



Annual Meeting & ToxExpo  
VIRTUAL EVENT • MARCH 2021

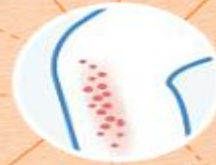
# DTSS RECEPTION

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Dermal Toxicology Specialty Section  
Virtual Reception  
March 17, 5-6 pm, 2021



Dermal Toxicology Specialty Section  
OF THE SOCIETY OF TOXICOLOGY



# Current Officers

President

**Neera Tewari-Singh, MS, PhD**



Vice President

**Sara Farahmand, PhD**



Vice President-Elect

Vacant

Secretary/Treasurer

**Yoke-Chen Chang, PhD**



Past President

**Michael Hughes, PhD, DABT**



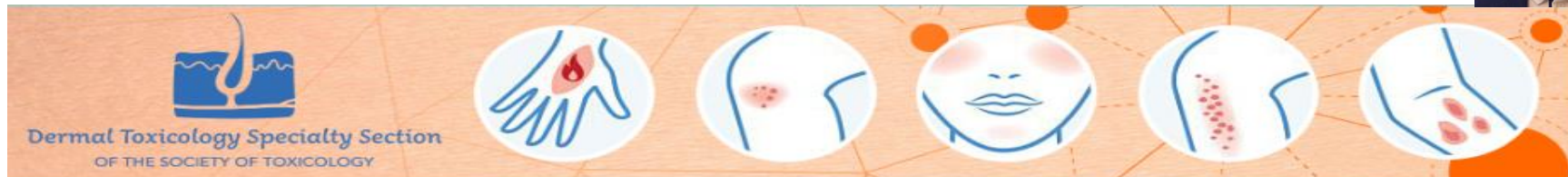
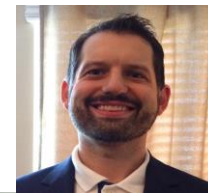
Senior Councilor

**Jeffrey Moehlenkamp, PhD, DABT**



Councilor

**Gabriel Knudsen, PhD, DABT**



# Current Representatives

- Postdoctoral Representative
  - **Ana Ferragut Cardoso, PhD**
- Graduate Student Representative
  - **Careen Khachatoorian, PhD**



# Thank You to DTSS Officers Rotating off the Committee!

**Michael Hughes**

**Jeffrey Moehlenkamp**



Dermal Toxicology Specialty Section  
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# Congratulations to New DTSS Officers!

- Vice President
  - **Sam Tadepalli**
- Councilor
  - **Michael D. Southall**

We need a volunteer for our Vice-President Elect position



Dermal Toxicology Specialty Section  
OF THE SOCIETY OF TOXICOLOGY



# Thanks to All Our Sponsors



Michael Hughes for Student support

# DTSS Activities 2020-2021

- **Sponsored workshop at 2021 Annual Virtual Meeting**

Applicability Domains and Future of Nonanimal Tests for Skin Sensitization” Wednesday, March 24<sup>th</sup> (11:45 am – 2:30 pm)

Chair(s): Victor J. Johnson, Burleson Research Technologies; and Marc Pallardy, Université Paris-Sud, France

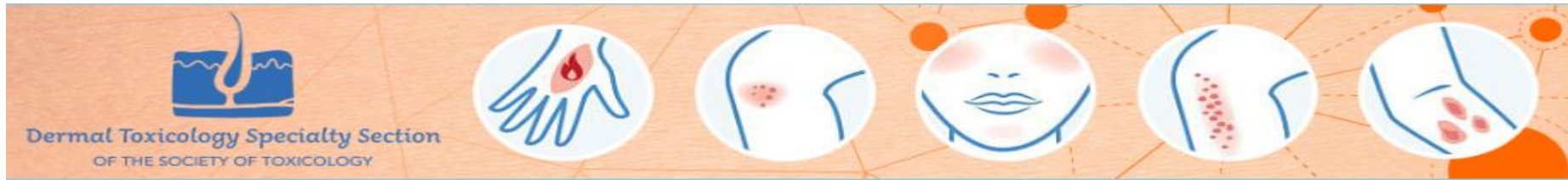


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# DTSS Activities 2020-2021

- Initiated Program to Sponsor Graduate Student Memberships
- Posted DTSS Officer Roles and Responsibilities on DTSS website
- Published DTSS Newsletter
- DTSS poster prepared for Annual Meeting
- Reviewed several proposals and papers for DTSS awards



# Skin and Dermal Toxicity Session

## **Poster Session:**

Skin and Dermal Toxicity  
Chair(s): Jeffrey Yourick, US FDA  
Tuesday, March 23<sup>rd</sup> (1- 2:45pm)

# Secretary/Treasurer's Report



Dermal Toxicology Specialty Section  
OF THE SOCIETY OF TOXICOLOGY



# Secretary/Treasurer's Report

- As of March 1, 2021, DTSS currently has 128 members (8 students, 3 post-doctoral fellows).
- At the end of 2020, DTSS had cash reserves of \$8,704  
Compared to \$3,880 at the end of 2019  
Current reserve is sufficient to cover the annual reception and student awards
- We encourage members to consider contributing to DTSS  
Send contributions to SOT, c/o Belinda Inscho and specifically note DTSS

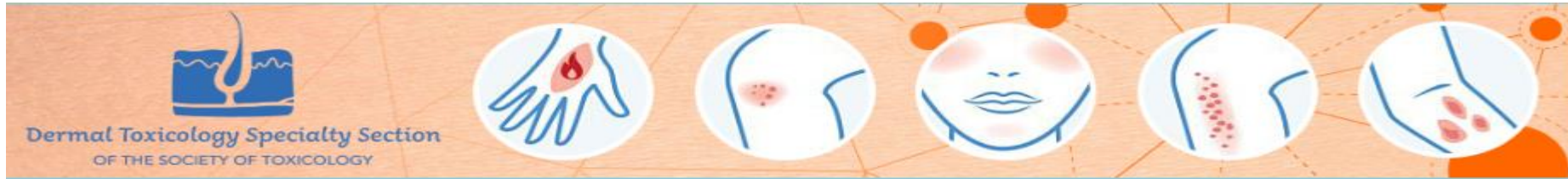


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# Special Program to Recruit Graduate Student Members

- The DTSS is offering a membership program to 6 graduate students for free membership to the specialty section
- If you have a lab colleague who might be interested in becoming a DTSS graduate student member, encourage them to contact Bo Inscho at SOT headquarters



# Session proposals for SOT 2022

- Symposia
- Workshops
- Roundtable
- Informational Session
- Continuing Education

Contact for more information or send proposals to Sara Farahmand at [farahmand.s@gmail.com](mailto:farahmand.s@gmail.com) or Neera Tewari Singh at [tewarsi@msu.edu](mailto:tewarsi@msu.edu) for feedback from DTSS

Please send proposals two-three weeks before the final deadline for SOT proposal submissions which might be late April or early May.



Dermal Toxicology Specialty Section  
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# Award Presentations

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- Informa Healthcare Award
- DTSS Paper of The Year Award
- Stratacor Postdoctoral Award
- DTSS Postdoctoral Award sponsored by Charles River
- DTSS Student Award sponsored by Charles River



Dermal Toxicology Specialty Section  
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# Informa Healthcare Award

In recognition of the best paper in dermal toxicology published  
in Cutaneous and Ocular Toxicology



## **Anti-inflammatory effect of Arnica montana in a UVB radiation-induced skin-burn model in mice**

J. da Silva, E.C. Bálsamo, F.R. Machado, M.R. Poetini, V.C.  
Bortolotto, S.M. Araújo, L. Londero, S.P. Boeira, C.P. Sehn, M.C. de  
Gomes, M. Prigol, L.C. Souza

Cutaneous and Ocular Toxicology, 2020 Jun;39(2):126-133.



# Paper of The Year Award

In Recognition of an Exceptional Publication in the Field of  
Skin Toxicology and Pharmacology

**Nancy Hopf, PhD., et al.**

University of Lausanne



*“Reflections on the OECD guidelines for in vitro  
skin absorption studies”*



# Stratacor Postdoctoral Award

In Recognition of Outstanding Postdoctoral Candidates  
for their Contribution to Skin-related Research

**Satyendra Singh, PhD**

Michigan State University

*“Mechanism mediating the Dermal  
Inflammation and Toxicity from Phosgene  
Oxime Exposure”*



# DTSS Student Award Sponsored by Charles River

In Recognition of an Outstanding Graduate Student  
for Skin-related Research

**Careen Khachatourian**

University of California, Riverside



*"Electronic cigarette fluids and exhaled residue cause an inflammatory response in both human keratinocytes and a 3D skin model"*



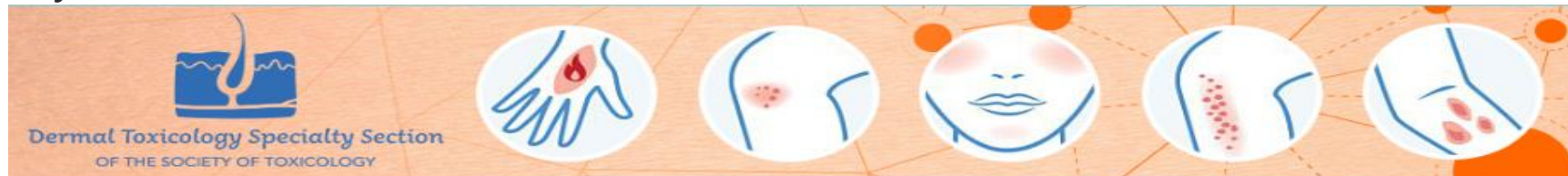
# DTSS Postdoctoral Fellow Award Sponsored by Charles River

In recognition of outstanding postdoctoral fellow  
for their contribution to skin-related research

**Swati Sharma, Ph.D.**

Michigan State University

*“Mechanisms contributing to skin inflammatory pathology  
following exposure to Environmental pollutant Benzo(a)  
Pyrene in Psoriatic mouse model”*



# Award Winners 2020



## Informa Healthcare Award

- Impaired skin barrier function caused by reactive oxygen species in mice with colonic tumours. **Satoshi Yokoyama, Keiichi Hiramoto, Yurika Yamate.** *Cutan Ocul Toxicol.* 2019 Dec;38(4):349-355

## DTSS Paper of the Year Award

- **Margaret EK Kraeling, PhD.** *In Vitro* Skin Penetration of Dendrimer Nanoparticles. *Applied In vitro Toxicology*, 2019 Sep; 5(3): 134-149.

## Stratacor Postdoctoral Award

- **Ana Cardoso, PhD (University of Louisville).** Alternative Splicing as a Key Mechanism in Arsenic-Induced Squamous Cell Carcinoma: Evidence from RNA-Seq and Proteomic Analysis.



# Award Winners 2020



## Student Research Award

- **Bryan Holloman (University of South Carolina, School of Medicine).** Role of Aryl Hydrocarbon Receptor ligands in allograft rejection.

## Charles River Student and Postdoctoral Fellow Travel Awards

- **Satyendra Singh, PhD (Michigan State University).** Toxicologic pathology and related mechanism following cutaneous exposure of phosgene oxime.
- **Rachel Baur (West Virginia University).** Alterations in the Mouse Skin and Gut Microbiome and Skin Integrity Following Dermal Exposure to the Antimicrobial Chemical Triclosan



## Reflections on the OECD guidelines for *in vitro* skin absorption studies

N.B. Hopf<sup>a</sup>, C. Champmartin<sup>c</sup>, L. Schenk<sup>b</sup>, A. Berthet<sup>a</sup>, L. Chedik<sup>c</sup>, J.L. Du Plessis<sup>i</sup>, A. Franken<sup>i</sup>, F. Frasc, S. Gaskin<sup>e</sup>, G. Johanson<sup>b</sup>, A. Julander<sup>b</sup>, G. Kasting<sup>h</sup>, S. Kilo<sup>d</sup>, F. Larese Filon<sup>f</sup>, F. Marquet<sup>c</sup>, K. Midander<sup>b</sup>, E. Reale<sup>a</sup>, A.L. Bunge<sup>g</sup>

<sup>a</sup> Centre for Primary Care and Public Health (Unisante), Department for Occupational and Environmental Health (DSTE), Exposure Science Unit, Switzerland

<sup>b</sup> Karolinska Institutet, Institute of Environmental Medicine, Unit of Integrative Toxicology, Sweden

<sup>c</sup> French National Research and Safety Institute for the Prevention of Occupational Accidents and Diseases (INRS), France

<sup>d</sup> Friedrich-Alexander University Erlangen-Nürnberg, Institute and Outpatient Clinic of Occupational, Social and Environmental Medicine, Germany

<sup>e</sup> University of Adelaide, School of Public Health, Health and Medical Sciences, Australia

<sup>f</sup> University of Trieste, Clinical Unit of Occupational Medicine, Department of Medical, Surgical and Health Sciences, Italy

<sup>g</sup> Colorado School of Mines, Chemical and Biological Engineering, USA

<sup>h</sup> University of Cincinnati, James L. Winkle College of Pharmacy, USA

<sup>i</sup> Occupational Hygiene and Health Research Initiative (OHHRI) North-West University, South Africa

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Centre universitaire de médecine générale  
et santé publique • Lausanne

**inrs**  
Institut National de Recherche et de Sécurité

  
**THE UNIVERSITY  
of ADELAIDE**

  
**Karolinska  
Institutet**

  
**University of  
CINCINNATI**

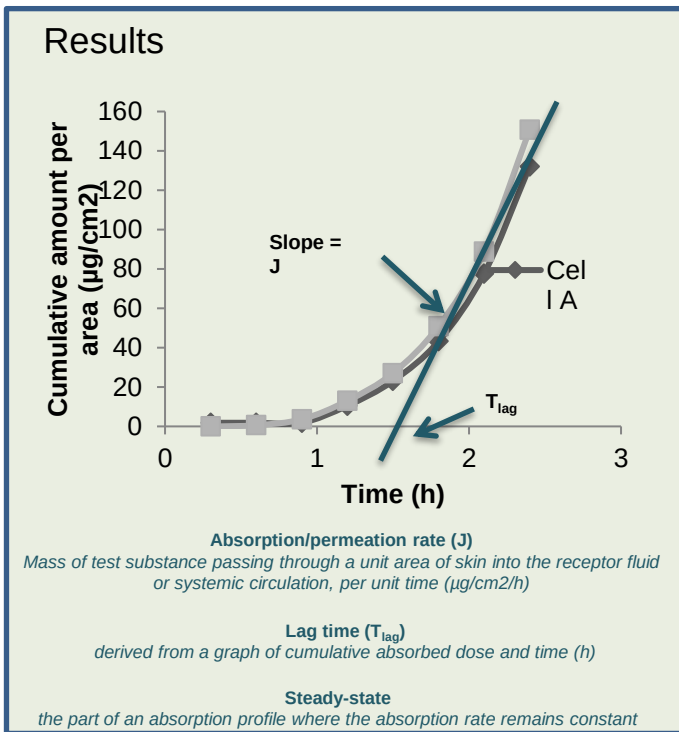
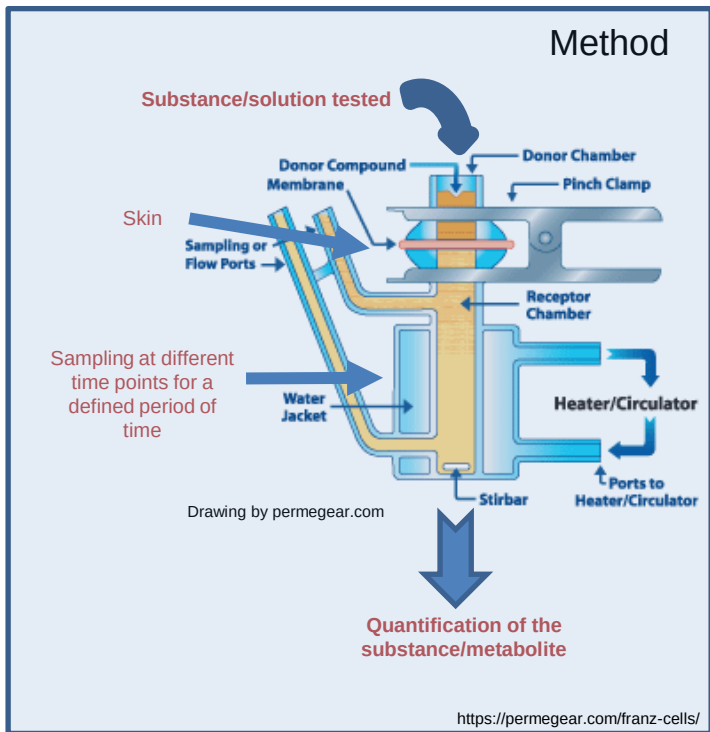
  
**COLORADO SCHOOL OF  
MINES**

**FAU**  
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ERLANGEN-NÜRNBERG  
MEDIZINISCHE FAKULTÄT

 **NWU®** | **OHHRI**

 **UNIVERSITÀ  
DEGLI STUDI DI TRIESTE**

# Background



Permeability coefficient:  $K_p [\text{cm}/\text{h}] = J_{\text{steady-state}} / (\text{applied conc. } [\mu\text{g}/\text{cm}^3])$

*$K_p$  represents the rate at which a chemical penetrates the skin*

# Goals

## Aims:

- 1) assist other skin absorption laboratories in planning their experiments considering factors that are currently not defined in the OECD documents; and
- 2) provide some practical insights to the OECD expert group that currently is revising the GN156-2019 guideline.

*The overall goal is to contribute to the harmonization of skin permeation experiments and standardization of reported outputs*

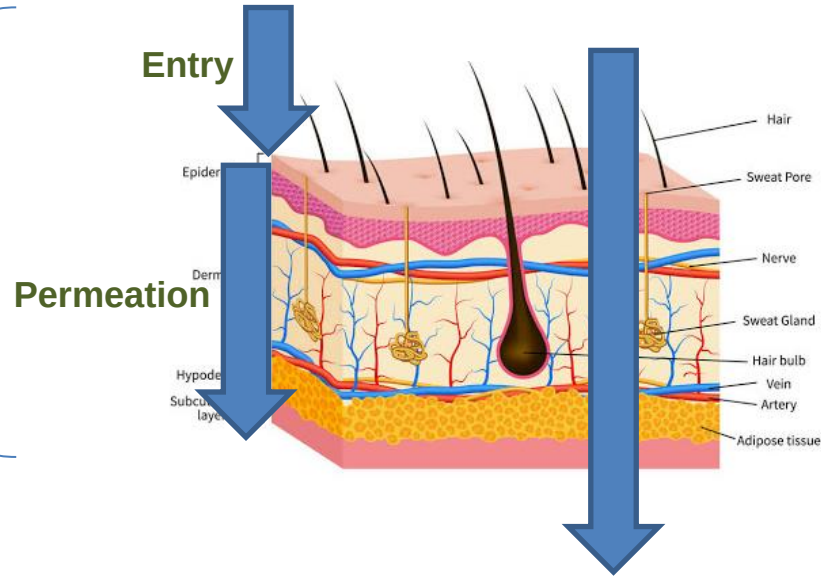
The paper discusses many OECD guidance themes:

- Terminology and scope
- Experimental equipment (diffusion cell, receptor fluid, sampling, temperature)
- Skin (skin procurement and preparation, skin thickness, skin integrity, skin viability)
- Substance application (test substance concentrations and formulations, application to the skin, recovery procedures, chemical analysis,)
- Statistics (data, replicates, and test report)
- Interpretation of *in vitro* data

# Ex. Terminology

- penetration, permeation, absorption

**Penetration** - entry of a substance into the stratum corneum and permeation through epidermis.



**Absorption** - a process that describes the passage of compounds across the skin and includes penetration

# Recommendations

## One overarching recommendation

- ❑ The GN156 should be revised to clearly address all types of chemicals tested for skin permeation (individual chemicals, formulations, pesticides, biocides, powders, mixtures)
- ❑ The GN156 revision should be followed by revisions of the GD28 and TGD428; as all three documents need to be updated and harmonized.

## Specifically,

- ❑ *Use the same terminology in all guidelines*
- ❑ *Add a section on theoretical basis of the skin permeation parameters and possible limitations in using these in risk assessment*
- ❑ *Add examples of appropriate vehicles and receptor fluid for poorly soluble analytes*
- ❑ *Provide examples of reliable methods for assessing skin viability and integrity, including criteria for acceptable integrity*
- ❑ *Include protocols describing how to conduct mass-balance, tape strip methods, and skin extractions.*

# **Mechanism Mediating the Dermal Inflammation and Toxicity from Phosgene Oxime Exposure**

Satyendra K Singh<sup>1</sup>, Dinesh G Goswami<sup>2,4</sup>, Claire R Croutch<sup>3</sup>,  
Rajesh Agarwal<sup>4</sup>, Erica L Noland<sup>5</sup>, Neera Tewari-Singh<sup>1</sup>

1. Department of Pharmacology and Toxicology, Michigan State University, East Lansing, MI; 2. Department of Molecular and Translational Medicine, Texas Tech University Health Sciences Center, El Paso, TX  
3. MRIGlobal, Kansas City, MO; 4. Department of Pharmaceutical Sciences, University of Colorado Denver, Aurora, CO; 5. Department of Pathobiology and Diagnostic Investigation, Michigan State University, East Lansing, MI

# Introduction

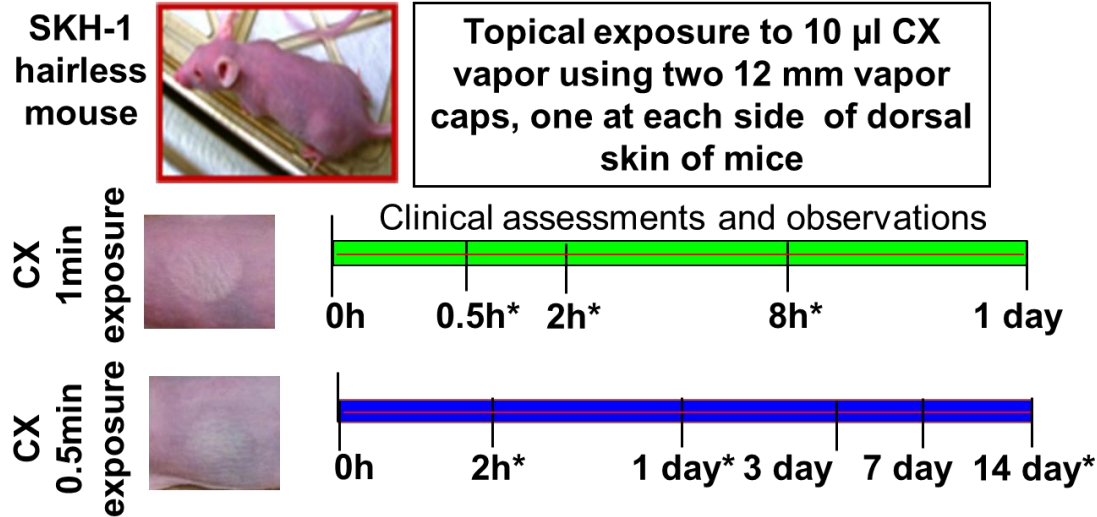
- Phosgene oxime (CX), a halogenated oxime, is an urticant or nettle agent with highly volatile, reactive, corrosive, and irritating vapor.
- CX is absorbed quickly through the clothing with faster cutaneous penetration compared to other vesicating agents causing instantaneous pain and severe tissue damage, and death.
- The skin urticaria from CX resembles urticaria caused by allergic and non-allergic reactions to various environmental substances.

| Chemical Agent        | Pain             | Tissue Damage                            | Blister            |
|-----------------------|------------------|------------------------------------------|--------------------|
| Sulfur Mustard        | Hours later      | Onset of clinical effects is hours (24h) | Fluid filled       |
| Lewisite              | Immediate        | Seconds to minutes                       | Fluid filled       |
| <b>Phosgene Oxime</b> | <b>Immediate</b> | <b>Seconds</b>                           | <b>Solid wheal</b> |

# Introduction

- It is one of the least studied warfare agent with no specific antidote available.
- Information on its dermal absorption and effects on human skin tissue is limited, and its mechanism of action is unknown.
- Our studies are focused on developing a well-defined mouse toxicity model of CX-skin exposure and a mechanistic base which could be employed for the identification of novel targets that could be explored for therapeutic intervention.
- Our current studies could have a profound impact on understanding the toxic effects, pathology and related molecular mechanism of CX cutaneous toxicity with significant translational implications towards designing intervention strategies.

# CX Exposure-Duration and Time-Response Study Paradigm



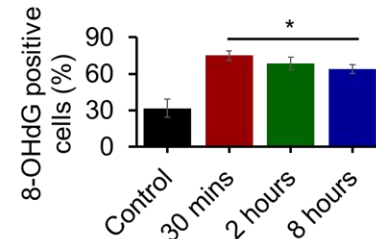
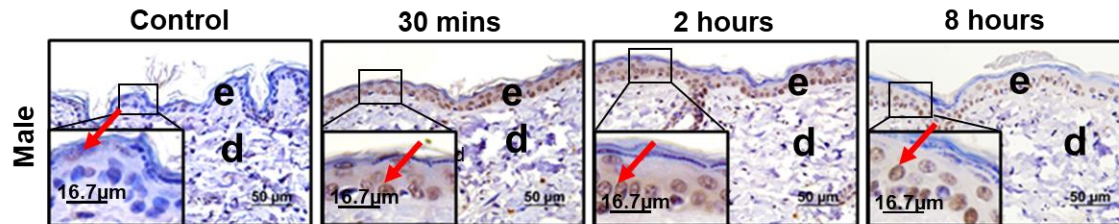
\*, time points at which mice were euthanized and skin tissues were collected for histopathological and molecular analyses



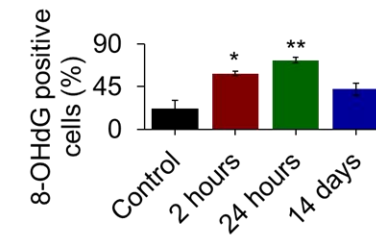
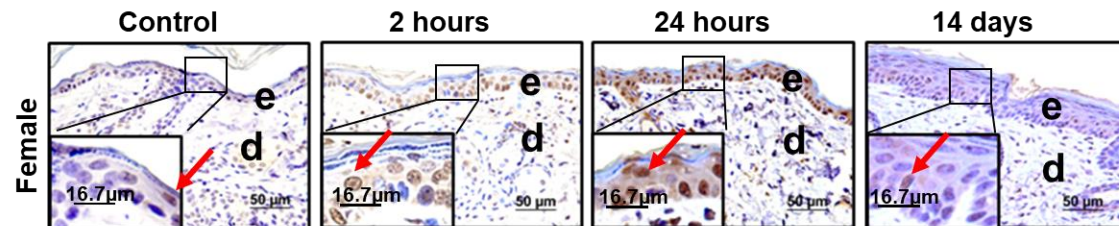
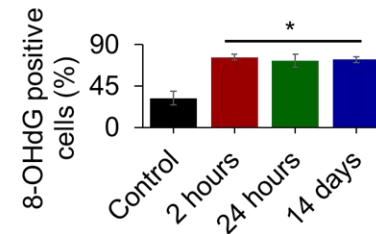
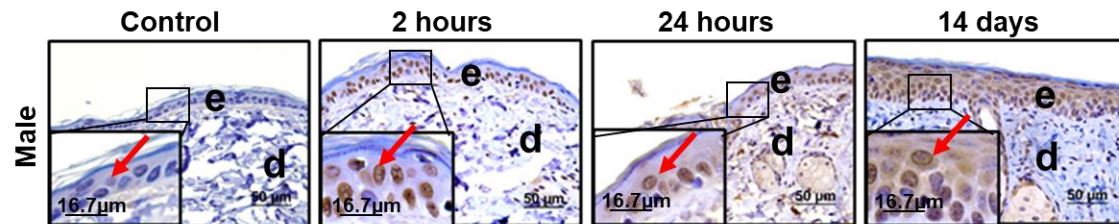
# CX skin exposure increased oxidative DNA damage

## 8-OHdG staining

1 min CX  
Exposure



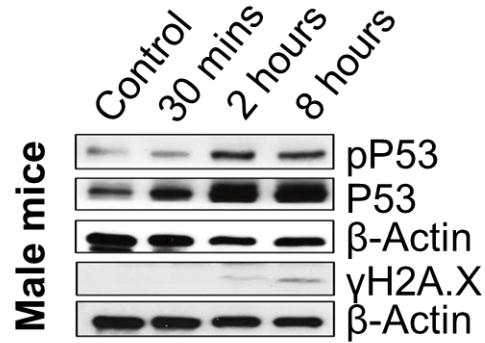
0.5 min CX  
Exposure



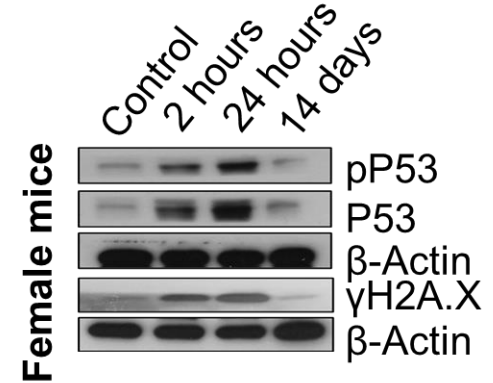
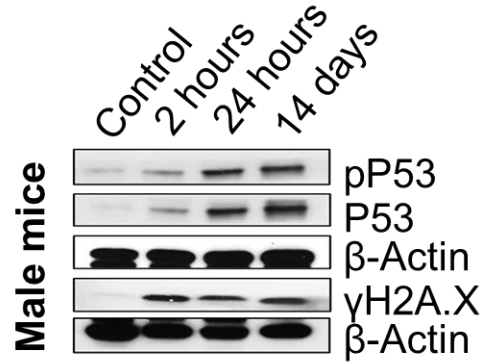
# CX skin exposure increased expression of DNA damage markers

## DNA damage markers

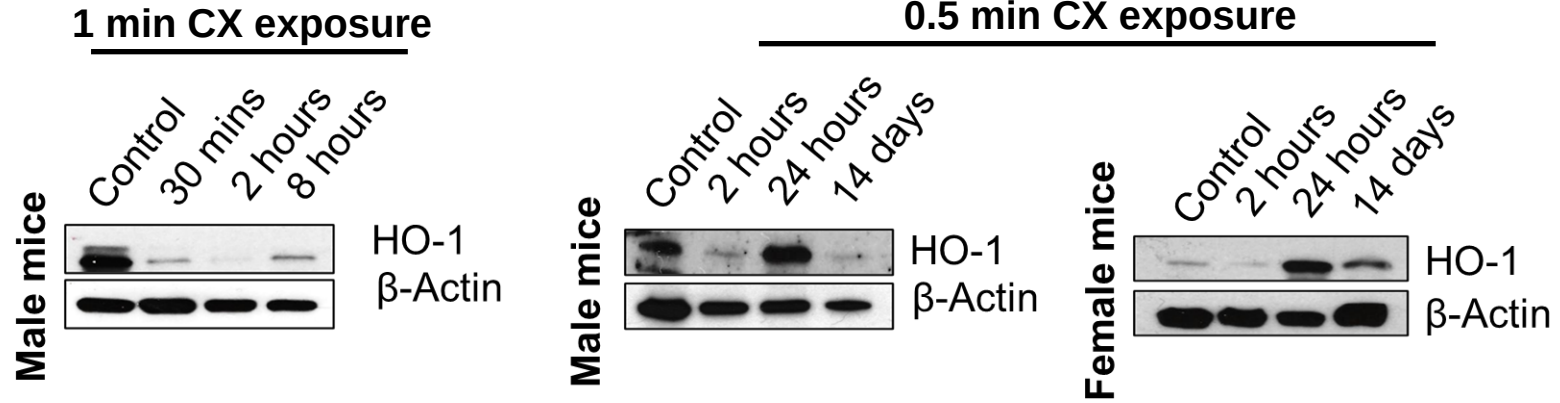
1 min CX exposure



0.5 min CX exposure

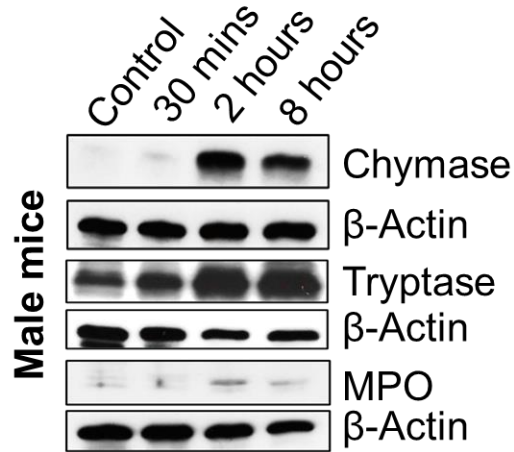


# CX skin exposure increased oxidative stress marker

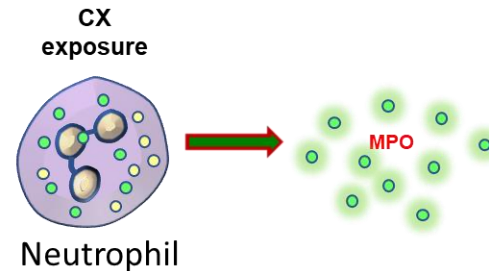
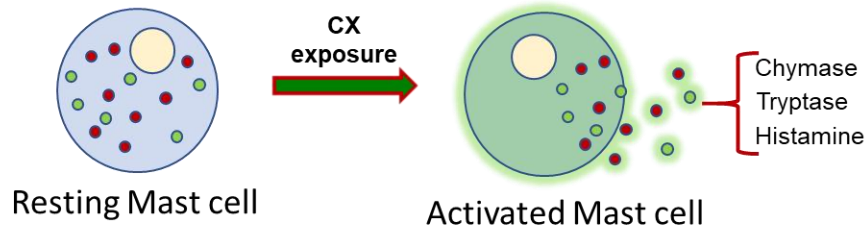
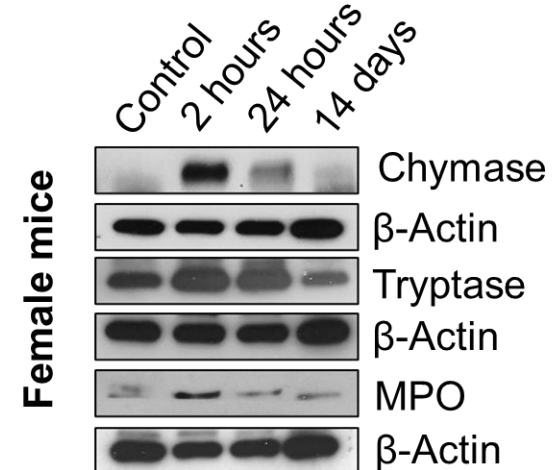
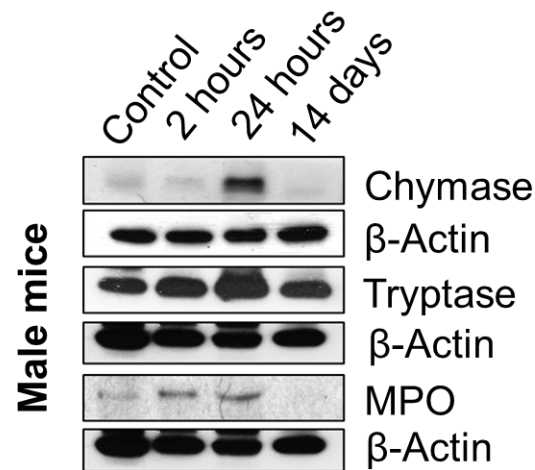


# CX skin exposure increased mast cell and neutrophils activation

## 1 min CX exposure



## 0.5 min CX exposure

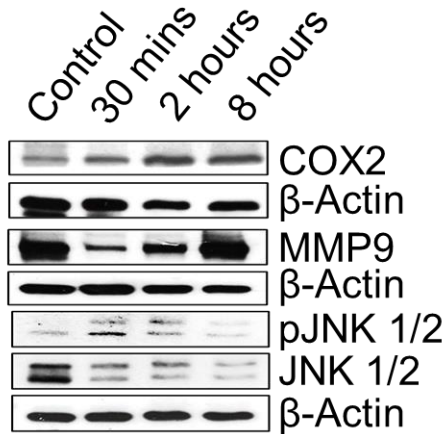


MPO, Myeloperoxidase

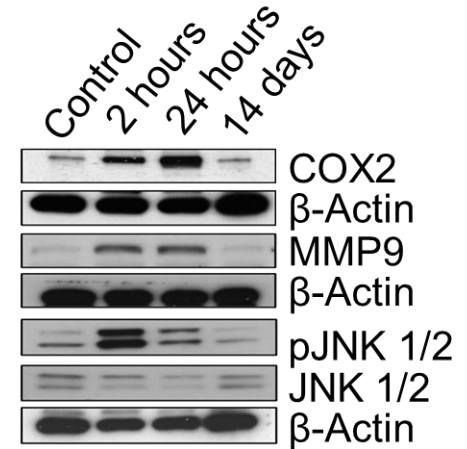
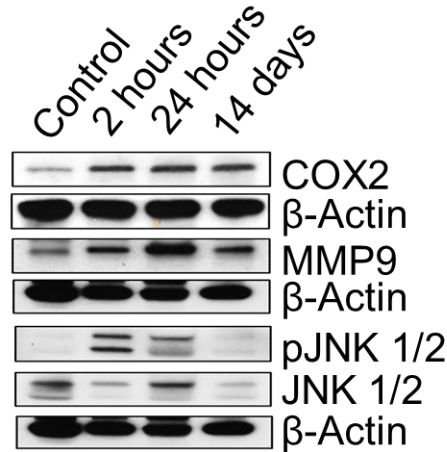
# CX skin exposure increased expression of DNA damage and inflammatory markers

## Inflammatory markers

### 1 min CX exposure

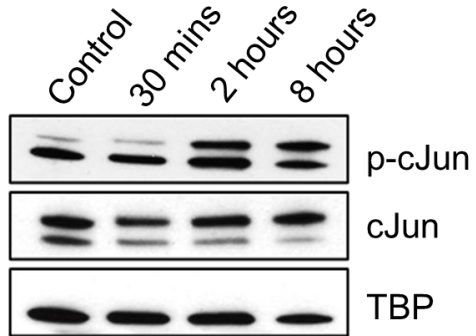


### 0.5 min CX exposure

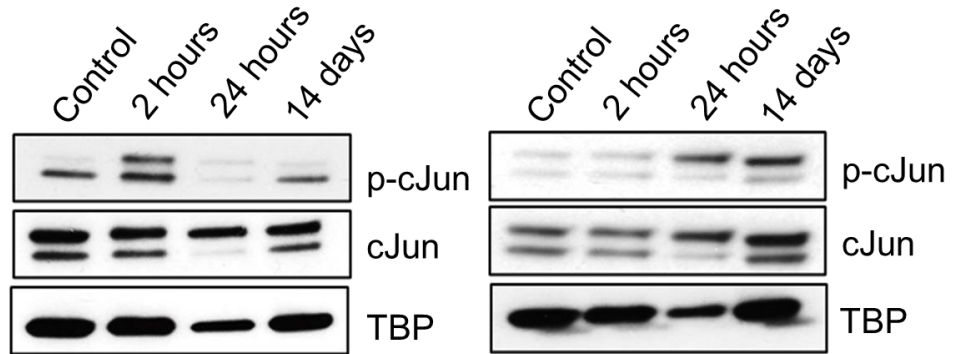


# CX skin exposure increased Activator Protein-1

## 1 min CX exposure



## 0.5 min CX exposure



# CX skin exposure increased Inflammatory cytokine

| Cytokines | 1 min CX exposure       |             |              | 0.5 min CX exposure     |              |              |                           |              |             |
|-----------|-------------------------|-------------|--------------|-------------------------|--------------|--------------|---------------------------|--------------|-------------|
|           | Male mice (fold change) |             |              | Male mice (fold change) |              |              | Female mice (fold change) |              |             |
|           | C vs. 30m               | C vs. 2h    | C vs. 8h     | C vs. 2h                | C vs. 24h    | C vs. 14D    | C vs. 2h                  | C vs. 24h    | C vs. 14D   |
| IL1       | <b>1.71</b>             | 0.94        | 0.64         | 1.06                    | 0.55         | <b>1.86</b>  | 0.94                      | 0.54         | <b>1.62</b> |
| IL6       | 0.25                    | <b>3.80</b> | <b>17.86</b> | <b>7.09</b>             | <b>6.50</b>  | <b>9.10</b>  | <b>9.03</b>               | <b>33.97</b> | <b>4.07</b> |
| CXCL11    | 0.53                    | <b>4.20</b> | <b>19.66</b> | <b>6.96</b>             | <b>11.08</b> | <b>48.19</b> | <b>2.85</b>               | <b>9.68</b>  | <b>5.38</b> |
| VEGF      | 0.80                    | 1.08        | <b>2.44</b>  | 0.33                    | <b>2.13</b>  | <b>15.68</b> | 0.64                      | <b>3.71</b>  | <b>5.42</b> |
| IL4       | 0.03                    | 0.15        | 0.15         | 0.42                    | 0.15         | 0.70         | 0.52                      | 0.24         | <b>1.43</b> |
| IL10      | 0.00                    | 0.05        | 0.68         | 0.00                    | 0.46         | 0.28         | 0                         | 0            | <b>1.68</b> |

# Summary

## **CX skin exposures in SKH-1 hairless mice causes:**

- Immediate skin lesions including urticaria, necrosis, blanching, erythema and edema, and mortality in long-duration exposed mice
- An increase in the skin epidermal and dermal plus hypodermal thickness
- Increases in the scab formation and hyperkeratosis
- Alterations of inflammatory, DNA damage and oxidative stress markers
- Alteration of inflammatory cytokine response
- An increase in skin mast cell activation
- These effects could be due to the activation of pathways related to mast cell activation, inflammation, and DNA damage

# Acknowledgements

## Funding

- Countermeasures Against Chemical Threats (CounterACT) Program, Office of the Director National Institutes of Health (NIH OD) and National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) [Grant Numbers R21 AR073544 and U01 AR075470].

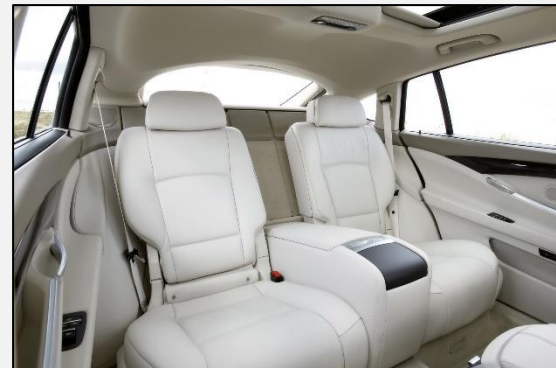
# E-CIGARETTE FLUIDS AND EXHALED RESIDUE CAUSE AN INFLAMMATORY RESPONSE IN BOTH HUMAN KERATINOCYTES AND A 3D SKIN MODEL

Careen Khachatoorian  
University of California, Riverside  
DTSS Reception  
March 17, 2021

# ECEAR ELECTRONIC CIGARETTE EXHALED AEROSOL RESIDUE



Nicotine

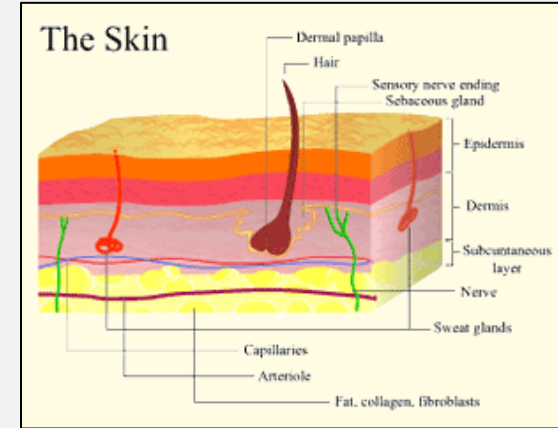


Flavor  
Chemicals

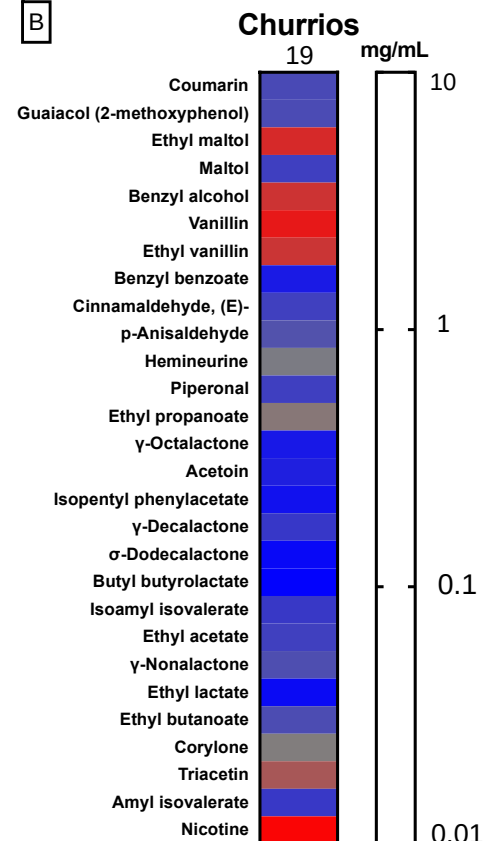
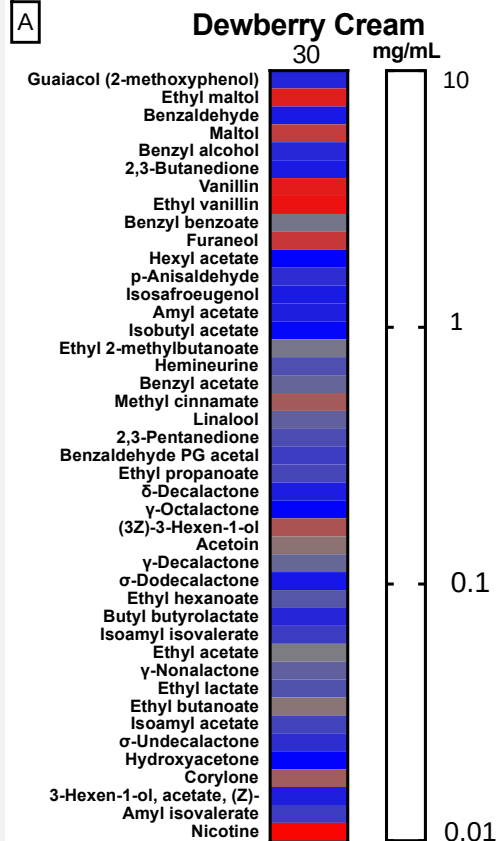
# ECEAR EXPOSURE ROUTE



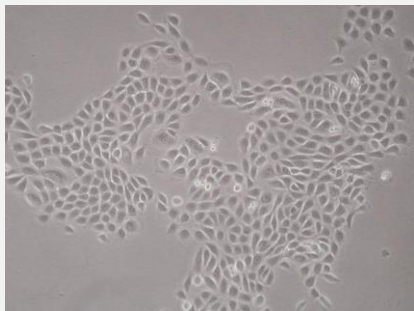
Epidermis



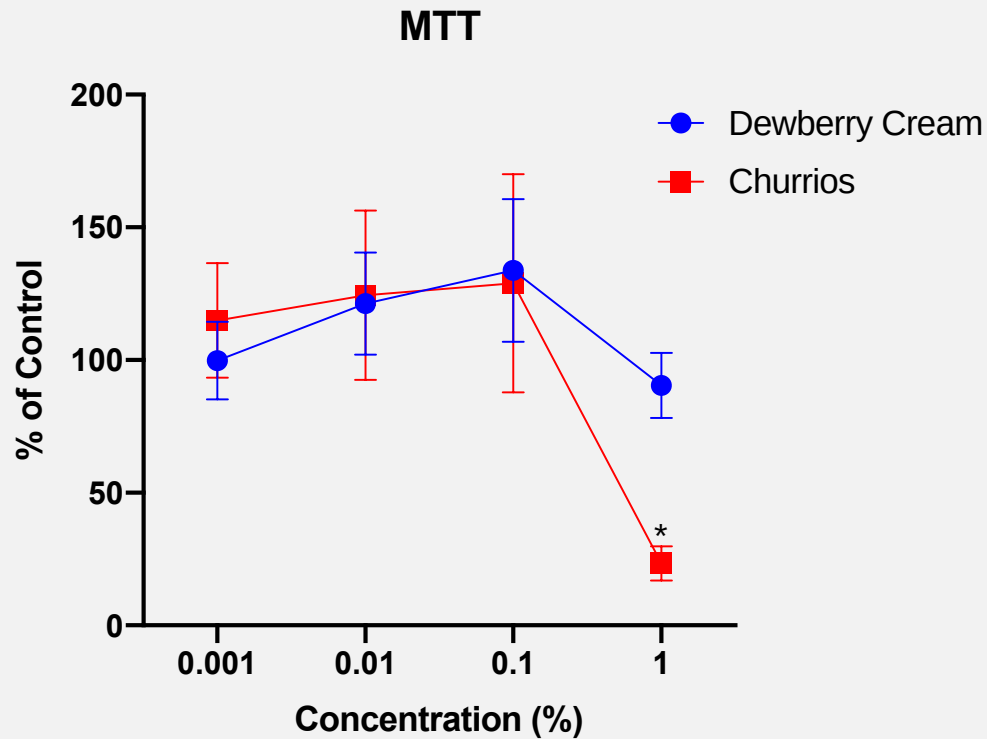
# DEWBERRY CREAM AND CHURRIOS REFILL FLUID CHEMICAL ANALYSIS



# MTT ASSAY

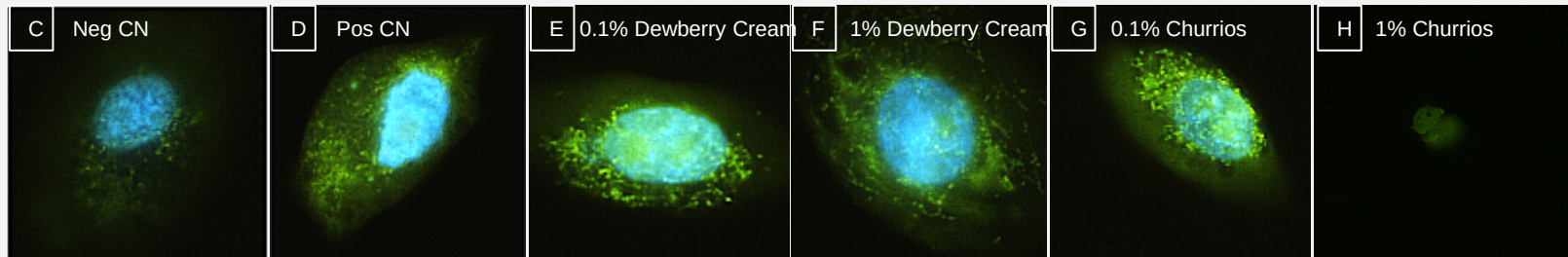
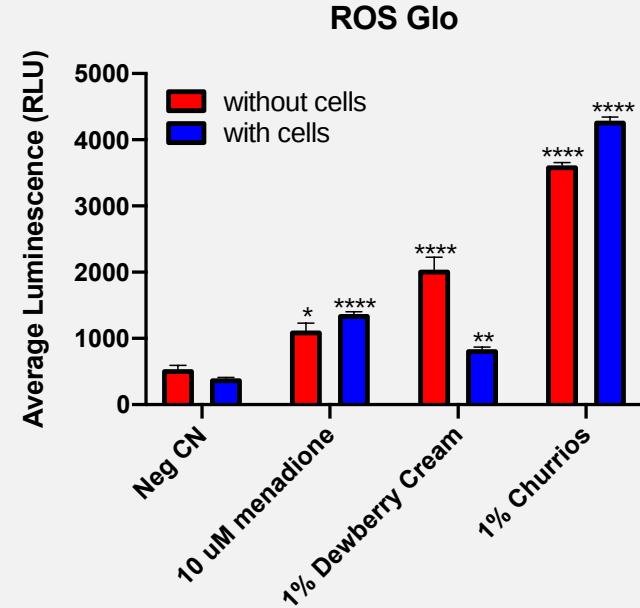


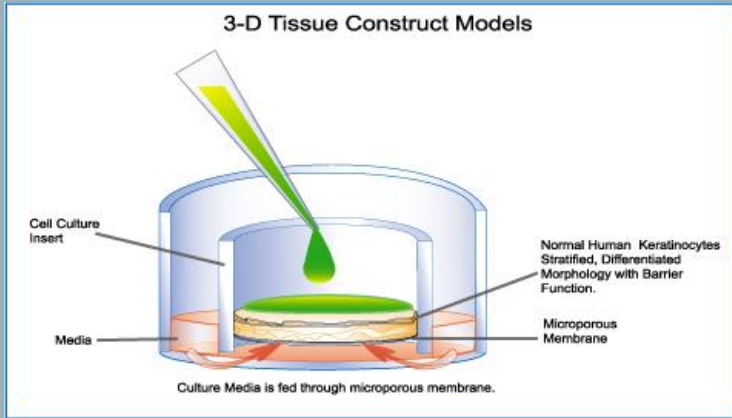
Human Keratinocytes  
CCD 1106 KERTr  
(ATCC® CRL-2309™)



# REACTIVE OXYGEN SPECIES

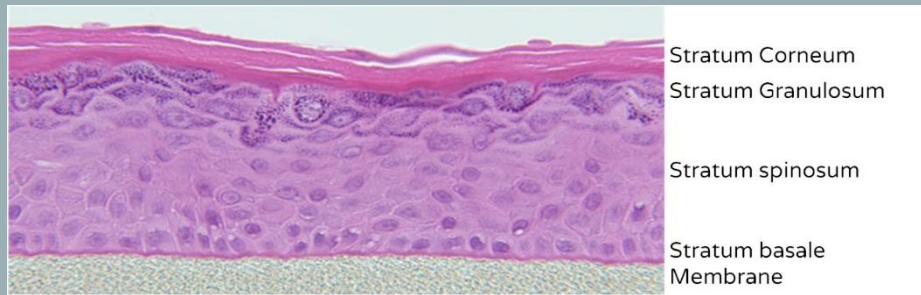
- ROS-Glo™ was used for  $\text{H}_2\text{O}_2$  measurement
- Upon addition of ROS-Glo™ Detection Reagent the luciferin reacts with Luciferase to generate a luminescent signal that is proportional to  $\text{H}_2\text{O}_2$  concentration.
- CellROX© Green for detection of oxidative stress in live cells
- CellROX® Green Reagent is a DNA dye, and upon oxidation, it binds to DNA; thus, its signal is localized primarily in the nucleus and mitochondria





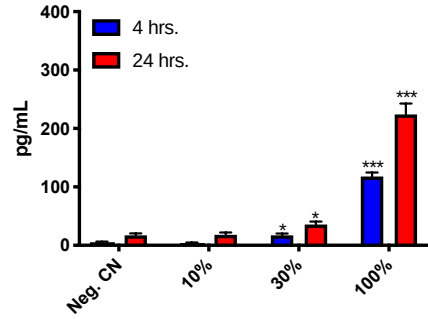
## MATTEK EPIDERM™

- *In vitro* model system for chemical, pharmaceutical and skin care product testing to replace rabbit skin *in vivo* experiments
- Exposure is done at the air liquid interface
- The *In Vitro* EpiDerm™ Skin Irritation Test was followed to determine irritation
- Tissue and culture medium can be assayed.

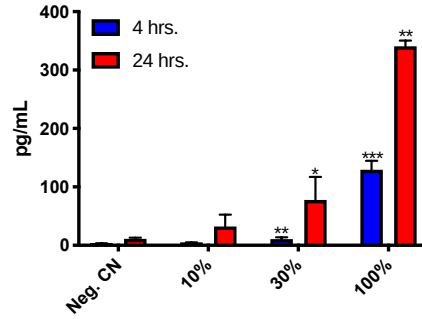


# EPIDERM™ SECRETIONS

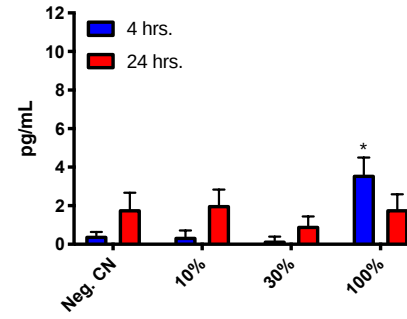
IL-1a Dewberry Cream



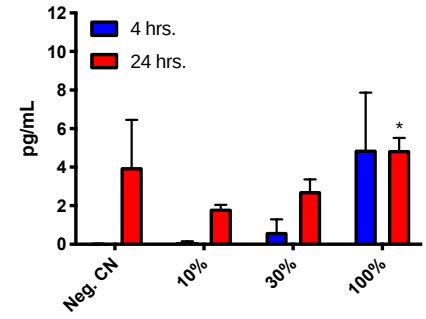
IL-1alpha Churrios



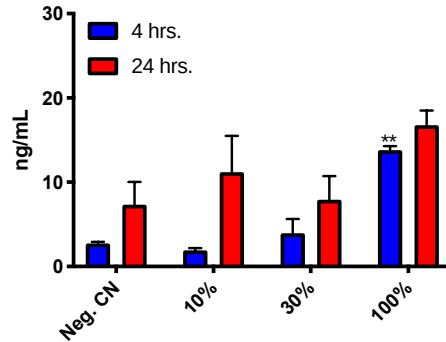
IL-6 Dewberry Cream



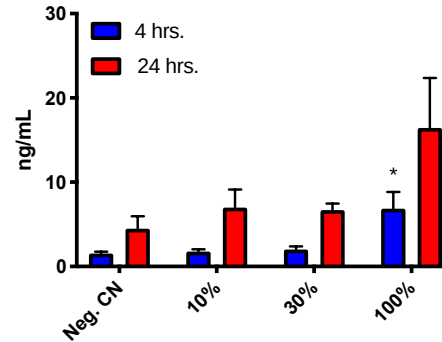
IL-6 Churrios



MMP-9 Dewberry Cream

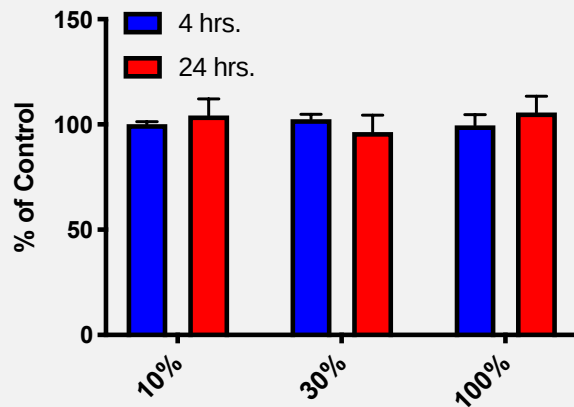


MMP-9 Churrios

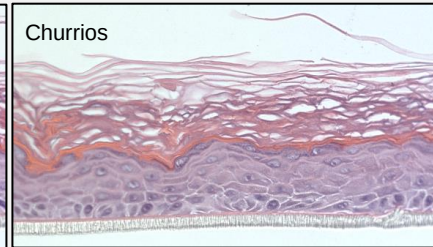
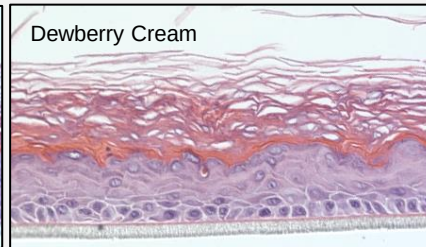
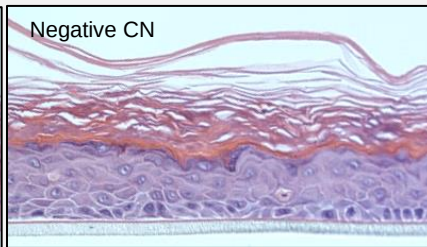
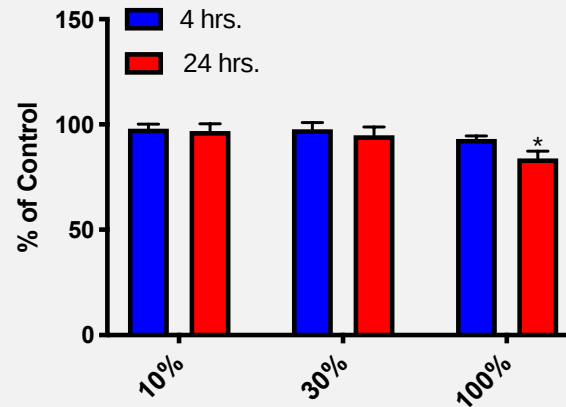


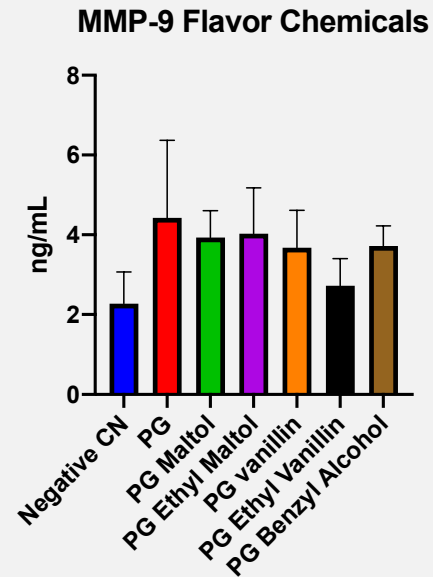
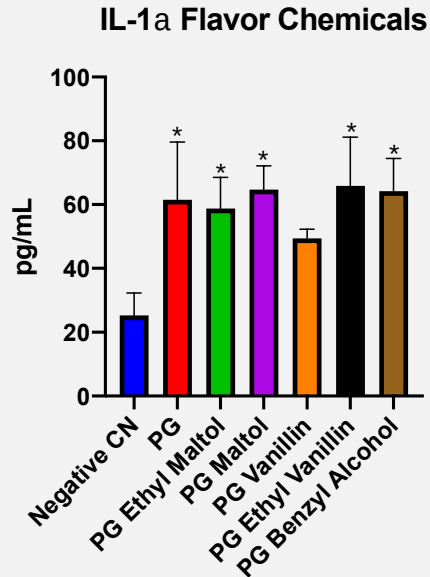
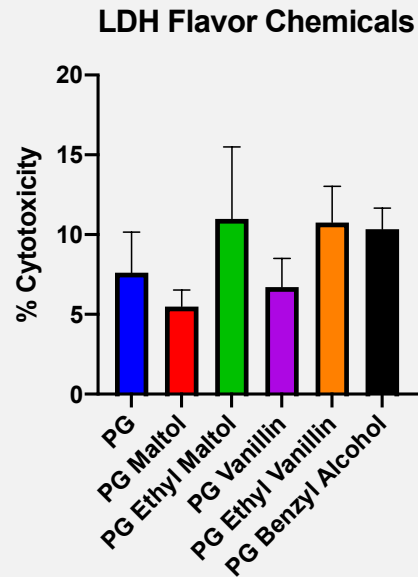
# EPIDERM™ EXPOSED TO REFILL FLUIDS

Dewberry Cream MTT



Churrios MTT





**EPIDERM™ EXPOSED TO LAB MADE  
REFILL FLUIDS**

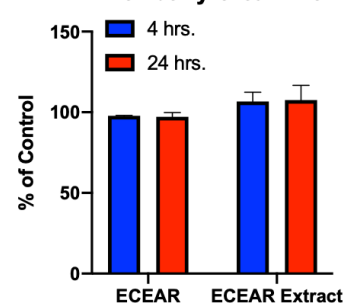
# EPIDERM™ EXPOSED TO ECEAR AND ECEAR EXTRACT

ECEAR treatments did not produce effects in the MTT or LDH assay when Dewberry Cream was used to create ECEAR.

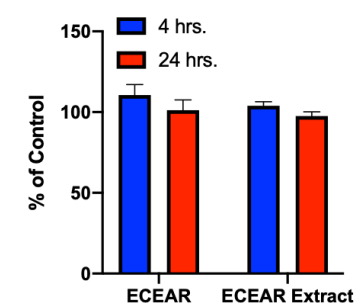
Similar results were obtained with ECEAR made from Churrios, except that there was a small (10%) (non-significant) increase in LDH activity in EpiDerm™ samples treated with ECEAR extracts for 24 hours.

IL-1 $\alpha$  secretion was increased in both Dewberry Cream and Churrios ECEAR extract samples treated for 4 and 24 hours, but significance was observed only in the 24-hour Churrios extract.

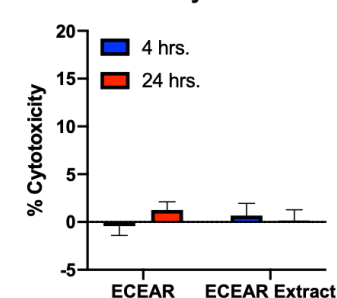
**A MTT Dewberry Cream ECEAR**



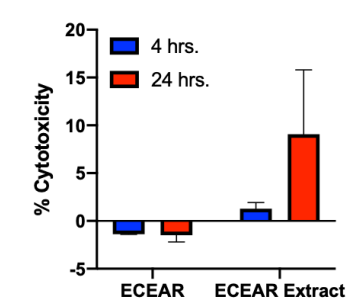
**B MTT Churrios ECEAR**



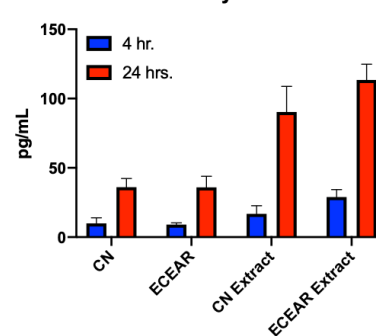
**C LDH Dewberry Cream ECEAR**



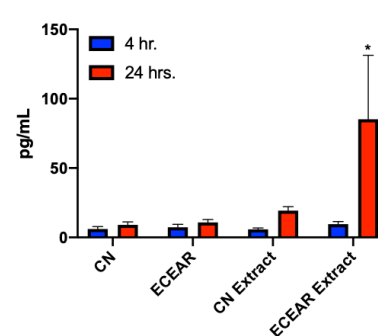
**D LDH Churrios ECEAR**



**E IL-1 $\alpha$  Dewberry Cream ECEAR**



**F IL-1 $\alpha$  Churrios ECEAR**

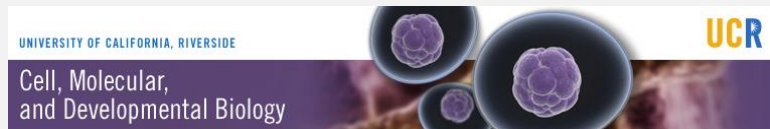


## SUMMARY

- Keratinocytes were exposed to refill fluids to determine cytotoxicity.
  - Churrios was more cytotoxic than Dewberry Cream at 1% concentration and both fluids induced ROS production.
- 3D skin tissues were exposed to refill fluids and lab made fluids.
  - Refill fluids and all lab made refill fluids increased inflammatory markers upon exposure.
  - Inflammation was caused by PG, which is found in all E-liquid products.
- Exposure due to leakage or spills can increase oxidative stress and release of inflammatory proteins.
- The accumulation of ECEAR contributed to inflammation in 3D skin tissues.
- Longer and increased exposures should be done to understand a full range of responses to ECEAR.

# ACKNOWLEDGMENTS

- DR. PRUE TALBOT
- TALBOT LAB
- DR. JIM PANKOW, DR. WENTAI LUO, KEVIN MCWHIRTER
- TAMMY NGUYEN
- FUNDING
  - TRDRP GRANT #26IR-0018
  - TRDRP THIRDHAND SMOKE CONSORTIUM #20PT-0184
  - ARMENIAN ENGINEERS AND SCIENTISTS OF AMERICA SCHOLARSHIP
- SOT DERMAL TOX SPECIALTY SECTION



# **Mechanisms Contributing to Skin Inflammatory Pathology Following Exposure to Environmental Pollutant Benzo(a) Pyrene in Psoriatic Mouse Model**

Swati Sharma<sup>1</sup>, Joshua A Klein<sup>1</sup>, Satyendra K Singh<sup>1</sup>, Dinesh G Goswami<sup>2</sup>,  
Leah N Braucher<sup>1</sup>, Holly N Wright<sup>1</sup>, Erica L Noland<sup>1</sup>; Rajesh Agarwal<sup>3</sup>; Neera  
Tewari-Singh<sup>1</sup>

1. Michigan State University, East Lansing, MI; 2. Texas Tech University Health Sciences  
Center, El Paso, TX; and 3. University of Colorado<sup>3</sup> Denver, Aurora, CO

# Background

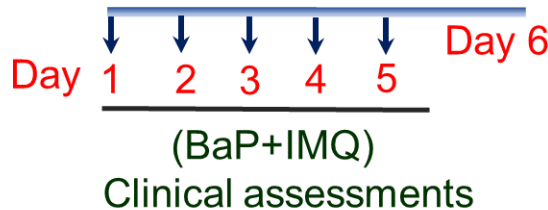
- Environmental chemicals like polycyclic aromatic hydrocarbons (PAHs) are a major concern as it could contribute to the pathophysiology of several chronic inflammatory skin diseases like atopic dermatitis and psoriasis.
- Benzo[a]pyrene (BaP), the main source of atmospheric PAH, and is generated mainly from cigarette smoke, wood-burning and automobile exhaust.
- BaP is known as one of the aggravating factor in inflammatory skin diseases which is characterized by neutrophil infiltration and induction of other proinflammatory cyto/chemokines.
- The toxicity of PAHs is known to affect a variety of organs and cells via the aryl hydrocarbon receptor (AhR).
- Information on its dermal absorption and effects on human skin tissue is limited, and its mechanism of action is unknown.

# Study Design

## Study Design 1: (BAP+IMQ)

**62.5mg IMQ and 64  $\mu$ g BaP in 50  $\mu$ L acetone  
topically once daily alone or in combination**

Dorsal surface of mice  
shaved 2 days before  
exposure

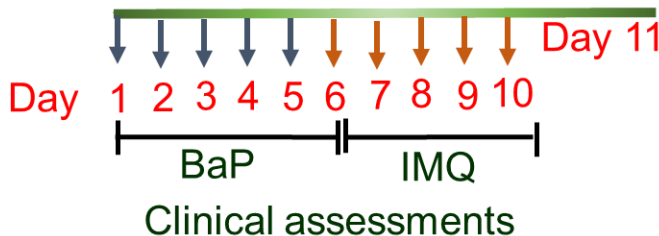


Mice sacrificed and the skin  
tissue was collected for  
analysis

## Study Design 2: BAP+IMQ

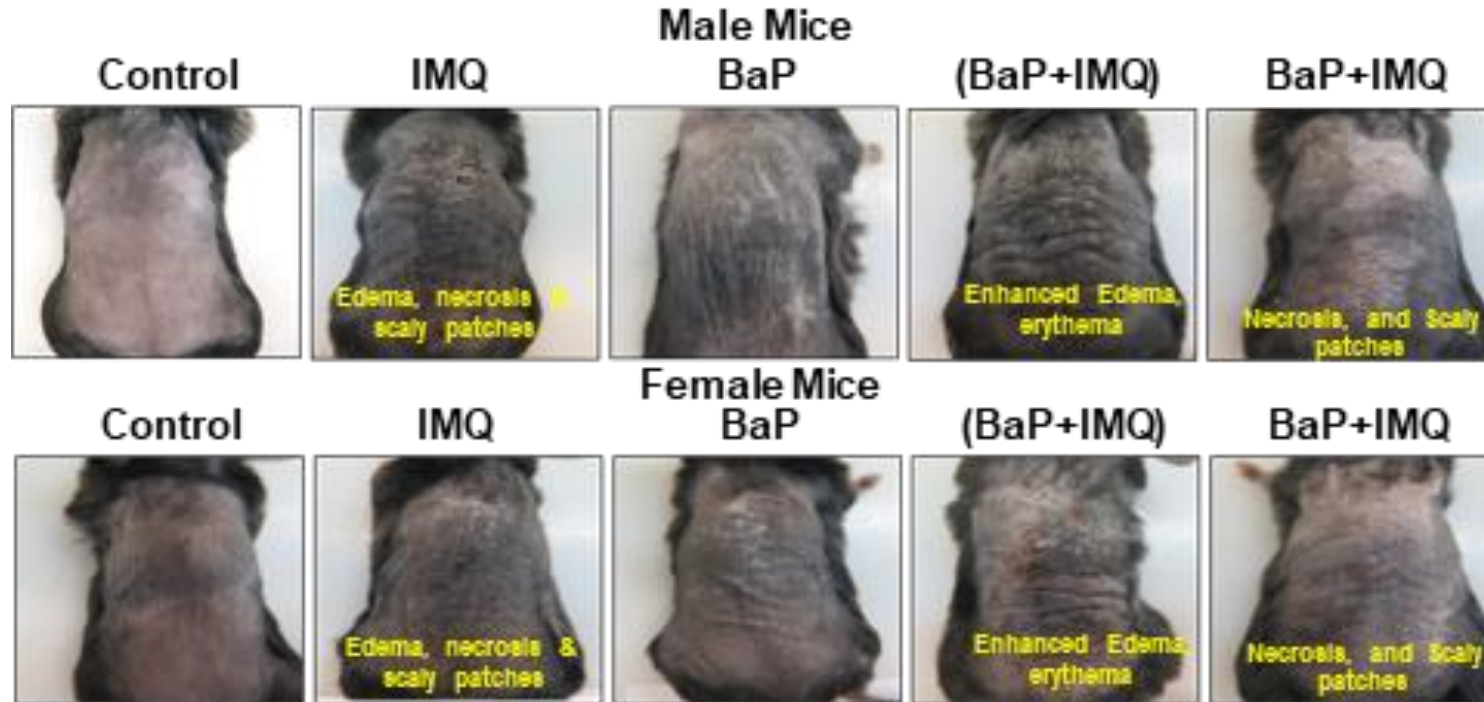
**64  $\mu$ g BaP in 50 $\mu$ L acetone once daily for 5 days  
followed by 62.5mg IMQ once daily for 5 days.**

Dorsal surface of mice  
shaved 2 days before  
exposure

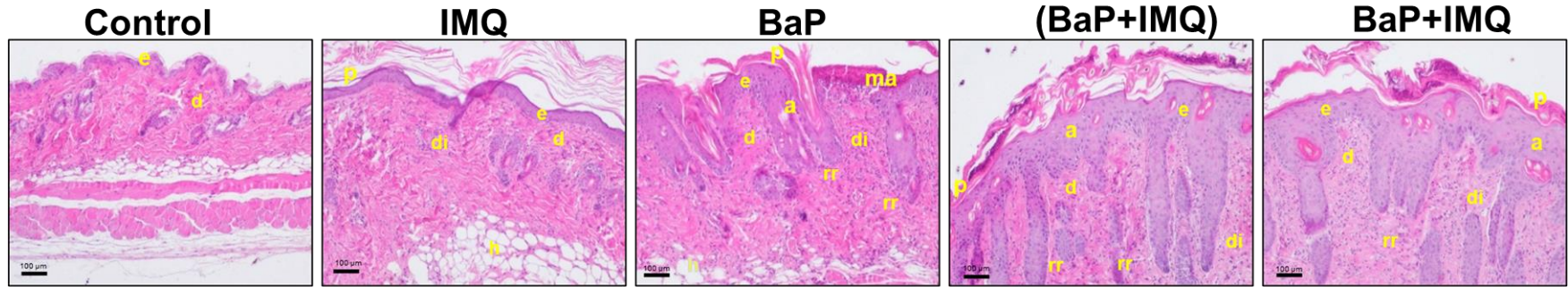


Mice sacrificed and the skin  
tissue was collected for  
analysis

# Effect of BaP Exposure on IMQ-induced psoriatic skin inflammation in C57BL/6 mice

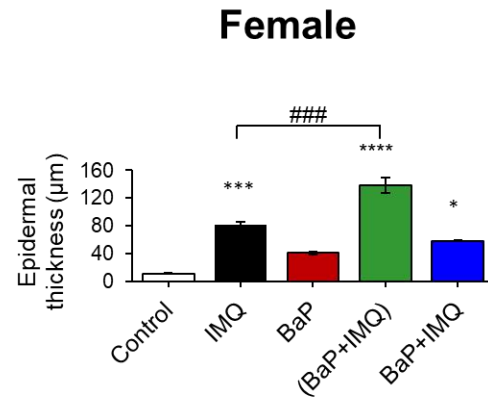
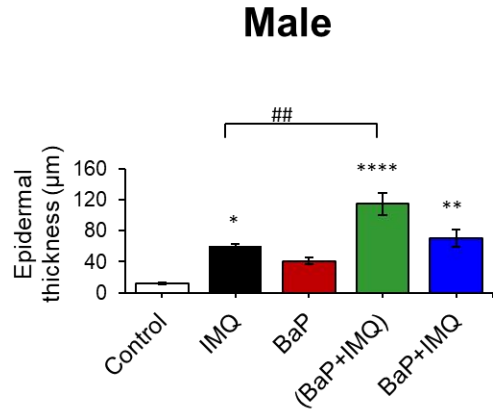
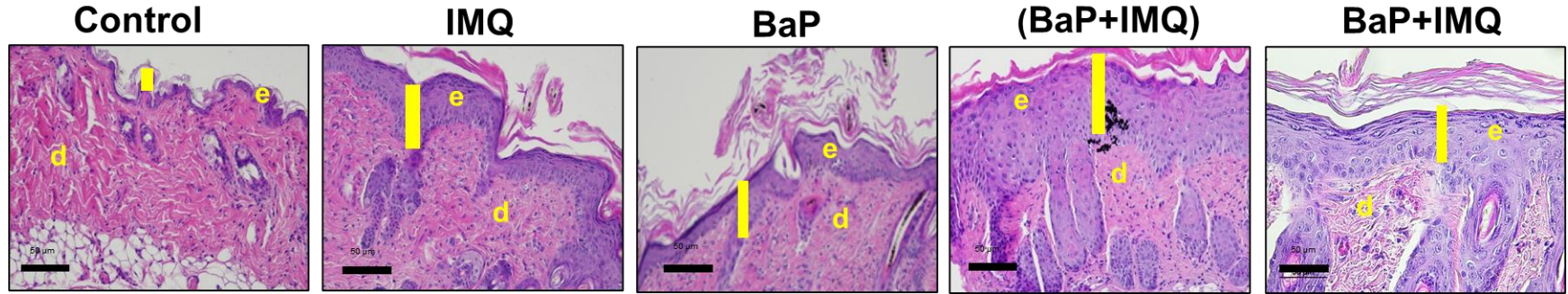


# Effect of BaP on IMQ- Induced Histopathological changes



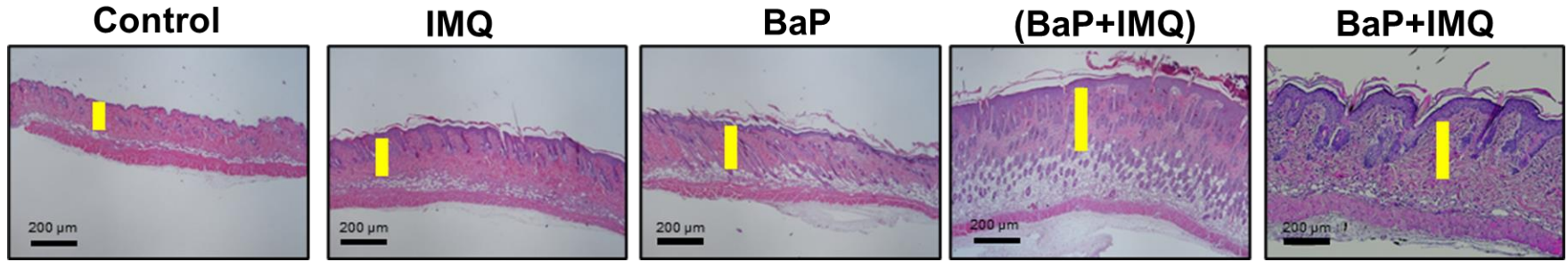
**Representative pictures showing histopathological changes in male C57BL/6 mice (10X magnification), rr, elongated rete ridges; a, acanthosis; di, dermal infiltrates; p, parakeratosis; ma, micro abscess; e, epidermis; d, dermis; h, hypodermis.**

# Effect of BaP on IMQ- Induced Epidermal Thickness

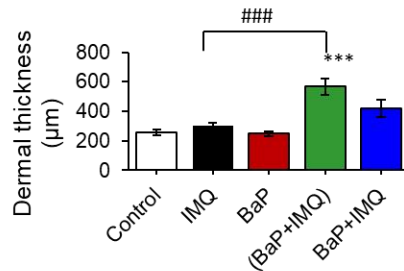


\*,  $P < 0.05$ ; \*\*,  $P < 0.01$ ; \*\*\*,  $P < 0.0005$ ; \*\*\*\*,  $P < 0.0001$  compared to control; ##,  $P < 0.01$ ; ###,  $P < 0.0005$  compared to IMQ

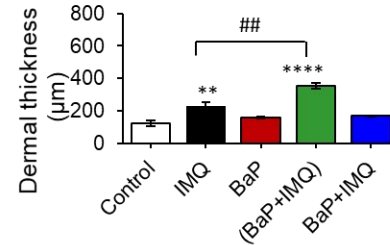
# Effect of BaP on IMQ- Induced Dermal Thickness



Male

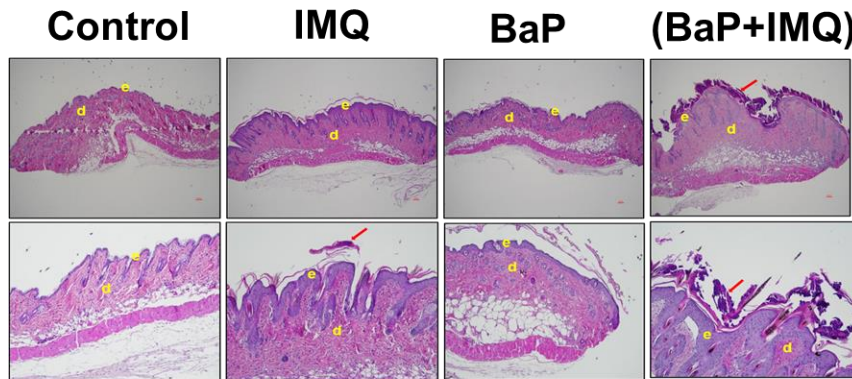


Female



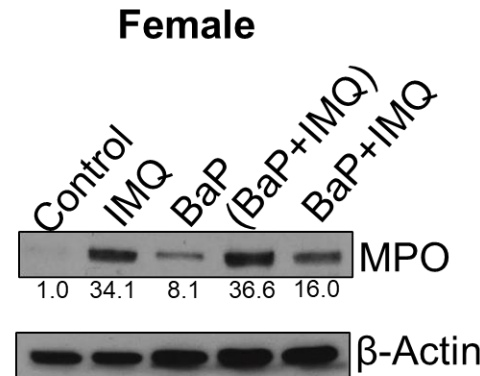
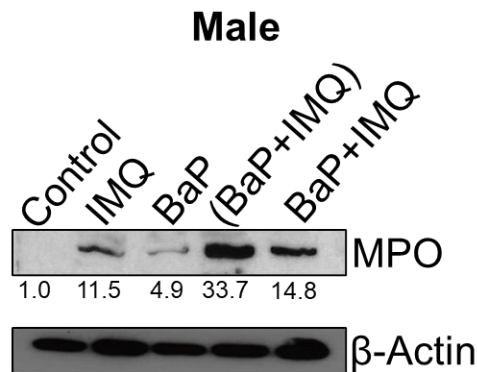
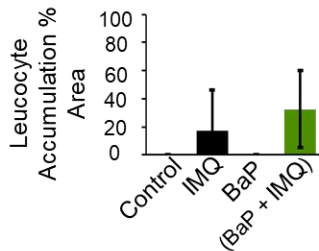
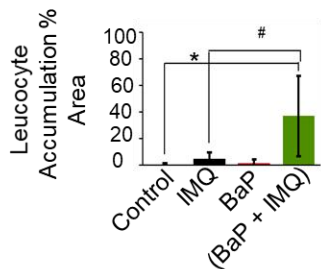
**\*\***,  $P < 0.01$ ; **\*\*\***,  $P < 0.0005$ ; **\*\*\*\***,  $P < 0.0001$  compared to control; **##**,  $P < 0.01$ ; **###**,  $P < 0.0005$  compared to IMQ

# Effect of BaP Exposure on IMQ-Induced Skin Leucocyte Accumulation



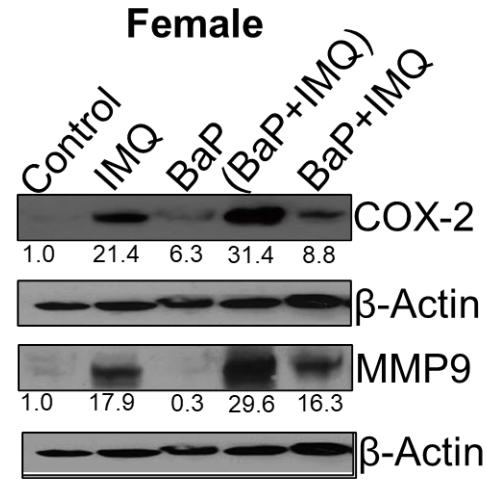
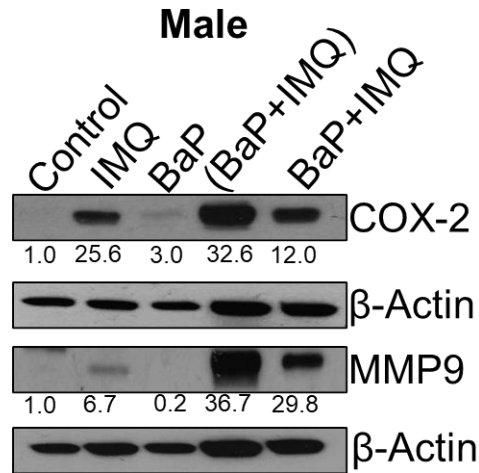
Male

Female



\*,  $p < 0.05$  compared to control; #,  $p < 0.05$  compared to IMQ

# Effect of BaP Exposure on the Expression of Inflammatory Markers



# Summary

- Exposure of BaP causes an increase in inflammation in mice and aggravates IMQ-induced histopathological changes.
- BaP exposure enhances skin edema, necrosis, and dermal and epidermal thickness in both male and female groups of psoriatic mouse model.
- Protein expression of inflammatory markers like COX-2 and MMP9 and myeloperoxidase(MPO) was elevated in both male and female of BaP exposed psoriatic mouse model.
- Further mechanistic studies and metabolomics analysis in the skin tissue is being carried out to determine the changes in metabolites and identify the pathways involved.

# Conclusion

- Present study reveals that exposure of BaP in IMQ-induced Psoriatic mouse model could activate inflammatory pathways by elevating the expression of inflammatory markers and further elevate the skin inflammation.
- Further mechanistic studies are needed to evaluate the pathways involved in BaP-induced exacerbation of psoriasis.

# Acknowledgements

- This work is supported (in part) by a grant from the Skaggs Scholars Program at the University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences.
- Startup funds from the Department of Pharmacology and Toxicology, Michigan State University to Dr. Neera Tewari-Singh.

# Closing Remarks

## Photos

thank  
=YOU=



Dermal Toxicology Specialty Section  
OF THE SOCIETY OF TOXICOLOGY

