

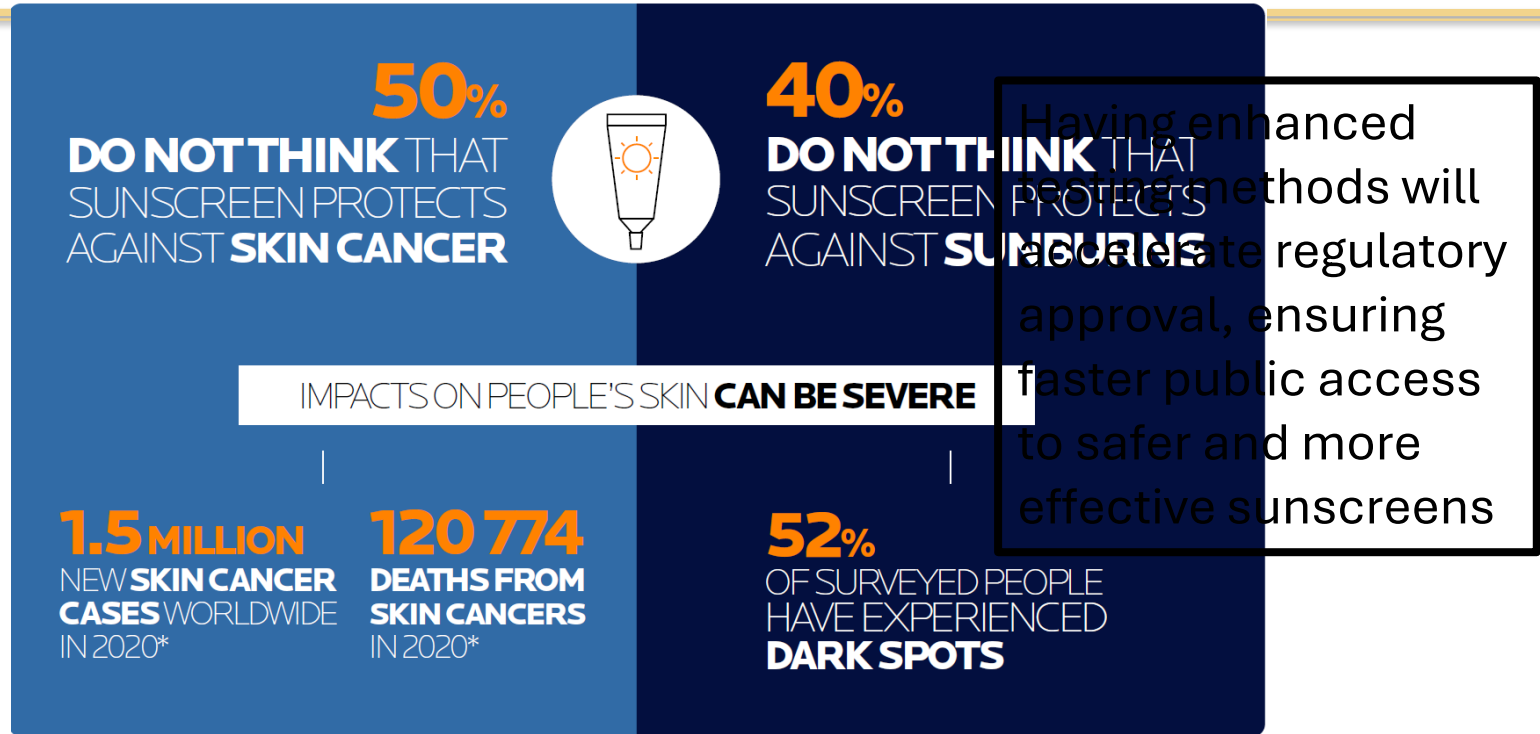
# UV & Me: Sun Safety Sleuths

*America's Got Regulatory Science Talent*  
Competition 2024

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# Importance of Sunscreen in Public Health



Sources: 1. Happi 2. Skin Cancer Foundation and 3. American Academy of Dermatology

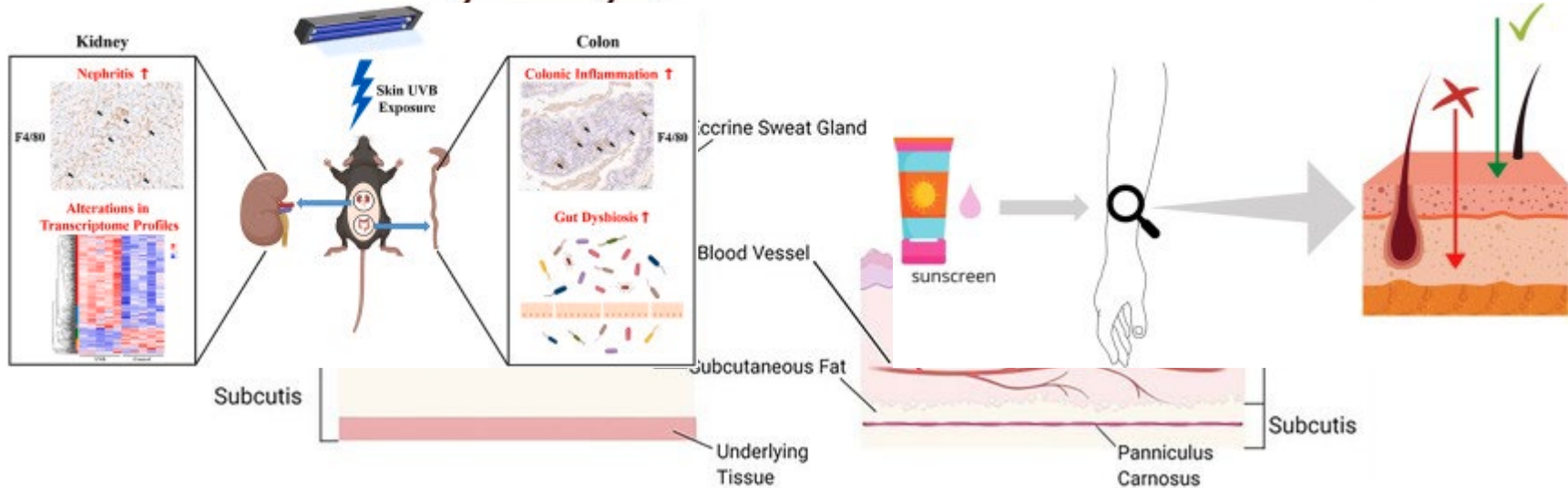


# Focus on Epidermal, Non-Systemic Sunscreen Exposure

## Mouse models fall short for non-systemic testing

Systemic Exposure Pathway  
(where mouse models are relevant)

Mouse (~25 $\mu$ m)  
Non-systemic, Epidermal Exposure  
Pathway



# Focus on Epidermal, Non-Systemic Sunscreen Exposure

Organotypic cultures are uniquely suited for non-systemic  
sunscreen testing

Mouse Models Limitations	Organotypic Culture Advantages
<b>Irrelevant for non-systemic exposure:</b> When active ingredients don't penetrate the skin barrier, systemic testing isn't needed. <b>Low predictive value for human skin:</b> Mouse skin differs structurally and functionally from human skin. <b>Ethical concerns:</b> The ethical implications of animal testing highlight the need for alternative methods	<b>Human-relevant physiology:</b> Mimics human skin structure and function. <b>Efficient and ethical:</b> Reduces time, cost, and reliance on animal testing. <b>Focus on dermal safety:</b> Directly evaluates skin-related outcomes, like barrier integrity and irritation.

Our proposed model addresses these challenges by exclusively focusing on exposure to the epidermis.



# FDA Regulatory Science Focus Areas

## **Novel Technologies to Replace, Reduce, and Refine Animal Testing:**

1. “We're committed to ensuring that our regulatory approaches are flexible and adaptable to incorporate new technologies and methods that can improve our ability to assess safety and efficacy.” – Former FDA Commissioner Stephen Hahn, MD
2. “The FDA is dedicated to reducing animal testing and promoting the use of alternative methods that can provide more accurate and relevant results for human health.” - FDA’s, “Alternative Methods for Animal Testing”

## **Product Safety Surveillance:**

1. “We're working to strengthen our product safety surveillance program to better identify and respond to potential safety issues with sunscreens and other topical products.” -Former FDA Commissioner Stephen Hahn, M.D.



# Comparing Organotypic Cultures (OTC) with Mouse Models

Organotypic skin models offer a viable alternative. They mimic the structure and function of human skin, providing a more physiologically relevant environment for testing.

Metric	Mouse Models	Organotypic Cultures
Timeline	6-24 months	2 months
Relevance to Human Skin	Low	High
Ethical Considerations	Animal-testing required	Animal free
Cost	Expensive	Cost-Efficient

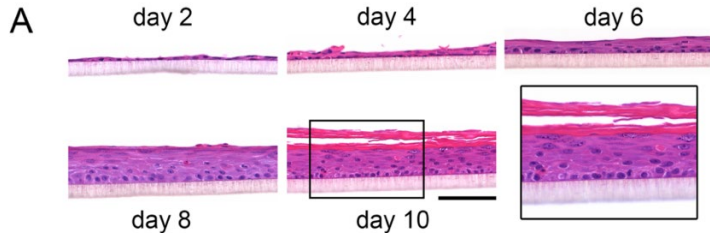


# OTCs are Efficient Alternatives to Animal Models for Sunscreen Regulation

1

## How to Generate OTCs

OTCs will be generated using immortalized keratinocyte cell line N/TERT-2G.



2

## Exposure to Sunscreen Active Ingredients

Cultures will be exposed to varying concentrations of active ingredients over acute (24 hours) and chronic (7-day exposure) periods

3

## Evaluation of Sunscreen Exposure Impact

Barrier function will be evaluated, and cultures will be harvested for mRNA- and protein-level analyses.

Smits *et al.*, 2017



# OTCs are Highly Translatable and Tractable

## Improved Skin Efficacy Testing

- a. These cultures are sophisticated, *in vitro* models **replicating complex interactions** within **human skin tissue**.
- b. These models allow us to **simulate real-world conditions**, such as sunscreen exposure, **more accurately** than current animal-based systems.

## Studying Skin Barrier Integrity

- a. Using organotypic cultures that replicate both healthy and diseased skin allows us to explore how **different active ingredients at different concentrations affect critical features of the skin**, such as **stratification** and **barrier function**, providing insight into skin barrier integrity.

## Future Research on Skin Health

- a. TUNEL Assays for Skin Cancer Research: **detects DNA fragmentation**, a key indicator of UV-induced apoptosis, allowing for the **evaluation of sunscreen efficacy** in **preventing cell death** and **potential cancer risk**





# OTCs Address FDA Focus Areas

## **Novel Technologies to Replace, Reduce, and Refine Animal Testing:**

The use of organotypic skin cultures directly contributes to the FDA's goal of reducing the reliance on animal models. By replicating human skin physiology more closely than animal models, these cultures offer a more predictive and ethical approach to currently used methods.

The transition to human-relevant, non-animal models is essential for improving the accuracy of non-clinical studies, particularly in products like sunscreen with UV filters where safety evaluations must closely mirror human responses.

## **Product Safety Surveillance:**

By identifying acceptable UV filter levels *in vitro*, we can predict potential skin irritations and allergic reactions before products reach the consumer market. This model provides an additional layer of safety oversight, enabling sunscreen manufacturers to ensure that their products meet regulatory standards for safety without the need for extensive animal testing.



# References

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2. FDA's Nonprescription Sunscreen Drug Products — Safety and Effectiveness Data
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5. Smits JPH, Niehues H, Rikken G, van Vlijmen-Willems IMJJ, van de Zande GWHJF, Zeeuwen PLJM, Schalkwijk J, van den Bogaard EH. Immortalized N/TERT keratinocytes as an alternative cell source in 3D human epidermal models. *Sci Rep*. 2017 Sep 19;7(1):11838. doi: 10.1038/s41598-017-12041-y. PMID: 28928444; PMCID: PMC5605545.

