	Low	Low
Study 2	Low	Low	Low	Low	Low
Study 3	Low	Low	Low	Low	Low
Study 4	Low	Low	Low	Low	Low
Study 5	Low	Low	Low	Low	Low

Table 4. Impact of Tetracycline on Cross-Resistance

Study	1	2	3	4	5
Study 1	Low	Low	Low	Low	Low
Study 2	Low	Low	Low	Low	Low
Study 3	Low	Low	Low	Low	Low
Study 4	Low	Low	Low	Low	Low
Study 5	Low	Low	Low	Low	Low

Table 5. Impact of Tetracycline on STI Incidence

Study	1	2	3	4	5
Study 1	Low	Low	Low	Low	Low
Study 2	Low	Low	Low	Low	Low
Study 3	Low	Low	Low	Low	Low
Study 4	Low	Low	Low	Low	Low
Study 5	Low	Low	Low	Low	Low

## Conclusions

- Oral tetracyclines minimally affects tetracycline and non-tetracycline resistance in subgingival, skin and GI flora, and is moderately efficacious at reducing STI incidence
- Next step is to summarize findings based on the burden of resistant isolates and microbial composition
- Our project will complement current clinical trials of doxycycline PEEP and inform clinicians and researchers of how much the use of these antibiotics as PEEP may add to the existing threat of AMR

## Acknowledgements

- RT and VT are supported by the Keenan Research Summer Student Program
- DMST is supported by New Investigator Awards from the CDR and OHTN

## References

- 1. [Reference 1]
- 2. [Reference 2]
- 3. [Reference 3]

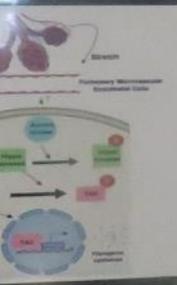
# Increased activation of Hippo signaling in lung microvascular endothelial cells – a novel mechanism of overventilation-induced pulmonary fibrosis

Razan Turki<sup>1,2</sup>, Michael Kofler<sup>1</sup>, Andras Kapus<sup>1,2,3,4</sup>, Wolfgang Kuebler<sup>1,2,5,6</sup>

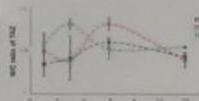
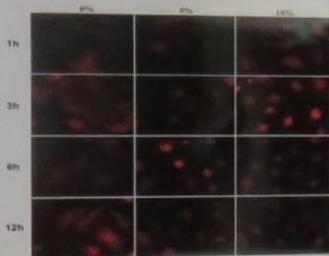
<sup>1</sup>Centre for Biomedical Science of St. Michael's Hospital, Canada; <sup>2</sup>Department of Physiology, University of Toronto, Canada; <sup>3</sup>Biochromer Ingelheim Pharma GmbH, Germany; <sup>4</sup>Department of Laboratory Medicine and Pathobiology, Interdepartmental Division of Critical Care Medicine and the Department of Medicine, University of Toronto, Canada; <sup>5</sup>Department of Surgery, University of Toronto, Canada; <sup>6</sup>Institute of Physiology, Charité – Universitätsmedizin Berlin, Germany

St. Michael's  
Inspired Care.  
Inspiring Science.

In acute respiratory distress syndrome ventilator induced lung injury study, we aimed to elucidate mechanisms. Specifically, we focused on Hippo-signaling pathway of Large Tumor Suppressor translocation to the nucleus. Underlying mechanisms and immediate cyclic stretch have not been investigated. We investigated translocation of TAZ in lung microvascular endothelial cells and downstream effects.



## 2) Endothelial stretch induces translocation of TAZ from the cytosol to the nucleus in a time and stretch dependent manner.

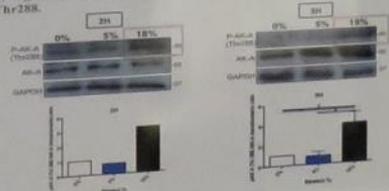


- At 5%, stretching HPMEC for 6h increases the N:C ratio of TAZ and this up-regulation decreased after 12h.
- At 18% TAZ N:C ratio was increased after 3h compared to the static control and this up-regulation decreased after 6h and 12h.

## 3) Treating endothelial with Src kinases or JNK inhibitors has NO effect on TAZ nuclear localization.



## 4) High stretch (18%) increases Aurora kinase-A (AK-A) phosphorylation at Thr288.



## RESULTS

### 5) High stretch induces LATS2 phosphorylation at S83 which was inhibited by the inhibition of Aurora kinases.



### 6) 18% stretch decreases TAZ phosphorylation at Serine 89 while Aurora kinase treatment increased its phosphorylation.



### 7) Inhibiting Aurora kinases reduces TAZ N:C ratio in stretched HPMEC for 3h at 18%.



- At 5%: Treating HPMEC with Aurora Kinases inhibitor has no effect on TAZ nuclear localization.
- At 18%: Treating HPMEC with Aurora Kinases inhibitor decreases TAZ nuclear localization after 3h of stretch compared to the control.

## SUMMARY & CONCLUSION

- Increased the total amount of TGF-β1 secretion in HPMECs exposed at 5% & 15% for 12h.
- Stretch enhances the N:C ratio of TAZ in a time and stretch % dependent manner, and the phosphorylation of AK-A at Thr288.
- The inhibition of Aurora Kinases decreased LATS2 phosphorylation at S83.
- The inhibition of Aurora Kinases decreased TAZ nuclear localization.
- Inhibiting Aurora kinases decreased TAZ nuclear translocation of TAZ on a result of stretch induced by mechanical overexpansion.

## ACKNOWLEDGEMENTS

St. Michael's  
Inspired Care.  
Inspiring Science.

Physiology  
UNIVERSITY OF TORONTO

St. Michael's  
Inspired Care.  
Inspiring Science.

RESEARCH CENTRE

St. Michael's  
Inspired Care.  
Inspiring Science.

## Expression and Function of DAR

Negar Khorasani, Nikki Zamani, Madeline Abou...  
Department of Laboratory Medicine and Pathobiology...  
Senior Research Centre for Biomedical Science

### Background

Vertically aligned fibroblasts (VAFs) were originally identified as endocardial fibroblasts in the embryonic heart, and later were demonstrated to be involved in the regulation of cardiac myocyte growth. The function of VAFs in the heart has been well established. A few years ago, it was shown that VAFs are involved in the regulation of cardiac myocyte growth.

### Methodology

Human VAFs were cultured in the presence of various growth factors and their effect on VAFs was studied. The function of VAFs in the heart was studied using various techniques.

### Results

The results showed that VAFs are involved in the regulation of cardiac myocyte growth. The function of VAFs in the heart was studied using various techniques.

### Mechanism of induction

The mechanism of induction of VAFs was studied using various techniques. The results showed that VAFs are involved in the regulation of cardiac myocyte growth.

### Conclusion

The conclusion is that VAFs are involved in the regulation of cardiac myocyte growth. The function of VAFs in the heart was studied using various techniques.



St. Michael's  
Inspired Care.  
Inspiring Science.

# Expression and Function of DARC in Endothelial Cells

<sup>1</sup> Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Canada  
<sup>2</sup> Keenan Research Centre for Biomedical Science, St. Michael's Hospital, Toronto, Canada



## Background

The Duffy Antigen Receptor for Chemokines (DARC) was originally identified on erythrocytes as a receptor for *Plasmodium vivax*, and later observed to be present on endothelial cells of the postcapillary venule<sup>1</sup>. The function of endothelial DARC has not been well established. Currently, it has been shown to play a role in leukocyte recruitment and transmigration<sup>2</sup>. However, there is limited research due to loss of DARC expression in cultured endothelial cells<sup>3</sup>.

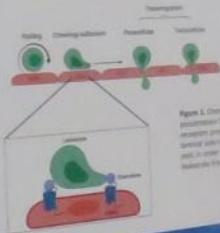


Figure 1. Chemokine presentation by chemokine inducible protein on the surface of endothelial cells in order to facilitate leukocyte transmigration.

## Hypothesis

Our lab discovered that incubation of endothelial cells with whole blood induces DARC expression<sup>4</sup>. Therefore, we hypothesize that the microenvironment of endothelial cells influences the expression of DARC in endothelial cells of the postcapillary venule.

### Objective Aims:

- 1) Elucidate the mechanism by which blood induces DARC expression in endothelial cells *in vitro*.
- 2) Elucidate the regulation of DARC protein and mRNA levels

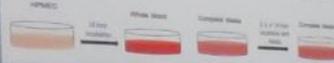
1. Haddley, T., et al. (1994). *J. Clin. Invest.*, 94, 985-991.
2. Pflüger, M., et al. (2009). *Immunology*, 121(1), 101-108.

## References

3. Lachy, D., et al. (2011). *Blood*, 117(21), 4164-4170.
4. Luban, A., et al. (2010). *Cell Physiol and Molec*, 193A-193 B.

## Methodology

Human Pulmonary Microvascular Endothelial Cells (HPMEC) used for all experiments



## Results

### Mechanism of Induction:

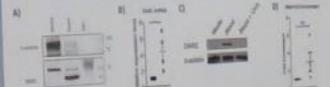


Figure 1. Increase DARC protein and expression in cells incubated with whole blood (WB) over control media (C) for 24 hours. (A) Western blot analysis of DARC protein levels in HPMEC cells treated with WB or C for 24 hours. (B) Western blot analysis of DARC protein levels in HPMEC cells treated with WB or C for 24 hours. (C) RT-PCR analysis of DARC mRNA levels in HPMEC cells treated with WB or C for 24 hours. (D) RT-PCR analysis of DARC mRNA levels in HPMEC cells treated with WB or C for 24 hours.

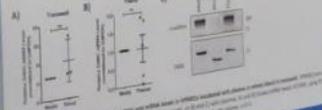


Figure 2. All significant changes in DARC protein and mRNA levels in HPMEC cells treated with whole blood (WB) over control media (C) for 24 hours. (A) Western blot analysis of DARC protein levels in HPMEC cells treated with WB or C for 24 hours. (B) Western blot analysis of DARC protein levels in HPMEC cells treated with WB or C for 24 hours. (C) RT-PCR analysis of DARC mRNA levels in HPMEC cells treated with WB or C for 24 hours. (D) RT-PCR analysis of DARC mRNA levels in HPMEC cells treated with WB or C for 24 hours.

## Conclusion

- DARC expression in endothelial cells is possibly induced by direct contact with blood. This suggests cell-cell interaction may be necessary for induction.
- DARC protein and mRNA are unstable and they are degraded upon removal of blood.
- DARC is not degraded through the proteasome pathway and is degraded by matrix metalloproteinases.

## Acknowledgments

Thank you to all members of the lab and to the members of the St. Michael's Hospital Research Centre for Biomedical Science.

## Results

### Regulation of DARC Protein and mRNA



Figure 3. All significant changes in DARC protein and mRNA levels in HPMEC cells treated with whole blood (WB) over control media (C) for 24 hours. (A) Western blot analysis of DARC protein levels in HPMEC cells treated with WB or C for 24 hours. (B) Western blot analysis of DARC protein levels in HPMEC cells treated with WB or C for 24 hours. (C) RT-PCR analysis of DARC mRNA levels in HPMEC cells treated with WB or C for 24 hours. (D) RT-PCR analysis of DARC mRNA levels in HPMEC cells treated with WB or C for 24 hours.



Figure 4. All significant changes in DARC protein and mRNA levels in HPMEC cells treated with whole blood (WB) over control media (C) for 24 hours. (A) Western blot analysis of DARC protein levels in HPMEC cells treated with WB or C for 24 hours. (B) Western blot analysis of DARC protein levels in HPMEC cells treated with WB or C for 24 hours. (C) RT-PCR analysis of DARC mRNA levels in HPMEC cells treated with WB or C for 24 hours. (D) RT-PCR analysis of DARC mRNA levels in HPMEC cells treated with WB or C for 24 hours.

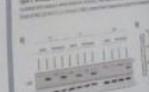
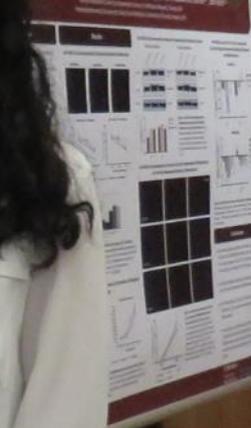


Figure 5. All significant changes in DARC protein and mRNA levels in HPMEC cells treated with whole blood (WB) over control media (C) for 24 hours. (A) Western blot analysis of DARC protein levels in HPMEC cells treated with WB or C for 24 hours. (B) Western blot analysis of DARC protein levels in HPMEC cells treated with WB or C for 24 hours. (C) RT-PCR analysis of DARC mRNA levels in HPMEC cells treated with WB or C for 24 hours. (D) RT-PCR analysis of DARC mRNA levels in HPMEC cells treated with WB or C for 24 hours.



Figure 6. All significant changes in DARC protein and mRNA levels in HPMEC cells treated with whole blood (WB) over control media (C) for 24 hours. (A) Western blot analysis of DARC protein levels in HPMEC cells treated with WB or C for 24 hours. (B) Western blot analysis of DARC protein levels in HPMEC cells treated with WB or C for 24 hours. (C) RT-PCR analysis of DARC mRNA levels in HPMEC cells treated with WB or C for 24 hours. (D) RT-PCR analysis of DARC mRNA levels in HPMEC cells treated with WB or C for 24 hours.

## Regulation of novel microRNAs regulating skeletal muscle regeneration in patients with sustained intensive care unit acquired weakness



## Vegetarian diet, growth, and serum lipids in childhood: A prospective cohort study

Laura J. Elliott, Jonathan L. Maguire, Catherine S. Birken, Charles D.G. Kacoun-Sherman, David J. Jenkins, on behalf of the TARGET Kids! Collaboration, St. Michael's Hospital, University of Toronto, and The Hospital for Sick Children

### INTRODUCTION

- Vegetarian diets are becoming increasingly popular. Diets rich in fruits and vegetables are associated with improved cardiovascular health and reduced risk of chronic disease.
- Present-day vegetarian diets vary in a variety of ways. Some are high in refined grains and added sugars, while others are high in whole grains, fruits, and vegetables.
- Free radicals have been associated with oxidative stress and chronic disease risk factors.

### OBJECTIVES

- To examine the relationship between vegetarian diet and height, weight, and BMI in children 8-10 years of age.
- To examine the relationship between vegetarian diet and serum lipids in children 8-10 years of age.
- To determine whether the relationship between vegetarian diet and height, weight, and BMI is modified by sex, age, and BMI.
- To determine whether the relationship between vegetarian diet and serum lipids is modified by sex, age, and BMI.

**Study Design and Population**

- Prospective cohort study of children 8-10 years of age.
- Participants were recruited from 2008-2010.
- Exposures - Vegetarian Diet
- Primary report of vegetarian diet

**Outcomes**

- Height and weight
- Age and sex-adjusted BMI
- Age and sex-adjusted serum lipids
- Age and sex-adjusted serum lipids

**Keywords:** vegetarian diet, growth, lipids, cardiovascular health, and engagement

- Vegetarian diet, growth, lipids, cardiovascular health, and engagement



### METHODS

Study 1: Cross-sectional study examining the relationship between vegetarian diet and BMI, height, and weight in children 8-10 years of age.

Characteristic	Vegetarian (n=100)	Non-vegetarian (n=100)
Age (years)	9.1 (0.5)	9.1 (0.5)
Sex (male)	50 (50%)	50 (50%)
Height (cm)	138.5 (5.5)	138.5 (5.5)
Weight (kg)	32.5 (5.5)	32.5 (5.5)
BMI (kg/m <sup>2</sup> )	17.5 (1.5)	17.5 (1.5)
Height (cm)	138.5 (5.5)	138.5 (5.5)
Weight (kg)	32.5 (5.5)	32.5 (5.5)
BMI (kg/m <sup>2</sup> )	17.5 (1.5)	17.5 (1.5)

### RESULTS

Table 1: Mean (SD) and 95% CI for BMI, height, and weight in children 8-10 years of age.

Characteristic	Vegetarian (n=100)	Non-vegetarian (n=100)
Mean (SD) BMI (kg/m <sup>2</sup> )	17.5 (1.5)	17.5 (1.5)
Mean (SD) Height (cm)	138.5 (5.5)	138.5 (5.5)
Mean (SD) Weight (kg)	32.5 (5.5)	32.5 (5.5)

Figure 1: Mean (SD) BMI (kg/m<sup>2</sup>) by sex in children 8-10 years of age.

Figure 2: Mean (SD) serum lipids (mmol/L) by sex in children 8-10 years of age.

Figure 3: Mean (SD) serum lipids (mmol/L) by sex in children 8-10 years of age.

### NON-NUTRITIVE SWEETENERS AND COMPARABLE DIET: A SYSTEMATIC REVIEW AND META-ANALYSIS

St. Michael's Hospital, University of Toronto

#### INTRODUCTION

Non-nutritive sweeteners (NNS) are used to sweeten foods and beverages without the calories of sugar. They are used in a variety of products, including soft drinks, fruit-flavored yogurts, and tabletop sweeteners. The use of NNS has increased significantly in recent years, particularly in children and adolescents. This systematic review and meta-analysis examined the relationship between NNS intake and body weight, blood glucose, and insulin resistance in children and adolescents.

#### METHODS

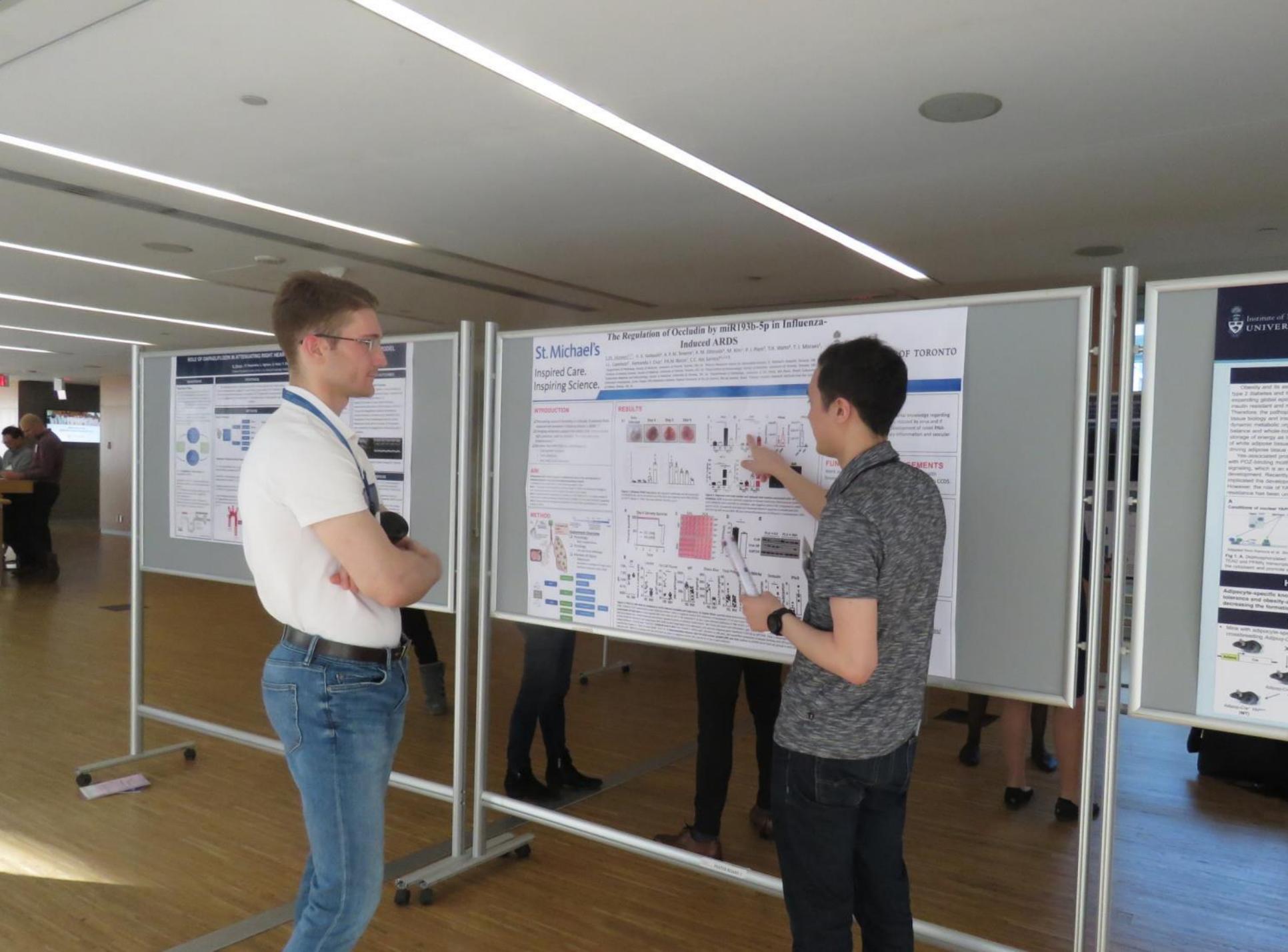
A systematic search of the literature was conducted to identify studies that examined the relationship between NNS intake and body weight, blood glucose, and insulin resistance in children and adolescents. The search was limited to English-language studies published between 2000 and 2015. The studies were screened based on their titles and abstracts. Full-text articles were obtained for studies that met the inclusion criteria. The studies were then assessed for their methodological quality using the Newcastle-Ottawa Scale (NOS). The results of the individual studies were pooled using a random-effects meta-analysis.

#### RESULTS

The search identified 10 studies that met the inclusion criteria. The results of the meta-analysis are summarized in the following table:

Outcome	Effect Size (95% CI)
Body weight (kg)	0.1 (0.0, 0.2)
Blood glucose (mmol/L)	0.1 (0.0, 0.2)
Insulin resistance (HOMA-IR)	0.1 (0.0, 0.2)





St. Michael's  
Inspired Care.  
Inspiring Science.

### The Regulation of Occludin by miR193b-5p in Influenza-Induced ARDS

L.J. Zhang<sup>1,2</sup>, H. K. Verhaeghe<sup>1</sup>, A. M. Sauer<sup>1</sup>, A. M. Zetterstrom<sup>1</sup>, M. Kim<sup>1</sup>, P. J. Pappas<sup>1</sup>, T.A. Wainwright<sup>1</sup>, Y. J. Minamide<sup>1</sup>, C.L. Cantor<sup>1</sup>, S. J. Kim<sup>1</sup>, P.M. Hwang<sup>1</sup>, C.C. Chiu<sup>1</sup>, S. J. Kim<sup>1,2,3,4</sup>

#### INTRODUCTION

ARDS is a leading cause of death in the ICU. The pathogenesis of ARDS is complex and involves multiple organ systems. The lung is the primary site of injury, but other organs, such as the liver, can also be affected. The liver plays a critical role in the regulation of the immune response and the production of acute phase reactants. The liver also plays a role in the regulation of the coagulation cascade. The liver is a central organ in the pathogenesis of ARDS.

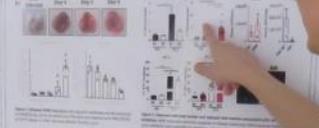
#### AIM

To investigate the role of miR193b-5p in the regulation of occludin in influenza-induced ARDS.

#### METHOD

ARDS was induced in mice by intratracheal instillation of influenza virus. The expression of miR193b-5p and occludin was measured by qPCR. The effect of miR193b-5p on occludin expression was determined by transfection of miR193b-5p into cells.

#### RESULTS



#### CONCLUSIONS

miR193b-5p regulates occludin expression in influenza-induced ARDS.

UNIVERSITY OF TORONTO

Institute of  
UNIVERSITY

#### Abstract

ARDS is a leading cause of death in the ICU. The pathogenesis of ARDS is complex and involves multiple organ systems. The liver plays a critical role in the regulation of the immune response and the production of acute phase reactants. The liver also plays a role in the regulation of the coagulation cascade. The liver is a central organ in the pathogenesis of ARDS.



Fig. 1. A. Immunofluorescence images of lung tissue at Day 1, Day 3, and Day 7. B. Bar graph of occludin mRNA levels at Day 1, Day 3, and Day 7. C. Bar graph of occludin protein levels at Day 1, Day 3, and Day 7. D. Bar graph of miR193b-5p levels at Day 1, Day 3, and Day 7. E. Bar graph of occludin mRNA levels in cells transfected with miR193b-5p. F. Bar graph of occludin protein levels in cells transfected with miR193b-5p.

Abstract (continued)

ARDS is a leading cause of death in the ICU. The pathogenesis of ARDS is complex and involves multiple organ systems. The liver plays a critical role in the regulation of the immune response and the production of acute phase reactants. The liver also plays a role in the regulation of the coagulation cascade. The liver is a central organ in the pathogenesis of ARDS.



Fig. 2. A. Bar graph of occludin mRNA levels in cells transfected with miR193b-5p. B. Bar graph of occludin protein levels in cells transfected with miR193b-5p. C. Bar graph of occludin mRNA levels in cells transfected with miR193b-5p and a luciferase reporter construct. D. Bar graph of occludin protein levels in cells transfected with miR193b-5p and a luciferase reporter construct.



### First Steps to Nanomedicine: Assessing Interactions between Protein-coated Nanoparticles and Albumin Receptors

**Abstract:** Nanoparticles (NPs) are used in drug delivery, diagnostics, and imaging. However, their interactions with biological systems are complex and often unpredictable. This study aims to understand the interactions between protein-coated NPs and albumin receptors, which are crucial for NP uptake and clearance. We investigated the binding of various protein-coated NPs to albumin receptors and their subsequent internalization. The results show that the presence of albumin receptors significantly affects the uptake and internalization of protein-coated NPs. This finding has important implications for the design and optimization of nanomedicines.

**Keywords:** Nanoparticles, Protein-coated, Albumin receptors, Interactions, Nanomedicine.



**Conclusion:** The study demonstrates that the interactions between protein-coated nanoparticles and albumin receptors are complex and highly dependent on the specific protein coating and the receptor. This knowledge is essential for the development of effective nanomedicines that can target specific cells and tissues.



# Surgeon management preferences for patella fractures in elderly, low-demand patients: a cross-sectional survey

Garrett F. Davidson PhD, David Wassenaar MD, Amir Khudbin MD, Patrick Henry MD, Emil Schemitsch MD, Milena Vízente RN, Aaron Nauth MD  
 St. Michael's Hospital, Toronto, Ontario, Canada

**Background**  
 Patella fractures are common orthopedic injuries with a high incidence in elderly, low-demand patients. The management of these fractures remains controversial, with a wide range of options available. The purpose of this study was to determine the management preferences of orthopedic surgeons for patella fractures in elderly, low-demand patients.

**Methods**  
 A cross-sectional survey of 100 orthopedic surgeons was conducted. The survey included questions regarding the degree of displacement, the degree of comminution, and the degree of articular surface involvement. The survey also included questions regarding the preferred management options for each scenario.

**Results**  
 The majority of surgeons (70%) preferred non-operative management for patella fractures in elderly, low-demand patients. The preferred management options were categorized by the degree of displacement, the degree of comminution, and the degree of articular surface involvement.

**Table 1. Consistency of Survey Responses (n=100)**

Question	Yes (%)	No (%)
Do you agree with the degree of displacement treatment?	85	15
Do you agree with the degree of comminution treatment?	75	25
Do you agree with the degree of articular surface involvement treatment?	80	20
Do you agree with the degree of displacement treatment?	85	15
Do you agree with the degree of comminution treatment?	75	25
Do you agree with the degree of articular surface involvement treatment?	80	20

**Table 2. Preferred preferences for varying fracture patterns in elderly, low-demand patients with all fracture mechanisms (%)**

Fracture Pattern	Non-operative (%)	Operative (%)
Displaced	65	35
Comminuted	55	45
Articular surface involvement	70	30

**Table 3. Common complications following operative and non-operative management of patella fractures in elderly, low-demand patients**

Complication	Operative (%)	Non-operative (%)
Malunion	15	5
Nonunion	10	5
Infection	5	2
Deep vein thrombosis	10	5
Pulmonary embolism	5	2
Postoperative pain	15	10
Postoperative swelling	10	5
Postoperative stiffness	10	5
Postoperative instability	5	2
Postoperative fracture	5	2
Postoperative hardware failure	5	2
Postoperative hardware migration	5	2
Postoperative hardware breakage	5	2
Postoperative hardware loosening	5	2
Postoperative hardware infection	5	2
Postoperative hardware migration	5	2
Postoperative hardware breakage	5	2
Postoperative hardware loosening	5	2
Postoperative hardware infection	5	2

Figure 1. Degree of displacement worsening reported by elderly low-demand patients with an impact colorbar



Figure 2. Factors influencing treatment decision



Table 3. Common complications following operative and non-operative management of patella fractures in elderly, low-demand patients

Complication	Operative (%)	Non-operative (%)
Malunion	15	5
Nonunion	10	5
Infection	5	2
Deep vein thrombosis	10	5
Pulmonary embolism	5	2
Postoperative pain	15	10
Postoperative swelling	10	5
Postoperative stiffness	10	5
Postoperative instability	5	2
Postoperative fracture	5	2
Postoperative hardware failure	5	2
Postoperative hardware migration	5	2
Postoperative hardware breakage	5	2
Postoperative hardware loosening	5	2
Postoperative hardware infection	5	2

## Discussion & Future Steps

- Consensus surrounding the degree of displacement management in this population is lacking.
- Recommendations established a need for further studies and standards in managing these fractures.

# Management preferences for patella fractures in elderly, low-demand patients: A cross-sectional survey

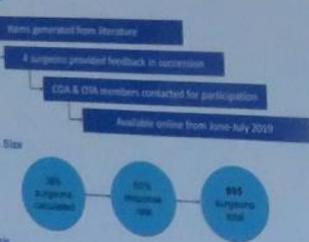
Authors: K. Chandhoke BHSc, David Wasserstein MD, Amir Khoshbin MD, Patrick Henry MD, Emil Schemitsch MD, Milena Vicente RN, Aaron Nauth MD, St Michael's Hospital, Toronto, Ontario, Canada

Patella fracture incidence increases with age, with elderly women the highest prevalence. Common mechanism of injury is low-energy trauma, such as falls. Treatment indicated for displaced fractures; non-operative is reserved for minimally displaced fractures with intact extensor mechanism.

Age is an independent risk factor for patellar fractures, and is associated with poor outcomes following ground-level fall injuries, shown to contribute to failure of fracture fixation; advanced age, low quality, comorbidities (diabetes, vascular disease), and retrospective review found patients >65 years of age having a higher complication rate following operative management.

Orthopaedic studies have challenged traditional surgical management of patella fractures in elderly, low-demand patients, and it is expected to rise with an aging population.

Current management practices and surgeon considerations for treating patella fractures in elderly (>65 years), low-demand patients



Statistical analysis: Fisher's exact tests used to compare differences across surgeons. Results summarized as proportions and stratified for analysis. Analysis performed on R Statistics programme (R Foundation for Statistical Computing, Vienna, Austria).

## Results

Table 1. Characteristics of Survey Respondents (n=115)

Characteristic	n	%
Age		
<40 years	26	22.6
41-60 years	26	22.6
61-80 years	33	28.7
>81 years	30	26.1
Sex		
Male	100	87.0
Female	13	11.4
Fracture not in eye	1	0.8
Practice Location		
Canada	83	71.8
International	21	18.4
Practice Type*		
Academy Hospital affiliated with a University	75	65.2
Community Public Hospital	41	35.3
Community Private Hospital	7	6.1
Years of Independent Practice		
Current fellow	2	1.7
< 5 years	32	27.8
6 - 15 years	30	26.1
16 - 25 years	22	19.1
> 25 years	29	25.2
Fellowship Training†		
Lower extremity	35	30.4
Trauma	62	53.9
Sports medicine	23	20.0
No training	11	9.6
Other	30	26.3

General consensus that non/minimally-displaced fractures should be conservatively managed (indicated by 80% of respondents), while displaced fractures require operative intervention (85% of respondents)

Table 2. Treatment preferences for varying displaced fracture patterns in elderly, low-demand patient with an intact extensor mechanism (%)

Fracture Pattern	Operative					Non-operative
	Other with VJ wires and TBW	Scarf fixation	Plate and screw fixation	Scarf and TBW	Other fixation (K-wire, nail)	
Transverse	62.4	1.0	4.0	51.3	3.0	16.2
Vertical	6.1	27.6	1.1	12.2	4.1	46.9
Comminuted	36.7	2.0	9.2	13.3	19.2	29.8
Pole	17.2	2.0	2.5	6.1	47.5	28.3

- Surgeons with both lower extremity and trauma fellowships were less likely to select surgery for displaced fractures (p=0.0208)
- Younger surgeons (<40 years of age) were less likely to treat displaced transverse, comminuted, and superior/inferior pole fractures operatively in comparison to older surgeons (all p<0.05)
- p-value approaching significance in the following relationships:
  - Lower extremity fellowship trained surgeons were less likely to select surgery for displaced transverse fractures (p=0.0588)
  - Canadian surgeons were less likely to treat displaced vertical fractures operatively in comparison to International surgeons (p=0.0546)

No agreement on the degree of displacement

Figure 1. Degree of displacement was not agreed upon by elderly, low-demand patients with an intact extensor mechanism



Figure 2. Factors influencing management preferences

- Open wounds
- Compromised soft tissue
- Intact extensor mechanism
- Patient compliance
- Number and size of fragments
- Fracture gap
- Comminution
- Displacement
- Fracture location
- Fracture type
- Fracture pattern

Table 3. Management preferences

Management preferences for various fracture patterns and patient characteristics.

# Research

Muhammad Mamdani, PharmD, MA, MPH  
Vice President, Data Science and Advanced Analytics, Unity Health Toronto  
Faculty Affiliate, Vector Institute  
Professor, University of Toronto

November 2019







Muhammad Mamdani, PharmD, MA, MPH  
Vice President, Data Science and Advanced Analytics, Unity Health  
Faculty Affiliate, Vector Institute  
Professor, University of Toronto

November 2019



- Oral Presentation Winner – Clinical/ Health Science Category
- Oral Presentation Runner Up – Clinical/ Health Science Category



Michael's



PERSUASION CODES

"Name"

5 things



St. Michael's  
Inspired Care.  
Inspiring Science.

The image shows three women standing behind a wooden podium. The podium has a silver panel with the St. Michael's logo and tagline. On the podium, there is a computer monitor, a microphone, and a printer. To the right of the podium, there is a table covered with a blue cloth, holding several colorful gift bags. The background is a large whiteboard.



PORT CODES  
\*Traine\*  
\*5 Things\*

EXIT

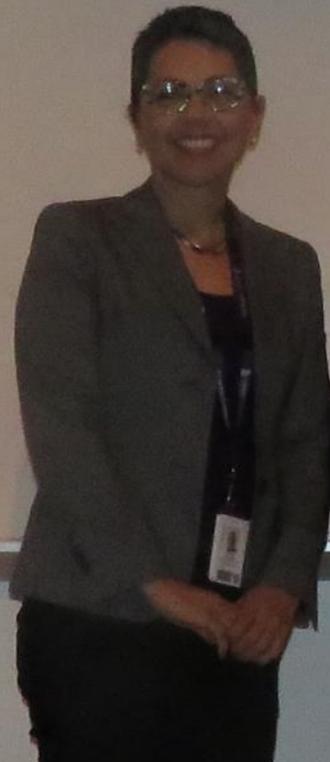


PASSPORT CODES

RTC Day "Tranee"

→ Franze  
Kypae "5 Things"





PASSPO  
RTC Day  
-Phoness  
Keynote





PASSPORT CODES

RTC  
airline  
Kings  
ings

# PASSPORT CODES

Day "Three"

