lipotype
Lipidomics for a better life

WHITE PAPER SERIES

White Paper: Lipotype Skin Lipidomics

The lipid composition of human skin is essential for its function. However, the simultaneous quantification of a wide range of *stratum corneum* and sebaceous lipids is not trivial. We developed and validated a quantitative high-throughput shotgun mass spectrometry-based platform for lipid analysis of tape-stripped skin samples. Lipotype analyzes also other types of skin samples, from monolayers to 3D models. It is now easy to investigate how the healthy skin lipidome is composed, how it changes in diseases or upon intervention with a drug or a cosmetic product. This lipidomic data can be used for cosmetic claim support, topical drug development and personalized cosmetics. More details about this method and its application can be found in:

Sadowski T. et al. "Large-scale human skin lipidomics by quantitative, high-throughput shotgun mass spectrometry." ***Scientific Reports*** **2017, doi: 10.1038/srep43761**

Ultra-broad coverage

Lipotype Shotgun Skin Lipidomics provides a broad coverage of *stratum corneum* and sebaceous lipids. Our analysis routinely covers 16 individual lipid classes (including all 12 ceramide sub-classes, but also triglycerides or cholesterol esters) on the level of lipid species (e.g. TAG 54:0;0) or subspecies (e.g. AS 10:1;2/16:0;1). With our method, in tape-stripped skin samples we typically identify and quantify 150 – 250 individual lipids

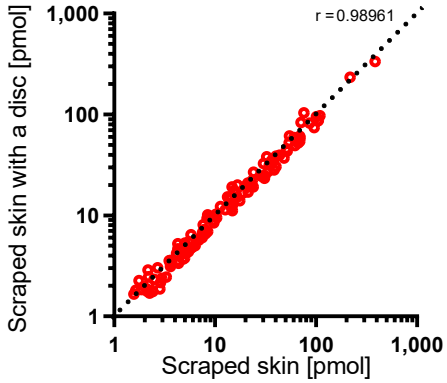
Lipid classes covered by our method in skin samples

NdS	-	non-hydroxy-dehydrosphingosine	EOdS	-	omegahydroxy-dehydrosphingosine
NS	-	non-hydroxy-sphingosine	EOS	-	omegahydroxy-sphingosine
NP	-	non-hydroxy-phytosphingosine	EOP	-	omegahydroxy-phytosphingosine
NH	-	non-hydroxy-6-hydroxy-sphingosine	EOH	-	omegahydroxy-6-hydroxy-sphingosine
AdS	-	alphahydroxy-dehydrosphingosine	TAG	-	triacylglycerol
AS	-	alphahydroxy-sphingosine	DAG	-	diacylglycerol
AP	-	alphahydroxy-phytosphingosine	CE	-	cholesteryl ester
AH	-	alphahydroxy-6-hydroxysphingosine	Cholesterol		

Easy sampling

Our method is compatible with the easiest and the most convenient skin sampling method – tape stripping. It is a non-invasive and painless method that allows control of the sampling depth (by collecting the appropriate *stratum corneum* layer) and collects comparable skin amounts. This facilitates collection of samples for screening and biomarker studies, increasing the statistical validity of results and conclusions.

Tape-sampling is comparable with scrape-biopsy

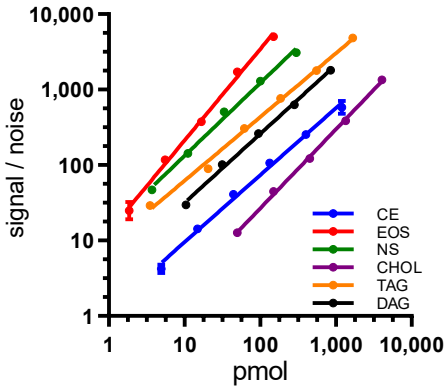


Pearson correlation of averaged lipid subspecies amounts determined for skin samples with and without stripping disc present. Every point represents the averaged amount of the individual lipid subspecies quantified from 5 independent extractions and acquisitions; only lipids present in all replicates were considered. Correlation coefficient (r) is given. The dashed diagonal represents slope of 1.
Lipids from a tape-stripped sample yield the same values as from a scraped sample.

Absolute quantification

The quantification is achieved using lipid class-specific internal standards allowing unbiased and direct quantitation of individual lipid molecules directly from their mass spectra intensities. Using this approach the method is capable of providing a quantitative read-out over 2 orders of magnitude. Lipotype delivers results expressed in absolute and not in relative values, which provides the basis for a direct comparison of different samples and experiments.

Lipids are quantifiable in wide ranges

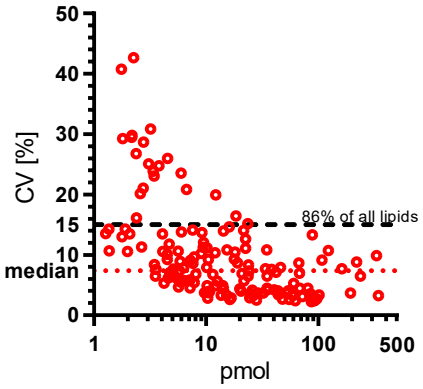


Dynamic range of different lipid classes. Various amounts of internal standards were added to the skin sample and their signal to noise ratio recorded. Linear dynamic range was defined as the concentration range at which the linearity of signal-to-noise values to pmol amount and the slope of the resulting function were close to 1. Data points show the mean of 5 independent experiments and error bars the standard deviation.
Quantification is both linear and proportional, and covers a wide range of lipid amounts.

Highest quality

Lipotype Shotgun Lipidomics Technology is highly reproducible, with a median coefficient of variation for quantified lipids of 7.4%. 86% of all lipids have a CV lower than 15%. This performance is ensured by rigorous quality controls. The high standard of the Lipotype platform is based on years of research experience both on the role of lipids in cellular processes and on the development of lipidomics technology.

Measurements are highly reproducible



Correlation between coefficients of variation and mean lipid amounts from 10 independent acquisitions and quantifications of pooled extracts of 3 different skin samples. Each point represents an individual lipid subspecies; only lipids present in all replicates were considered.

The majority of lipids is quantified with with a c.v. <15 %.

Full high-throughput

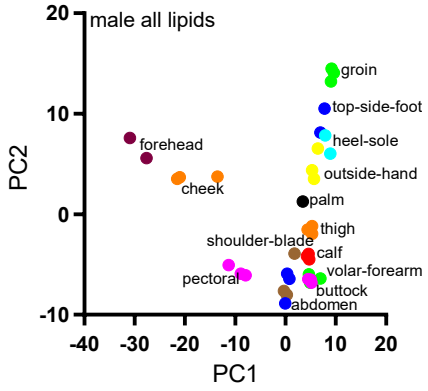
Lipotype uses Shotgun Lipidomics Technology without time consuming chromatographic separation of lipids before analysis. We utilize the advantages of cutting-edge mass spectrometry, combined with automated sample extraction, processing and data analysis. In this way our exquisitely standardized platform allows the complete analysis of 100 skin samples per day, offering unprecedented delivery time of weeks, instead of months, for complete results and associated reports.

Individual skin lipid profiles

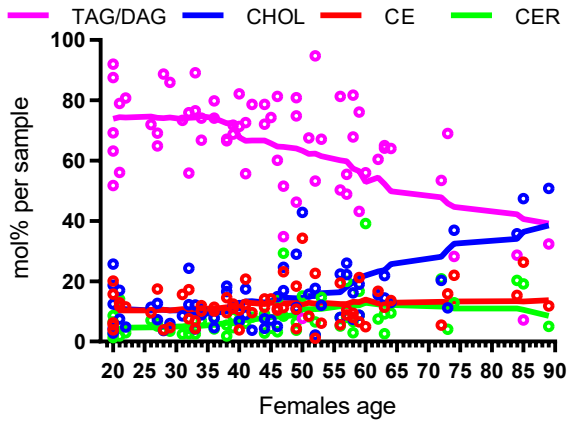
With Lipotype Skin Lipidomics, interesting observations on skin lipid physiology can be made almost effortlessly. Using the advantage of high-throughput and wide coverage, Lipotype analysed skin from 14 body sites to gain insight into the lipidomic variation of healthy human skin. Not surprisingly, different body parts have different skin lipidomes. An analysis of people of different age revealed that their skin lipids change with age, highlighting that different people have a unique and individual skin lipidome.

Various body spots have different lipid composition

Principal component analysis of the male body site lipidomes. Skin from different body sites can be differentiated based on lipids. Each site was measured in triplicate, and these triplicates cluster together showing comparability of skin lipidomes over a site.



Skin lipid composition changes with age



Profiles of lipid groups of 65 females of different age. Lines represent 0-order polynomial smoothing function with 8 neighbours averaged.

TAG/DAG – summed tri-/diacylglicerides.

CHOL – cholesterol

CE – cholesterol esters

CER – summed all ceramide subclasses

Sebum lipids TAG and DAG content decreases with age, while cholesterol content increases.

Advantages of Lipotype Skin Lipidomics

WIDE COVERAGE

- Covering 12 ceramide subclasses, tri- and diacylglycerol, cholesterol, cholesterol ester
- 250 individual lipid species per sample

FULL HIGH-THROUGHPUT

- Cutting-edge mass spectrometry, automated sample extraction, processing and data analysis
- 100 skin samples per day
- 2 weeks turnaround time

ABSOLUTE QUANTIFICATION

- Quantification via internal standards
- Results in mol% and pmol
- Technical variation <10%

EASY SAMPLING VIA TAPE-STRIPPING

- Reproducible
- Controlled sampling site in all planes
- Non-invasive

Applications of Lipotype Skin Lipidomics

Dermatological pharmacology:

- Influence of drugs on the skin lipidome;
- Deeper understanding of skin physiology and pathophysiology;
- The action of substances influencing skin lipid metabolism or the skin microbiome-lipidome relation;
- Lipid markers for diagnosis or stratification of skin disease;
- Skin lipidome as suitable clinical end point for drug development.

Cosmetics and skin research:

- Impact of cosmetic substances on the skin lipidome;
- Innovative claim support based on response of skin composition to product;
- Distinction and stratification of consumer groups based on skin lipid composition;
- Development of personalized cosmetics.

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