VOLUME 101 | SUPPLEMENT 1 | MARCH 2021

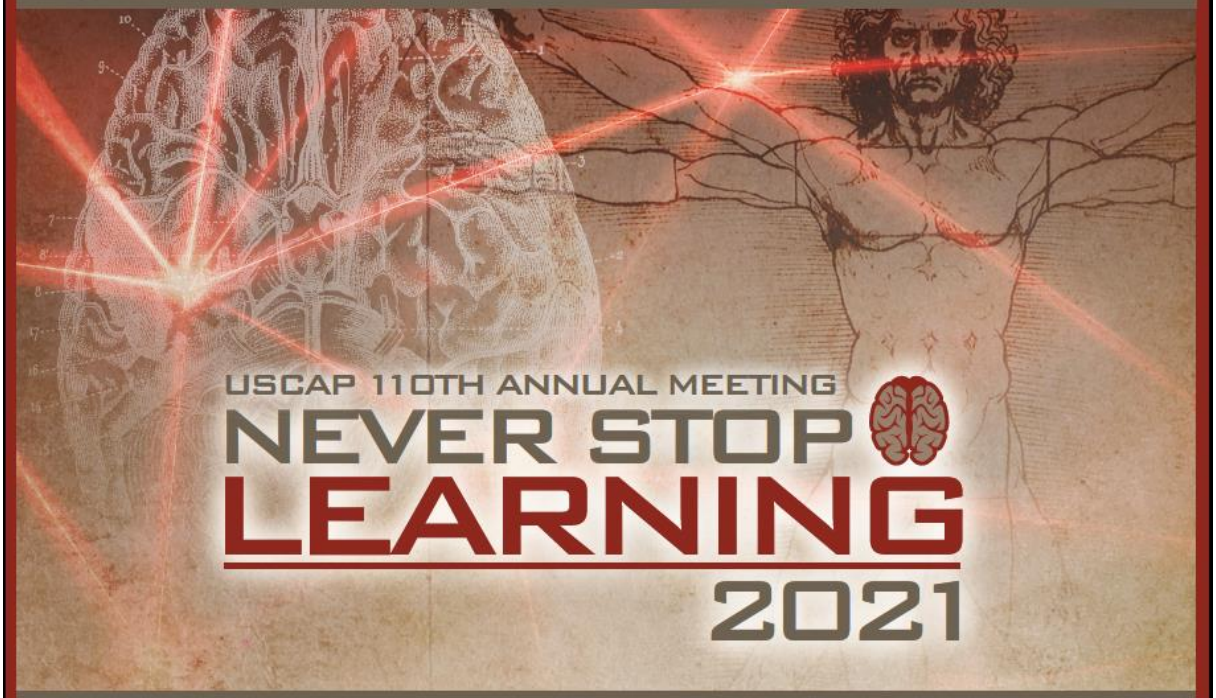
LI

LABORATORY INVESTIGATION

THE BASIC AND TRANSLATIONAL PATHOLOGY RESEARCH JOURNAL

ABSTRACTS

MEDICAL RENAL PATHOLOGY
(INCLUDING RENAL TRANSPLANTATION)
(828-847)



MARCH 13-18, 2021 | VIRTUAL AND INTERACTIVE

Published by
SPRINGER NATURE
www.ModernPathology.org

USCAP Creating a Better Pathologist
AN OFFICIAL JOURNAL OF THE UNITED STATES AND CANADIAN ACADEMY OF PATHOLOGY

EDUCATION COMMITTEE

Jason L. Hornick
Chair

Rhonda K. Yantiss, Chair
Abstract Review Board and Assignment Committee

Kristin C. Jensen
Chair, CME Subcommittee

Laura C. Collins
Interactive Microscopy Subcommittee

Raja R. Seethala
Short Course Coordinator

Ilan Weinreb
Subcommittee for Unique Live Course Offerings

David B. Kaminsky
(Ex-Officio)
Zubair W. Baloch
Daniel J. Brat
Sarah M. Dry
William C. Faquin
Yuri Fedoriw
Karen Fritchie
Jennifer B. Gordetsky
Melinda Lerwill
Anna Marie Mulligan
Liron Pantanowitz
David Papke,
Pathologist-in-Training
Carlos Parra-Herran
Rajiv M. Patel
Deepa T. Patil
Charles Matthew Quick
Lynette M. Sholl
Olga K. Weinberg
Maria Westerhoff
Nicholas A. Zoumberos,
Pathologist-in-Training

ABSTRACT REVIEW BOARD

Benjamin Adam
Rouba Ali-Fehmi
Daniela Allende
Ghassan Allo
Isabel Alvarado-Cabrero
Catalina Amador
Tatjana Antic
Roberto Barrios
Rohit Bhargava
Luiz Blanco
Jennifer Boland
Alain Borczuk
Elena Brachtel
Marilyn Bui
Eric Burks
Shelley Caltharp
Wenqing (Wendy) Cao
Barbara Centeno
Joanna Chan
Jennifer Chapman
Yunn-Yi Chen
Hui Chen
Wei Chen
Sarah Chiang
Nicole Cipriani
Beth Clark
Alejandro Contreras
Claudiu Cotta
Jennifer Cotter
Sonika Dahiya
Farbod Darvishian
Jessica Davis
Heather Dawson
Elizabeth Demicco
Katie Dennis
Anand Dighe
Suzanne Dintzis
Michelle Downes
Charles Eberhart
Andrew Evans
Julie Fanburg-Smith
Michael Feely
Dennis Firchau
Gregory Fishbein
Andrew Folpe
Larissa Furtado
Billie Fyfe-Kirschner
Giovanna Giannico
Christopher Giffith
Anthony Gill
Paula Ginter
Tamar Giorgadze
Purva Gopal
Abha Goyal
Rondell Graham
Alejandro Gru
Nilesh Gupta
Mamta Gupta
Gillian Hale
Suntrea Hammer
Malini Harigopal
Douglas Hartman
Kammi Henriksen
John Higgins
Mai Hoang
Aaron Huber
Doina Ivan
Wei Jiang
Vickie Jo
Dan Jones
Kirk Jones
Neerja Kambham
Dipti Karamchandani
Nora Katabi
Darcy Kerr
Francesca Khani
Joseph Khoury
Rebecca King
Veronica Klepeis
Christian Kunder
Steven Lagana
Keith Lai
Michael Lee
Cheng-Han Lee
Madelyn Lew
Faqian Li
Ying Li
Haiyan Liu
Xiuli Liu
Lesley Lomo
Tamara Lotan
Sebastian Lucas
Anthony Magliocco
Kruti Maniar
Brock Martin
Emily Mason
David McClintock
Anne Mills
Richard Mitchell
Neda Moatamed
Sara Monaco
Atis Muehlenbachs
Bita Naini
Dianna Ng
Tony Ng
Michiya Nishino
Scott Owens
Jacqueline Parai
Avani Pendse
Peter Pytel
Stephen Raab
Stanley Radio
Emad Rakha
Robyn Reed
Michelle Reid
Natasha Rekhtman
Jordan Reynolds
Andres Roma
Lisa Rooper
Avi Rosenberg
Esther (Diana) Rossi
Souzan Sanati
Gabriel Sica
Alexa Siddon
Deepika Sirohi
Kalliopi Siziopikou
Maxwell Smith
Adrian Suarez
Sara Szabo
Julie Teruya-Feldstein
Khin Thway
Rashmi Tondon
Jose Torrealba
Gary Tozbikian
Andrew Turk
Evi Vakiani
Christopher VandenBussche
Paul VanderLaan
Hannah Wen
Sara Wobker
Kristy Wolniak
Shaofeng Yan
Huihui Ye
Yunshin Yeh
Anjana Yeldandi
Gloria Young
Lei Zhao
Minghao Zhong
Yaolin Zhou
Hongfa Zhu

To cite abstracts in this publication, please use the following format: **Author A, Author B, Author C, et al. Abstract title (abs#). In "File Title."** ***Laboratory Investigation*** **2021; 101 (suppl 1): page#**

Background: Current diagnosis of primary podocytopathies (Px), such as Minimal Change Disease (MCD), Primary Focal Segmental Glomerulosclerosis (FSGS, pFSGS), and Lupus Podocytopathies (LPs), currently relies on technically-exhaustive electron microscopy analysis to determine both disease entity and severity. We and others have observed punctate IgG immunoreactivity (P-IgG) on routine immunofluorescence in many Px cases, that may represent disease-specific autoimmunoreactivity. However, P-IgG may be interpreted as epithelial protein reabsorption and its significance as a potential marker for Px may be missed. We sought to characterize key features of protein reabsorption granules (PRGs) and P-IgG, which may help to differentiate these features and facilitate the rapid diagnosis of Px through immunofluorescence microscopy (IF).

Design: We investigate these two morphologic features in a study of archival material.

We conducted IF on archived biopsies from cases of Px and control cases including secondary FSGS (sFSGS). Anti-human IgG and anti-human albumin staining was evaluated by assessing key morphologic characteristics such as location, distribution, and size of stained punctate features.

Results: The P-IgG pattern was seen in almost all MCD cases but was absent in the sFSGS. Protein reabsorption granules were present across case types in glomerular and tubular epithelial cells, in the absence or presence of the P-IgG. The albumin PRGs were usually coarse and clustered, and were observed focally and segmentally in the glomeruli. In contrast, the P-IgG was finer (smaller in size), more uniform in size, and almost always diffuse and global in the glomeruli

Difference in Morphological Characteristics between P-IgG and PRGs		
Characteristic	**P-IgG**	**PRG**
Disease Type	Px	sFSGS; Px
Location	Podocyte	Tubules; Glomeruli
Distribution	Diffuse; Global	Focal; Segmental
Size	Fine	Coarse
Shape	Punctate	Clustered
Expected Protein Composition	IgG; kappa & lambda	Albumin in combination with various immunoreactants

Conclusions: The PRGs, as shown by anti-albumin staining, did not colocalize with P-IgG. P-IgG is distinct from PRGs in makeup, location, and size, indicating separate etiology. Therefore the P-IgG observed in Px is highly likely to represent a distinct process from epithelial protein reabsorption. Additional studies using antibodies for megalin and cubilin, specific markers for PRGs, are underway.

839 Squalene in Prevention of Podocyte Injury

Resmiye Irmak Yuzuguldu[1], Osman Yılmaz[2], Mehtat Unlu[2], Hatice Kolatan[1], Hulya Ellidokuz[2], Caner Cavdar[2], Hulya Guven[1], Sulen Sarioglu[3]
[1]Dokuz Eylul University School of Medicine, Izmir, Turkey, [2]Dokuz Eylul University School of Medicine, Balcova, Turkey, [3]Dokuz Eylul University School of Medicine, Balçova, Turkey

Disclosures: Resmiye Irmak Yuzuguldu: None; Osman Yılmaz: None; Mehtat Unlu: None; Hatice Kolatan: None; Hulya Ellidokuz: None; Caner Cavdar: None; Hulya Guven: None; Sulen Sarioglu: None

Background: Focal segmental glomerulosclerosis (FSGS) is a frequent renal disease related to podocyte injury. There is no treatment regimen that can provide remission in all FSGS patients, and the rate of recurrence can be up to 40%. Squalene is an isoprenoid compound found mainly is shark liver and olive oil. Studies related to squalene are focused on antioxidant and antitumoral effects. This study aims to investigate the effects of olive oil (SQ-O) and shark-derived squalene (SQ-S) on podocyte injury in an experimental animal model.

Design: Wistar rats with similar weights (300-350 g) were grouped as follows: control (n=7), SQ-S (n=7), SQ-O (n=6), Adriamycin (ADR) (n=7), SQ-S+ ADR (n=6) and SQ-O+ADR (n=7). Squalene was administered at a total dose of 0.4 ml/day for 14 days. One week after the SQ, intravenous ADR (7.5 mg/kg) was administered. Urine proteinuria, creatinine and urea values were analyzed in 24-hour urine on the 14th and 22rd days. Blood creatinine, blood urea nitrogen (BUN), total protein and albumin values were analyzed at the 23rd (sacrifization day).

Hematoxylin & eosin, periodic acid schiff (PAS), trichrome, silver metanamine (PAMS) and Wilms' tumor 1 protein (WT-1) stained sections from the kidney tissues were evaluated by light microscopy (Figure-1). Bowman and glomerular tuft area were measured digitally. The mean segmental sclerosis scores were determined separately in PAS and PAMS stained sections (Figure-2). WT-1 positive podocytes were counted in 30 glomeruli. Tubular atrophy, interstitial fibrosis and inflammation, tubular damage was scored and thrombotic microangiopathy (TMA) findings were noted.

Results: All parameters were increased in ADR group compared to control, except for urine creatinine, urea; blood total protein, albümin and glomerular WT-1counts which were decreased as expected (p<0,05). There was no statistically significant difference between the SQ-O+ADR and the control group for most parameters; except for urine creatinine, urea and blood total protein, albumin values but all parameters were better than ADR group. Urine proteinuria and BUN in SQ-S+ADR were increased compared to ADR group, all other parameters were better than ADR group. Urine creatinine, urea, protein and blood BUN, total protein, albumin values between groups SQ-S+ADR worse than control group, probably related to the TMA findings detected in 3 rats belonging to SQ-S+ADR group (Table-1).

Groups	Control	SQ-S	SQ-O	ADR	SQ-S+ADR	SQ-O+ADR
14.rd day U_P (g/24h)	0.029 ± 0.006	0.024 ± 0.01	0.028 ± 0.02	0.725 ± 0.11	0.877 ± 0.14	0.662 ± 0.09
22.th day U_P (g/24h)	0.024 ± 0.004	0.021 ± 0.006	0.025 ± 0.01	0.824 ± 0.26	-	0.32 ± 0.06
BUN (mg/ dl)	18.3 ± 1.94	17.1 ± 1.96	19.0 ± 4.31	34.9 ± 11.8	71.9 ± 53	35.4 ± 10.5
Blood creatinine (mg/dl)	0.26 ± 0.051	0.28 ± 0.03	0.26 ± 0.02	0.44 ± 0.06	0.32 ± 0.1	0.33 ± 0.03
Bowman area	15001 ±1507	16362 ±661	15683 ±1638	10316 ±1115	15433 ±2448	13395 ±1613
Glomerular tuft area	10540 ±1507	11427 ±348	10849 ±1134	6803 ± 1076	9109 ± 748	8516 ± 841
SSS - PAS	0.0017 ± 0.002	0.0021 ± 0.001	0.0038 ± 0.003	0.2957 ± 0.09	0.115 ± 0.78	0.1083 ± 0.26
SSS - PAMS	0.001 ± 0.001	0.001 ± 0.001	0.004 ± 0.002	0.282 ± 0.079	0.103 ± 0.095	0.101 ± 0.014
WT-1	11.51 ± 0.14	11.51 ± 0.14	14.71 ± 1.52	7.15 ± 0.64	9.99 ± 2.51	11.86 ± 1.50

Table-1: Mean Values of the Clinicopathological Parameters Evaluated in Wistar Rat Groups.

All data are presented as mean ± SD.

Abbreviations: SQ: Squalane; SQ-S: Shark derived SQ administered group; SQ-O: Olive oil derived SQ administered group; ADR: Adriamycin administered group; SQ-S+ADR: Shark derived SQ and Adriamycin administered group; SQ-O+ADR: Olive oil derived SQ and Adriamycin administered group, U_P, urinary protein; BUN: *Blood urea* nitrogen; SSS: segmental sclerosis score.

* There was no statistical differences between any of these three groups (p< 0.05).
** Since 3 of the rats belonging to this group died early, urine samples of the remaining rats could not be collected and were sacrificed early (20th day).
[¥] There was no statistical differences between control vs. SQ-O+ADR (p< 0.05).
[φ] There was no statistical differences between control vs. SQ-O+ADR (p< 0.05).
[Θ] There was no statistical differences between control vs. SQ-S+ADR and control vs. SQ-O+ADR (p< 0.05).
[τ] There was no statistical differences between control vs. SQ-S+ADR and control vs. SQ-O+ADR (p< 0.05).
[Ƥ] There was no statistical differences between control vs. SQ-S+ADR and control vs. SQ-O+ADR (p< 0.05).
[¶] There was no statistical differences between control vs. SQ-S+ADR and control vs. SQ-O+ADR (p< 0.05).
[§] There was no statistical differences between control vs. SQ-S+ADR and control vs. SQ-O+ADR (p< 0.05).
[€] ADR vs. SQ-O+ADR, p=0.031.

Figure 1 - 839

Figure-1: Significant loss of podocytes in group receiving Adriamycin (B), compared to control group (A). Note the preservation of the podocytes in groups receiving Adriamycin + Shark derived squalene (C) and Adriamycin + Olive oil derived squalene (B).
(IHC, WT1 original magnification X40)

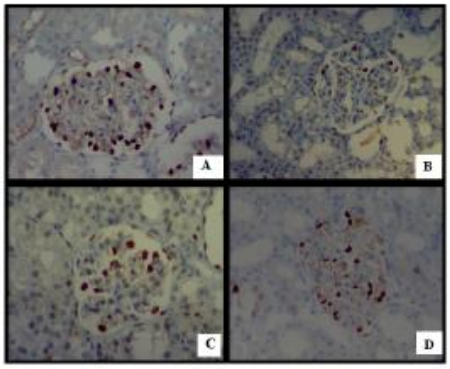
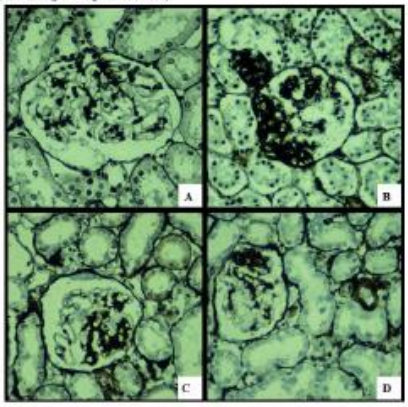


Figure 2 - 839

Figure-2: Glomeruli in control group (A), Adriamycin group (B) with severe segmental sclerosis affecting more than 75% of the tuft area. Less severe segmental sclerotic lesions in groups receiving Adriamycin + Shark derived squalene (C) and Adriamycin + Olive oil derived squalene (D).
(IHC, PAMS original magnification X40)



Conclusions: Olive oil derived squalene seems to be a valuable compound against podocyte injury which deserves further investigation to understand effector mechanisms and clinical availability.

840 Urinary Proteomics Data Guides AI to Discover New Digital Biomarkers for Diabetic Nephropathy Classification

Nicholas Lucarelli[1], Brandon Ginley[1], Seung Seok Han[2], Pinaki Sarder[1]
[1]SUNY Buffalo, Buffalo, NY, [2]Seoul National University College of Medicine, Seoul, South Korea

Disclosures: Nicholas Lucarelli: None; Brandon Ginley: None; Seung Seok Han: None; Pinaki Sarder: None

Background: Diabetic Nephropathy (DN) is one of the most common causes of end stage renal disease (ESRD). The Tervaert classification is a system for classifying the severity of DN using glomerular lesions. However, the resulting diagnoses do not perfectly predict patient progression. Significant literature suggests tubules are important to the pathogenesis of DN, but common assessment methods are limited to semi-quantitative estimation of IFTA. Further, urinary proteomics have proven to be a powerful tool to monitor disease progression. We used machine learning to study the structural changes in renal glomeruli, tubules, and urine of DN patients and their association with patient outcome.

Design: We studied whole slide images (WSIs) of periodic acid-Schiff stained renal biopsies from 56 DN patients matched with 2038 proteins measured from each patient's urine. Using Seurat, we identified proteins that were differentially expressed in patients that developed ESRD within 2 years after biopsy. Glomeruli, globally sclerotic glomeruli, tubules, arteries and arterioles, and interstitium were segmented from WSI using our previously published HAIL (human-AI-loop) for convolutional network training and prediction on WSIs. For each glomerulus, 315 handcrafted digital image features were measured, and for tubules, 207 features. Glomerular and tubular image features were used separately as inputs to a recurrent neural network to predict the patient's ESRD status within 2 years post-biopsy. Differentially expressed urine proteins were also used as inputs to a fully connected neural network to predict ESRD within 2 years.