FlashNote

Identify hidden markers by time series experiments

Multifactorial study designs (e.g. different cell lines, different culture media, or individuals) along a time series are common in (bio)pharma, metabolomics, lipidomics and phenomics research. These enable, for example, to investigate clinically relevant markers for immune cells responses to pathogen attacks that would otherwise remain undiscovered.

MetaboScape® provides support for evaluating multifactorial time series experiments with intuitive visualization to readily determine relevant changes.

Challenge

How to evaluate data from time series experiments and readily spot relevant differences?

Solution

MetaboScape enables the quick determination of relevant changes occurring over time in multiparametric experimental designs with intuitive workflow design and dedicated plots. Time series plots go hand in hand with the complementary correlation analysis plots to provide insights on biochemical relations.


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"The activation of immune cells, for example in response to a pathogen, is an inherently dynamic situation. We regularly use time series metabolomics experiments to study these dynamics on the molecular level. The new time series feature in MetaboScape allows us to easily visualize and compare trends across a large number of metabolites. Simultaneously plotting time course data for biological replicates helps us to detect shifts in timing that are otherwise hidden. The client-server setup of MetaboScape is ideal for us as a core facility, because we can easily provide interactive access to metabolomics data to many users."

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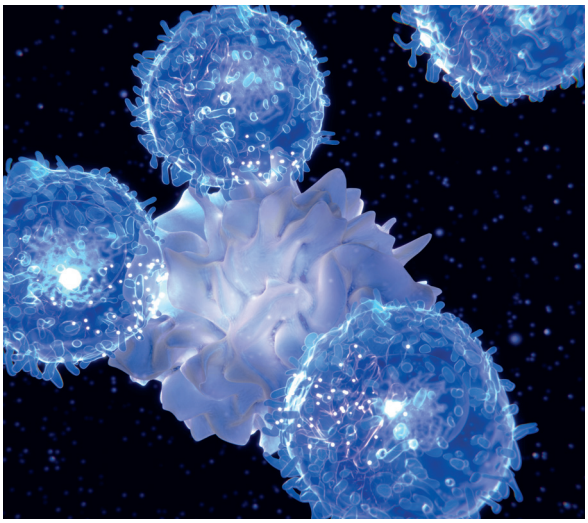
Find and ID dynamic changes that remained hidden!

MetaboScape enables investigating dynamic molecular changes in time course experiments. Automatic annotation routines for high confident metabolite annotation within the same software package make it a fully integrated all in one solution.

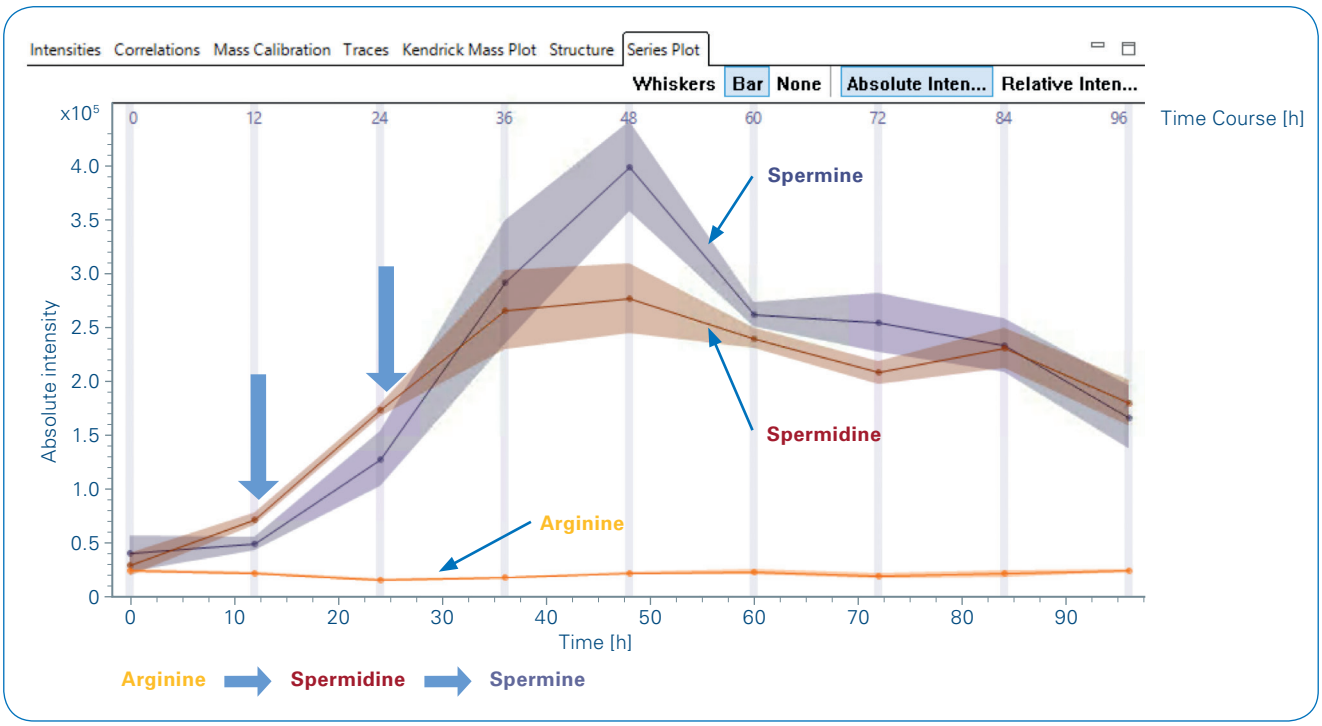


Cytotoxic (CD8+) T cells play a key role in the immune response. They are activated by antigen-presenting cells and can kill cancer cells or body cells that have been infected by a virus. To better understand the metabolic adaptation that occurs during the activation, we simulated the activation in vitro and observed intracellular metabolites over 96 hours.

- Three members of the polyamine pathway could be detected and identified by spectral library matching and comparison of retention times to single standards.

- We observe a strong enrichment of spermidine and spermine, while their precursor arginine remains largely unchanged. The earlier intermediate spermidine slightly precedes its product spermine in peak intensity over time (see arrows in plot below).

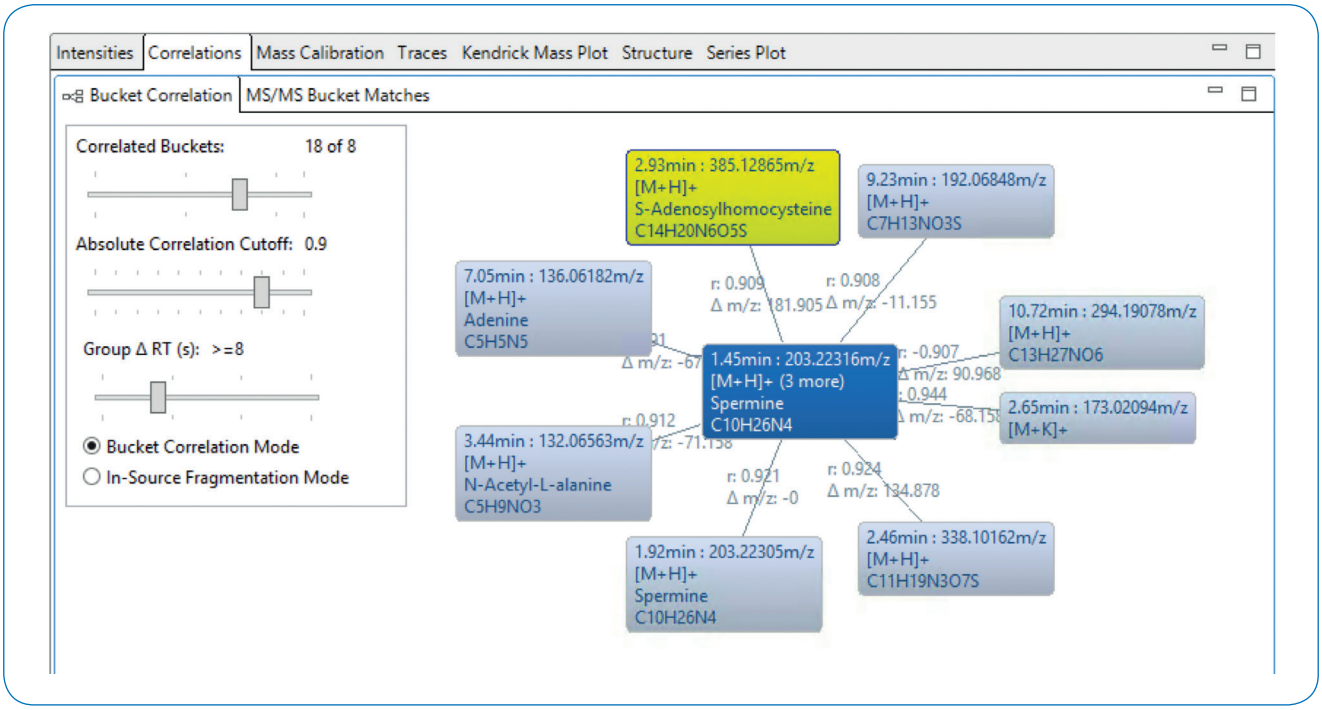
Δm/z [...	mSigma	Ions	MS/...	Name	Molecular F...	Annotations	AQ
0.139	2.3			Spermine	$C_{10}H_{26}N_4$	AL SF SL	
0.153	1.7			Spermidine	$C_7H_{19}N_3$	AL SF SL	
0.058	7.6			Arginine	$C_6H_{14}N_4O_2$	AL SF SL	



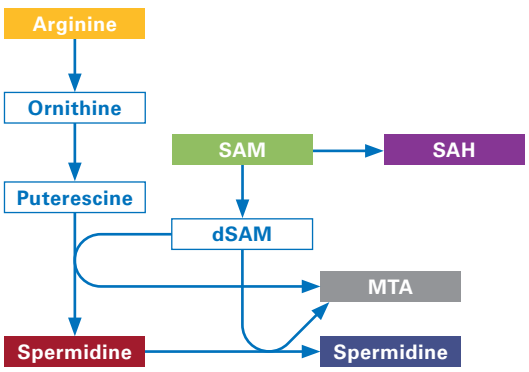
- Using a correlation analysis several features were determined to correlate with spermine, i.e. these compounds follow a similar intensity behavior over the time course.

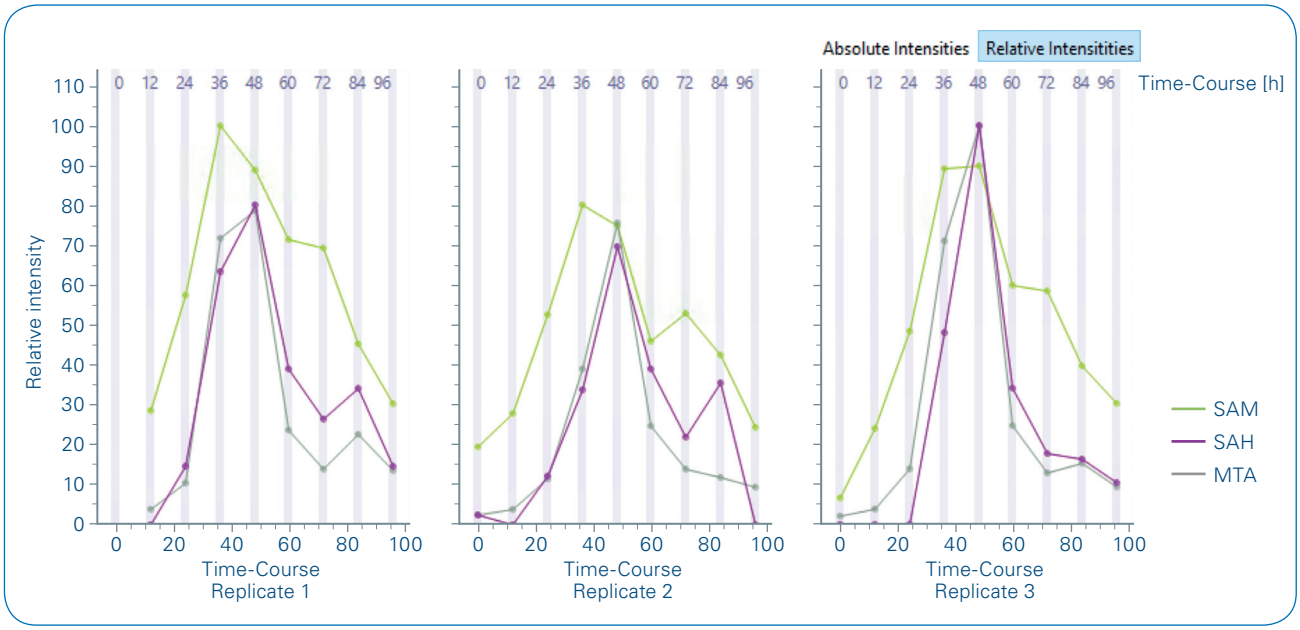
- Direct links between correlation analysis and time series plots allows to readily investigate these similar intensity changes over time

Name	Molecular For...	Annotatio...	AQ
S-Adenosylmethionine	$C_{15}H_{22}N_6O_5S$	SL SF AL	
5' Methylthioadenosine	$C_{11}H_{15}N_5O_3S$	SL SF	
S-Adenosylhomocysteine	$C_{14}H_{20}N_6O_5S$	SL SF	



- One of these features (highlighted in yellow above) was subsequently annotated as S-adenosyl homocysteine (SAH). This compound is related to S-Adenosyl methionine (SAM). SAM and its derivatives play important biological roles, for example, in RNA modification. A detailed search in the bucket table led to the annotation of 2 further compounds: SAM and 5'-methylthioadenosine (MTA) are directly involved in polyamine biosynthesis.





- The 3 SAM derivatives have greatly different signal intensities. However, plotting their relative intensities shows that they all follow a similar time profile as the polyamines. In addition, plotting the data from 3 biological replicates separately confirms the high reproducibility of the experiment.

- In summary, the time course experiment of T-Cell activation revealed that:
  - Arginine, a precursor for polyamine biosynthesis, stayed largely constant with a slight decrease at 24 and 36 hours
  - The earlier intermediate spermidine slightly precedes its product spermine in peak intensity over time
  - Bucket correlation analysis enabled to pinpoint and identify initially unassigned metabolites
  - Combining time course and bucket correlation analysis using MetaboScape linked two biologically important pathways: polyamine biosynthesis and S-adenosyl methionine metabolism, thus establishing a possible mechanistic link between immune cell function and RNA modification

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