

Probing the Skin with ToF-SIMS: Skin Lipid Composition Upon Exposure to Metal Allergens

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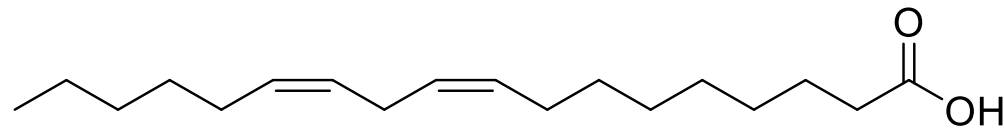
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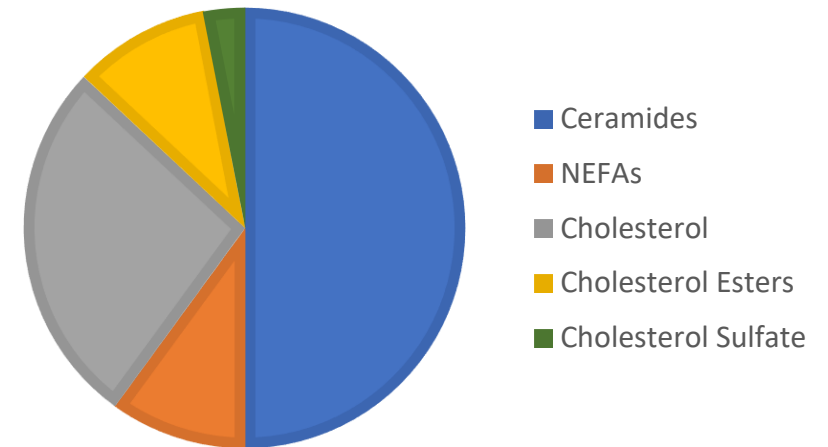
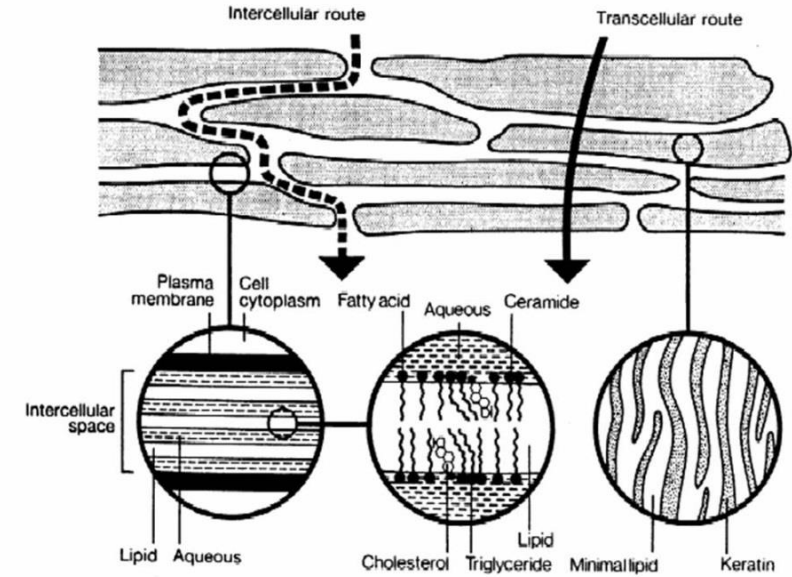


INTRODUCTION | LIPIDS IN SKIN

- Epidermis is a lipid-rich environment
- Huge variability in lipid composition depending on many factors
- Lipid changes in many skin diseases are known



Linoleic Acid
(a polyunsaturated fatty acid)



Lipid composition of healthy **stratum corneum** by dry weight as a percentage of total lipid content.

INTRODUCTION | METAL ALLERGENS



Nickel (II) sulfate
hexahydrate
($\text{NiSO}_4 \cdot 6\text{H}_2\text{O}$)

CAS: 10101-97-0

14.5%



Cobalt (II) chloride
hexahydrate
($\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$)

CAS: 7791-13-1

2.2%



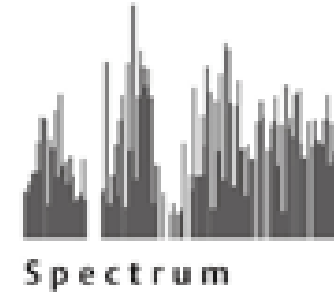
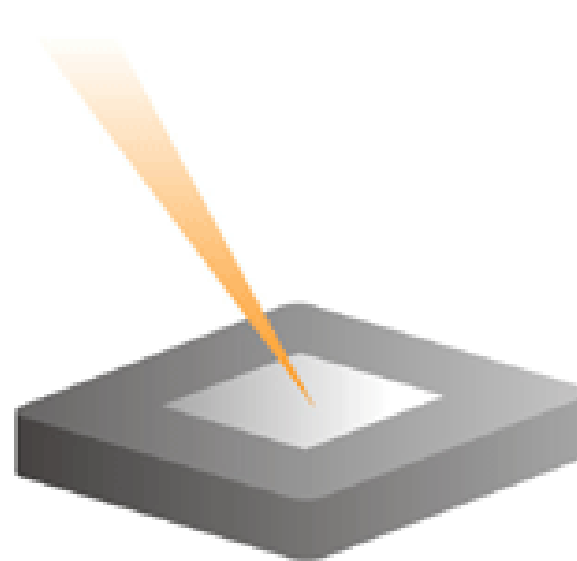
Chromium (III)
chloride hexahydrate
($\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$)

CAS: 10060-12-5

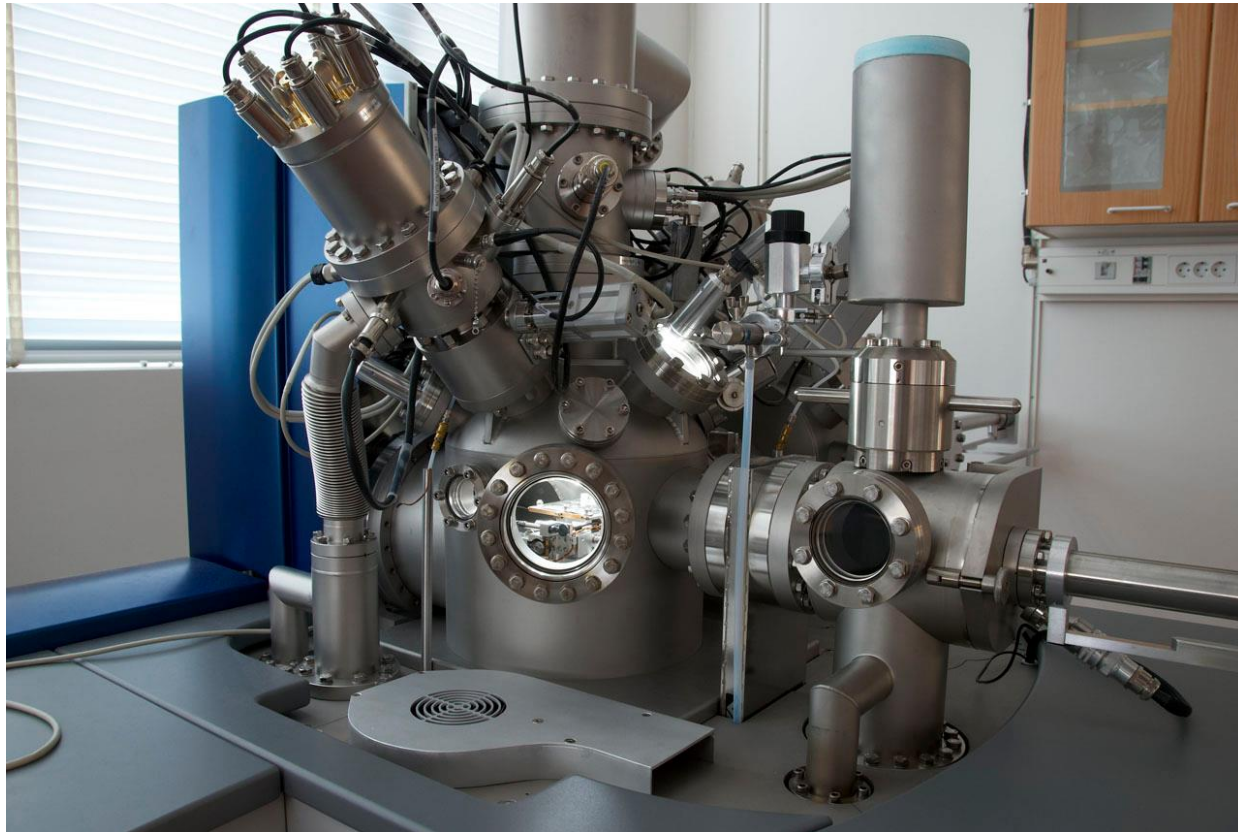
0.8%

INSTRUMENTATION | ToF-SIMS

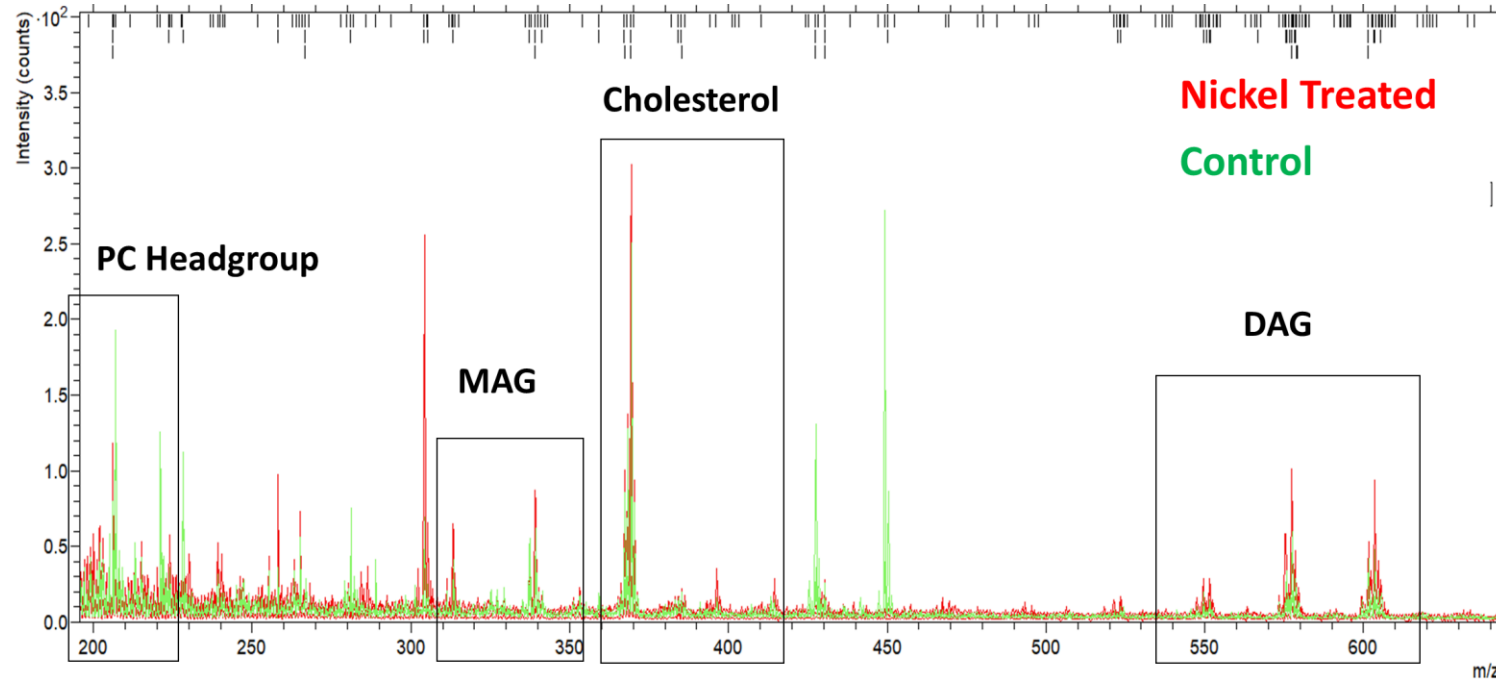
- Time-of-Flight Secondary Ion Mass Spectrometry
- *Ex vivo* Human Skin (female breast tissue)



INSTRUMENTATION | ToF-SIMS



TYPICAL DATA | NICKEL TREATED

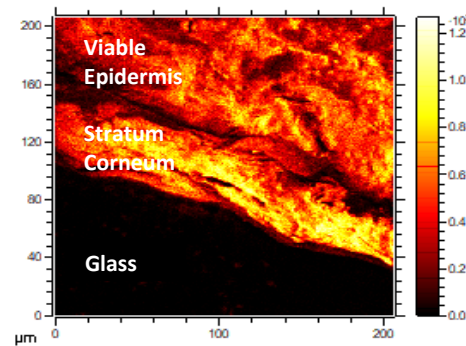


Overlaid m/z spectra of *ex vivo* human skin untreated (green) or treated with nickel(II) sulfate hexahydrate for 24 hr at 32°C (red). Phosphatidylcholine (PC) headgroup, monoacylglycerol (MAG), cholesterol and diacylglycerol (DAG) fragment regions are highlighted.

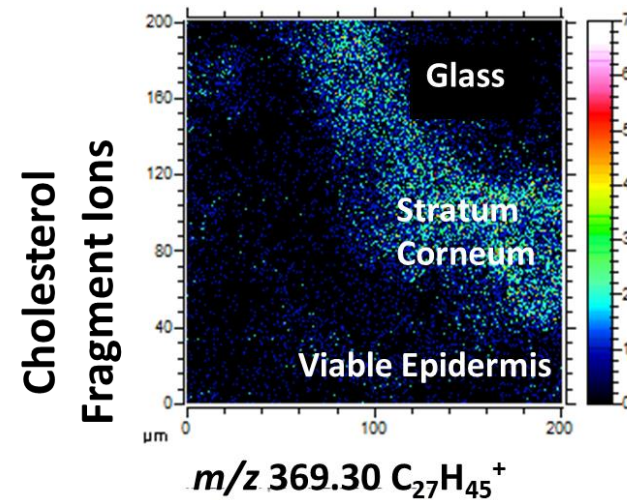
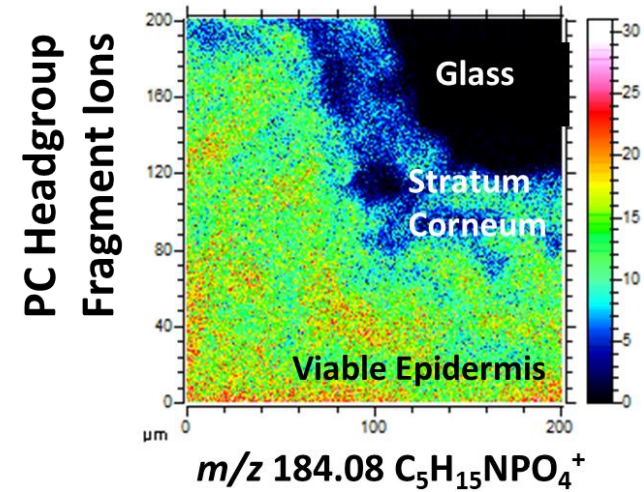
DATA ANALYSIS

Analysis possible based on mass/charge ratio (m/z)

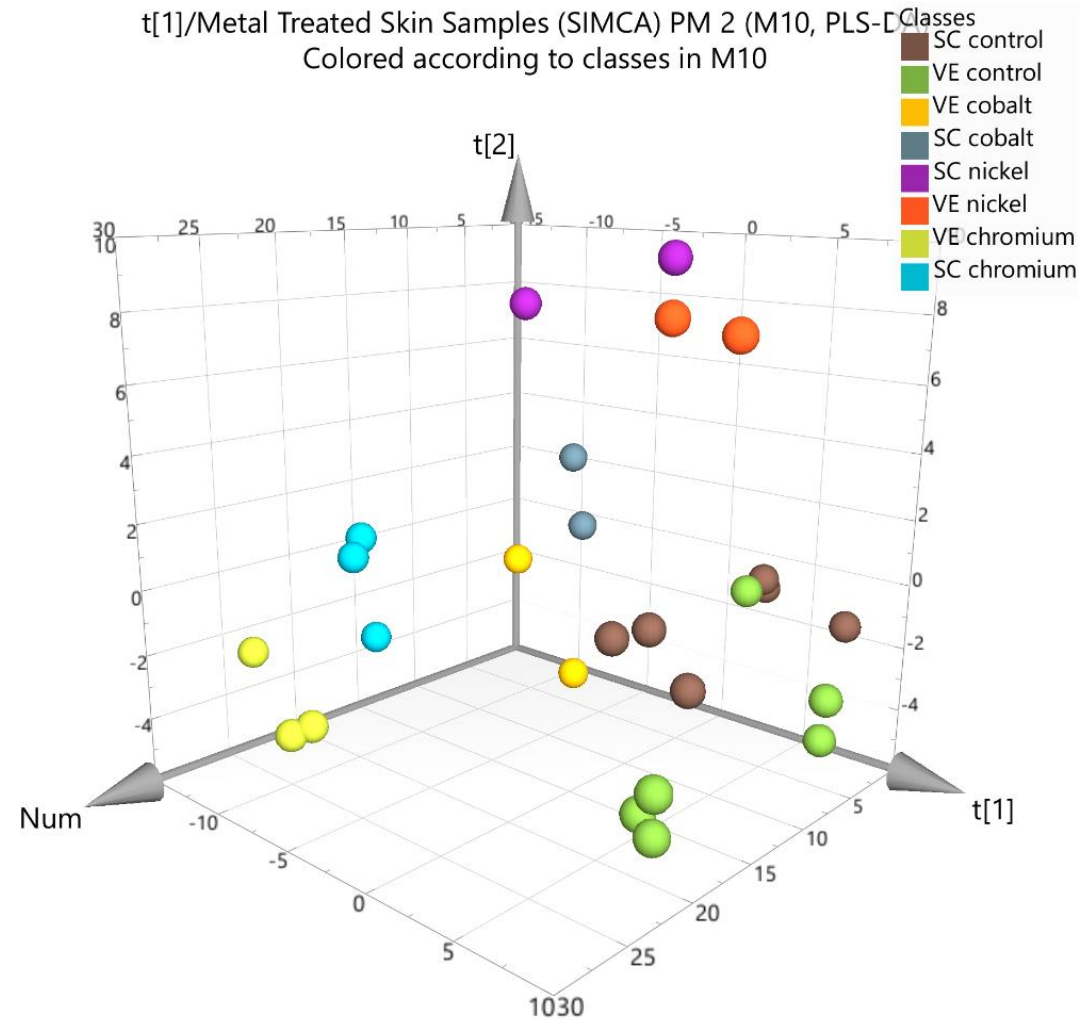
- Total ion intensity
- Selected ion intensity



Ex vivo human skin (control sample, 200 μM²) coloured by total ion intensity showing the stratum corneum and viable epidermis.



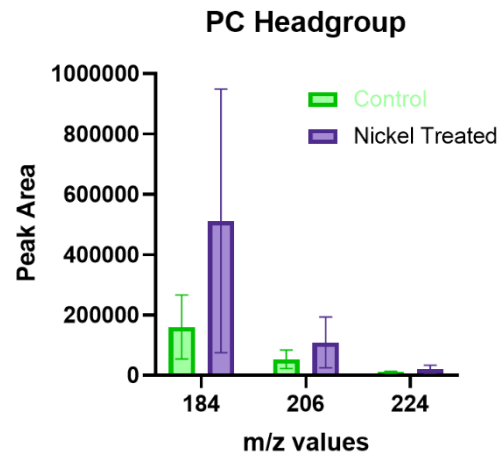
MULTIVARIATE ANALYSIS



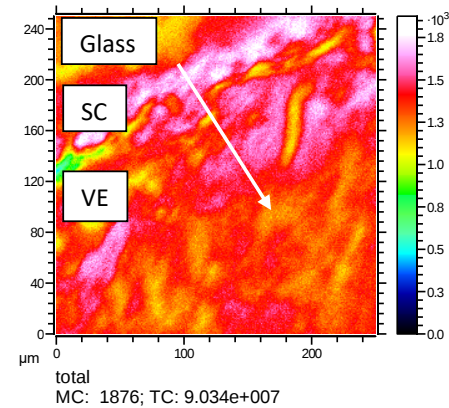
SC: Stratum Corneum
VE: Viable Epidermis

RESULT | LIPID IONS IN SKIN

Viable Epidermis

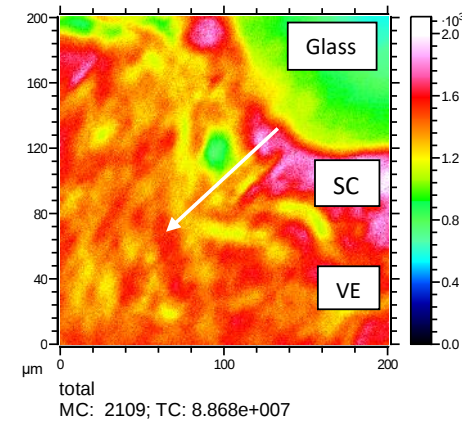


Control (Untreated) Skin

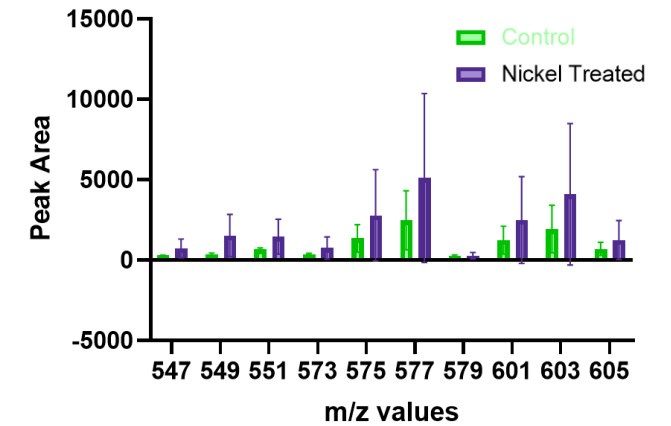


Nickel-Treated Skin

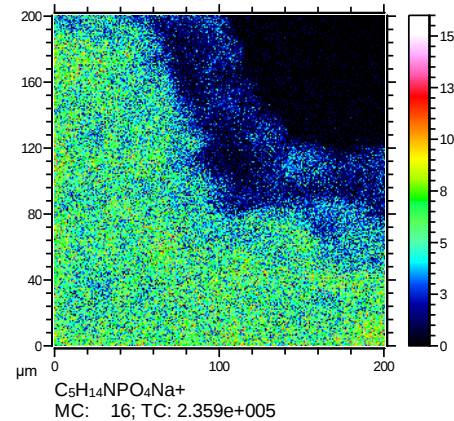
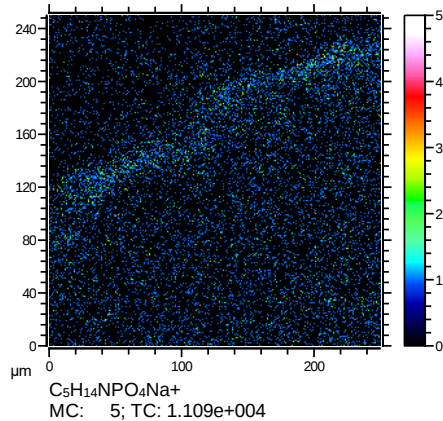
A. Total



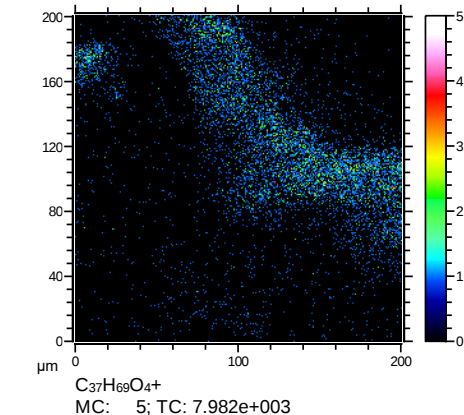
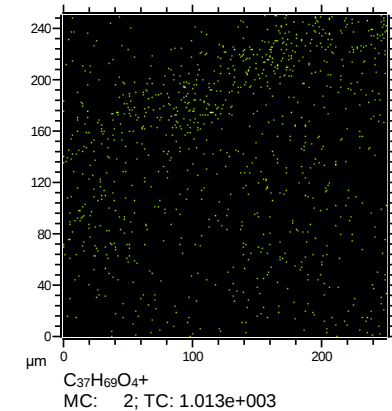
DAG



PC Headgroup Example – m/z 206



DAG Example – DAG 34:1 – m/z 577



RESULT | DIACYLGLYCEROLS IN METAL-TREATED SKIN

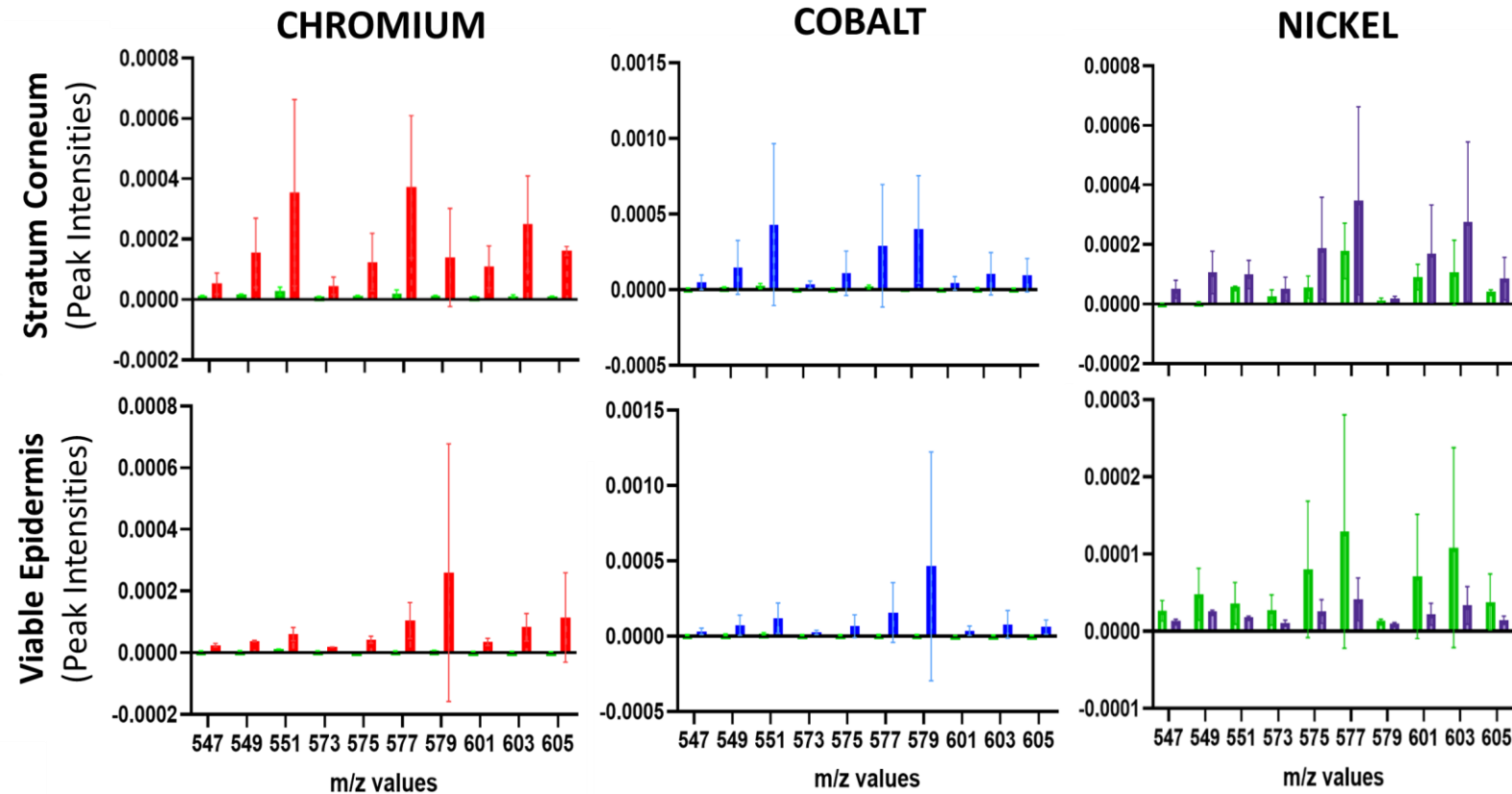


Figure 6. Quantification of diacylglycerol (DAG) fragments from chromium (*red*), cobalt (*blue*) and nickel (*purple*) treated skin compared to untreated (*green*) stratum corneum (top) and viable epidermis (bottom)

RESULT | SUMMARY TABLE

	PC headgroup	Cholesterol	MAG	DAG	Fatty Acids	Sphingomyelin	Phospholipids
<u>Stratum Corneum</u>							
Nickel	NS	NS	NS	NS	↑	↑	NS
Chromium	NS	NS	NS	↑	--	--	--
Cobalt	NS	↑	NS	↑	--	--	--
<u>Viable Epidermis</u>							
Nickel	NS	NS	↓	↓	NS	↑	NS
Chromium	NS	NS	NS	↑	--	--	--
Cobalt	NS	↑	↑	NS	--	--	--

Table X1. Summary of the changes that occur when skin samples are treated with metal ions *ex vivo*

NS: not statistically significant using an unpaired corrected Welch t-test.

SUMMARY | FUTURE WORK

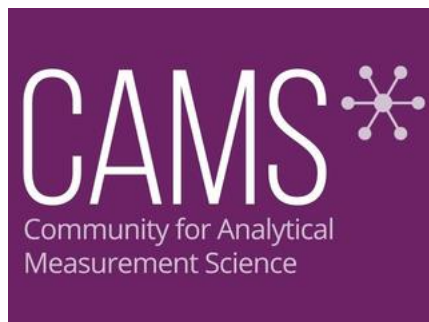
Metal allergens induce changes to the lipid composition of *ex vivo* human skin. Our future plans will:

- Expand the range of allergens
- Expand the range of lipids (e.g. ceramides)
- Explore mechanisms for the observed changes

ionTOF



Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin



UNIVERSITY OF GOTHENBURG

THANK YOU FOR LISTENING

Ms. Sophie Knox, BSc (Pharm)

Dr. Lina Hagvall

University of Gothenburg, Sweden

Dr. Per Malmberg

Chalmers Technological University, Sweden

Prof. Ann-Therese Karlberg

Skin Tissue Donors – we are very grateful