Prä-analytische Qualitätskontrolle in Blutplasma Proben in Biobanken mittels Metabolomics Technologie

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2. Nationales Biobanken Symposium

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a BASF Group Company

metanomicshealth

The Impact of the Pre-Analytical Phase on Sample Quality [2]

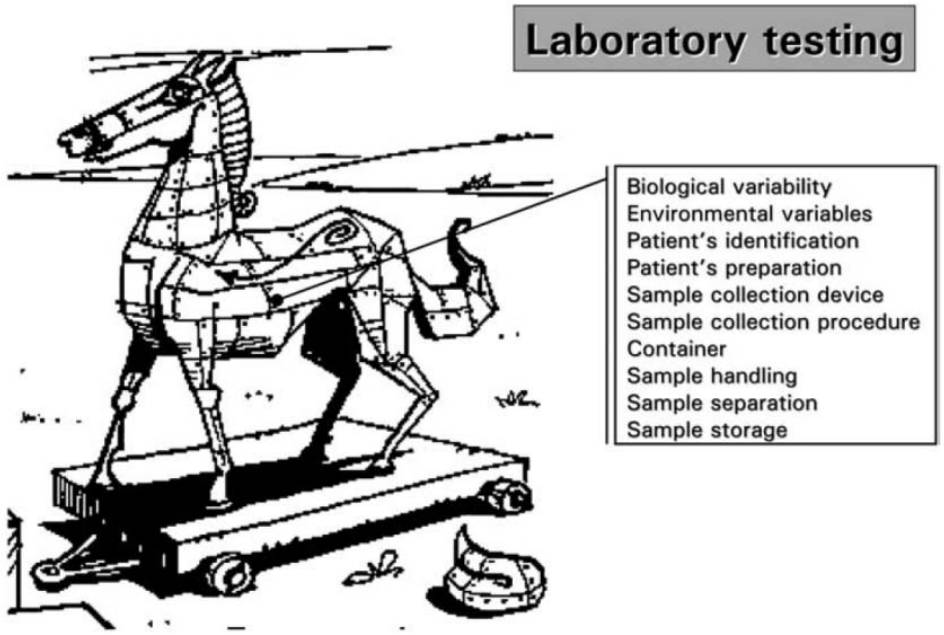


Figure 1 Preanalytical variables and laboratory testing.

Clin Chem Lab Med 2006;44(4):358–365 © 2006 by Walter de Gruyter • Berlin • New York. DOI 10.1515/CCLM.2006.073

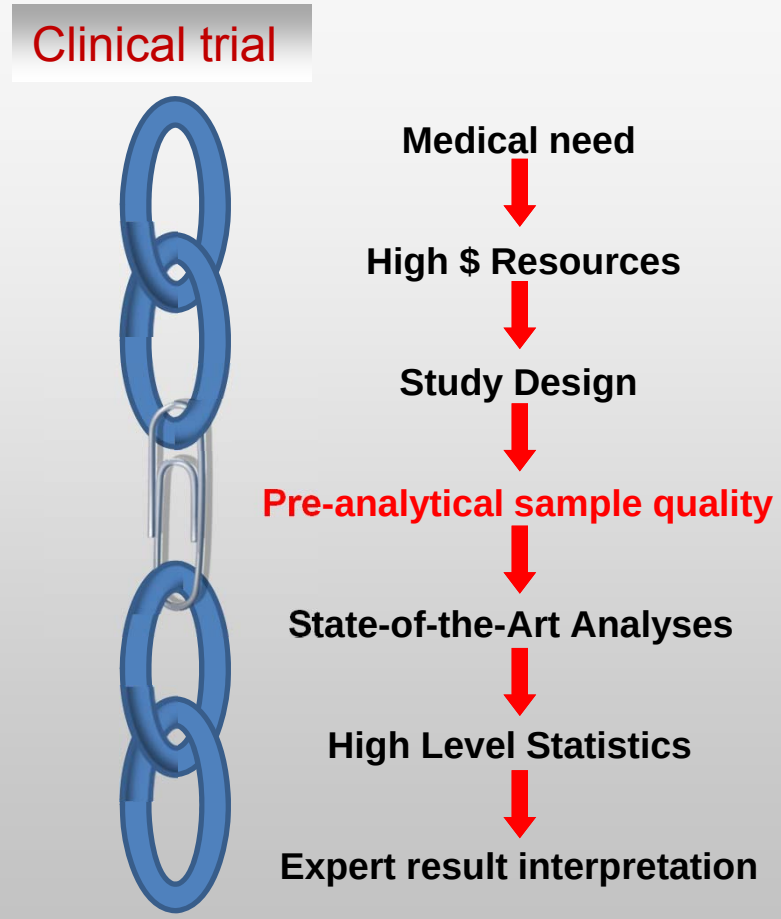
Review

Preanalytical variability: the dark side of the moon in laboratory testing

Giuseppe Lippi[1,*], Gian Cesare Guidi[1], Camilla Mattiuzzi[2] and Mario Plebani[3]

The medical error

-Analytics the Weakest Part of Your Research Pipeline?



evance of Human Blood Sample Quality for Clinical marker Research

lood is easily accessible, collection is inexpensive and minimally invasive

- Ideal for clinical assays

lood biomarkers are standard for diagnosis, prediction and monitoring of many seases (including cancer)

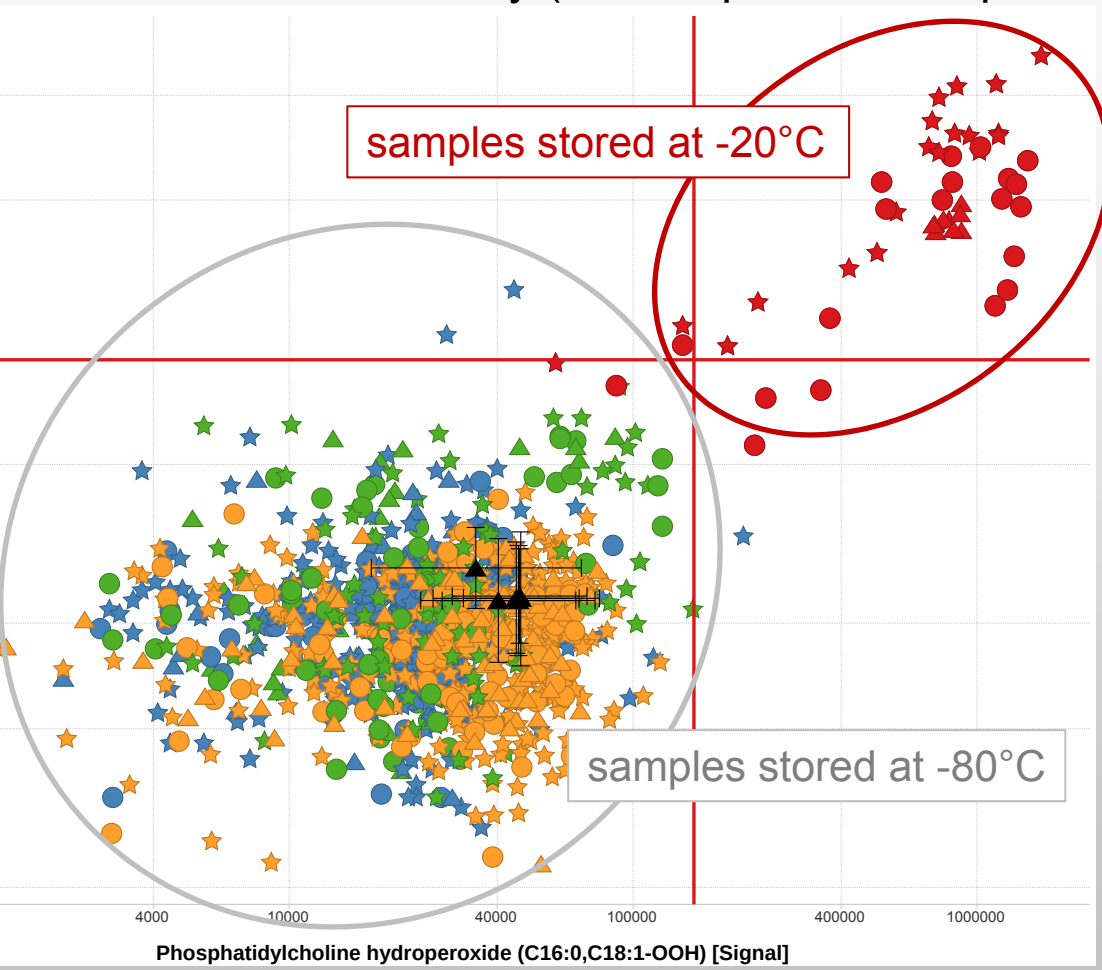
esults of targeted and -omics experimental approaches are influenced by pre-nalytical variations

he success of any biomarker study will depend in large part on the ality of the biospecimen analyzed"

uilar-Mahecha et al. 2012, PLoS ONE 7, 1-10

mple of a Quality Issue: Lipid Peroxidation

narker identification study (human plasma samples from an academic partner)



- Metabolite profiling of >1200 human plasma samples
- Batch 1 of samples presented lipo-hydroperoxides above the estimated thresholds
- Oxidation most likely due to inadequate storage temperature of -20°C

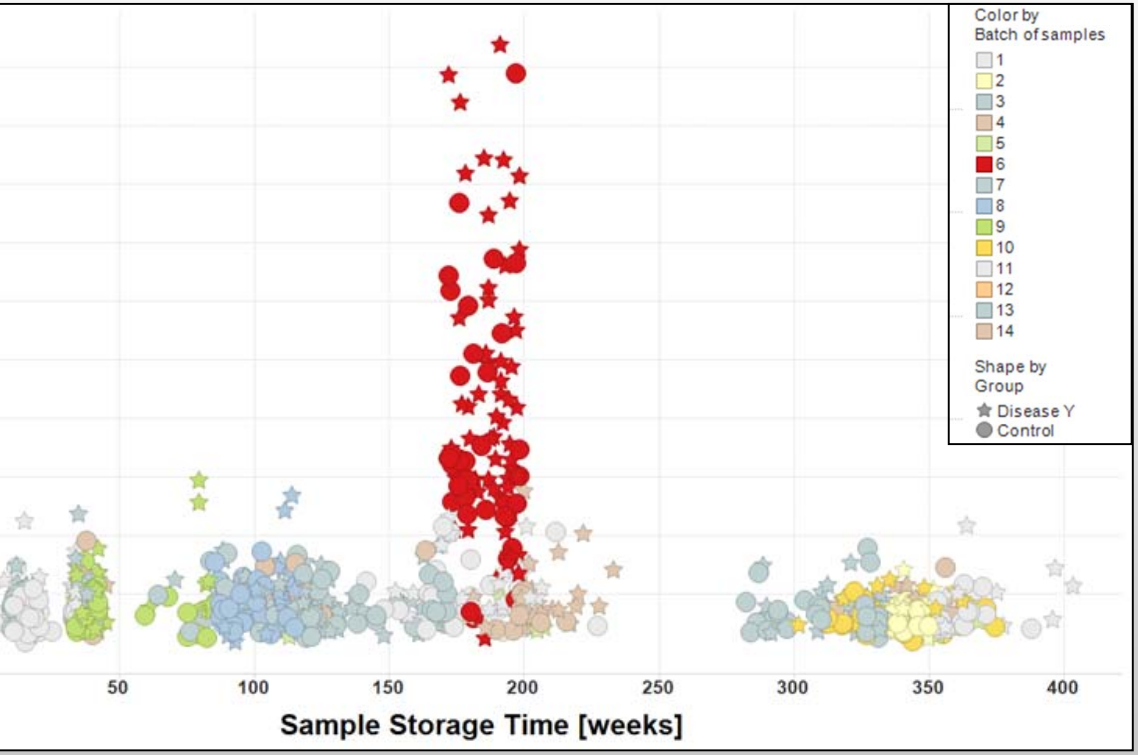
Color by
Sample Batch
Sample batch 1
Sample batch 2
Sample batch 3
Sample batch 4
SOP conform plasma, Median±SD

Shape by
Sample Group
Control
Disease X
Project pool
SOP conform plasma, Median±SD

Horizontal Line:

xample of a Quality Issue: Batch-to-Batch Variability

narker identification study (human plasma samples from a biobank)



- Human plasma samples stored in a biobank were thawn, split into aliquots and sent in batches to metanomics GmbH
- A quality marker is increased in a single batch (#6) of samples
- Independent of disease and storage time

ntification of pre-analytical failure in one batch of a major biomarker study

etanomics Health: Because Quality Matters Initiative

Quality Assurance (QA) Service: standardization of pre-analytical processing steps, addressing key confounders for metabolomics research

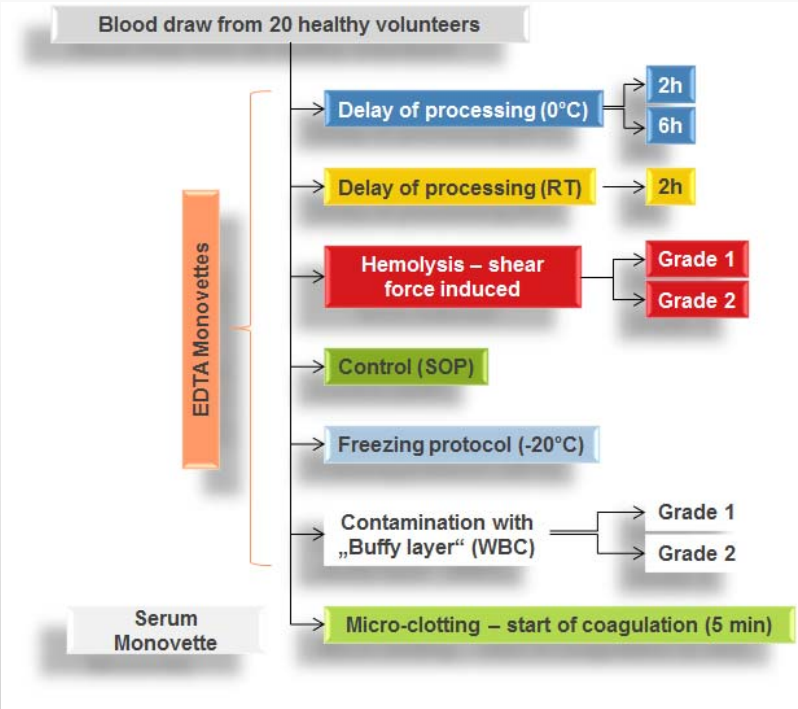
→ **SOP guidance, sample repository quality assessment, consulting**

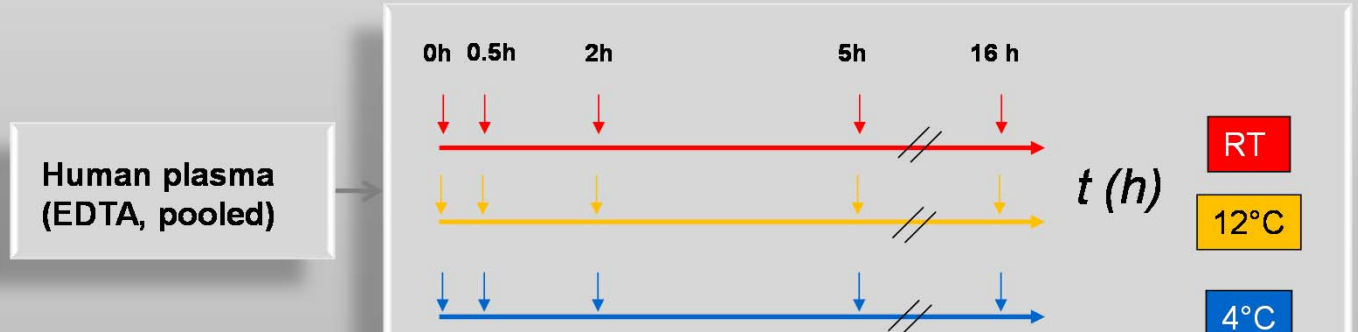
Quality Control (QC) Service: effectively assess the quality of biobank samples, e.g. pre-testing for quality markers or multivariate identification and exclusion of outliers

→ **QC biomarkers, sample quality report, outlier elimination**

esigns of Framework Studies – Quality Markers

erimental designs analyzing
act of pre-analytical variables
he plasma metabolome
ood processing
asma processing
abolomics analysis
xP™ Broad Profiling
xP™ Catecholamines
xP™ Eicosanoids
xP™ Lipids (sphingoid fraction)





esults: Percentage of Metabolome Changes

Clinical Chemistry 60:2
000–000 (2014)

Other Areas of Clinical Chemistry

Quality Markers Addressing Preanalytical Variations of Blood and Plasma Processing Identified by Broad and Targeted Metabolite Profiling

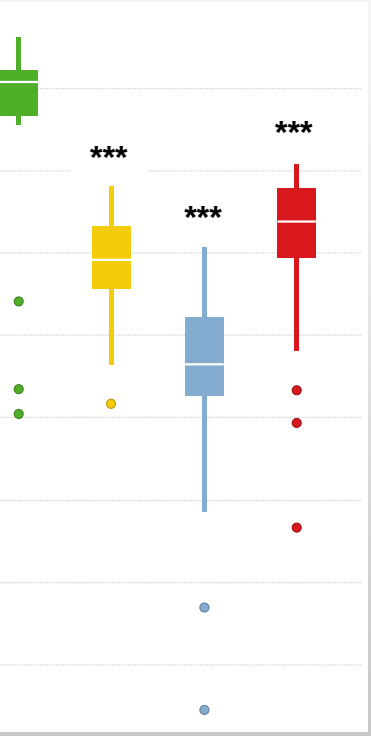
Beate Kamlage,[1*] Sandra González Maldonado,[1] Bianca Bethan,[1] Erik Peter,[1] Oliver Schmitz,[1] Volker Liebenberg,[2] and Philipp Schatz[2]

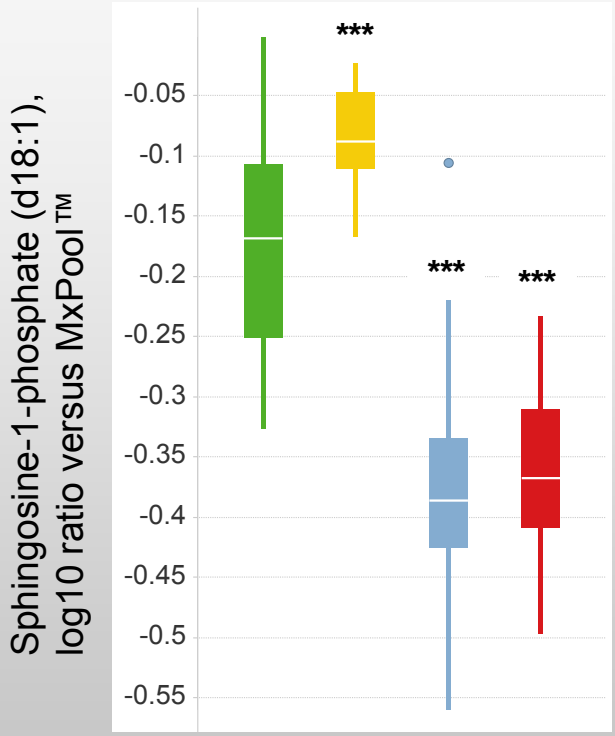
Table 1. Number and percentage of statistically significant metabolite changes after applying defined preanalytical confounders out of 267 metabolites for the blood and 262 metabolites for the plasma processing experiment.[a]

		Significantly changed metabolites (increase/decrease)[b]	
Material	Preanalytical variable applied	Number	Percent change
Blood	Microclotting	31 (3/28)	12 (1/10)[c]
	Room temperature, 2 h	59 (27/32)	22 (10/12)
	Wet ice, 2 h	44 (12/32)	16 (4/12)
	Wet ice, 6 h	46 (17/29)	17 (6/11)
	Hemolysis, grade 1	47 (15/32)	18 (6/12)
	Hemolysis, grade 2	81 (50/31)	30 (19/12)[c]
	Contamination with buffy layer, grade 1	0 (0/0)	0 (0/0)
	Contamination with buffy layer, grade 2	8 (8/0)	3 (3/0)
EDTA plasma	4 °C, 0.5 h	0 (0/0)	0 (0/0)
	4 °C, 2 h	7 (7/0)	3 (3/0)
	4 °C, 5 h	16 (12/4)	6 (5/2)[c]
	4 °C, 16 h	30 (24/6)	11 (9/2)
	12 °C, 0.5 h	1 (1/0)	0 (0/0)
	12 °C, 2 h	7 (7/0)	3 (3/0)
	12 °C, 5 h	14 (11/3)	5 (4/1)
	12 °C, 16 h	37 (29/8)	14 (11/3)
	Room temperature, 0.5 h	4 (4/0)	2 (2/0)
	Room temperature, 2 h	28 (25/3)	11 (10/1)
	Room temperature, 5 h	47 (27/20)	18 (10/8)
	Room temperature, 16 h	61 (41/20)	23 (16/8)[c]

esults: Examples of Blood Processing

otonin and sphingosine-1-phospate levels in plasma are influenced by pre-
ytical blood processing





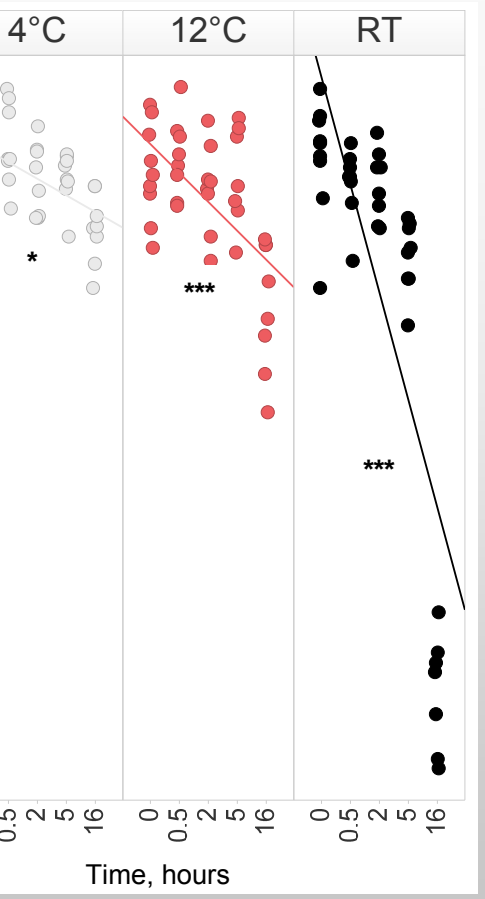
Color by Confounder
- Control
- Prolonged blood processing at room temperature
- Prolonged blood processing on ice
- Shear force induced hemolysis

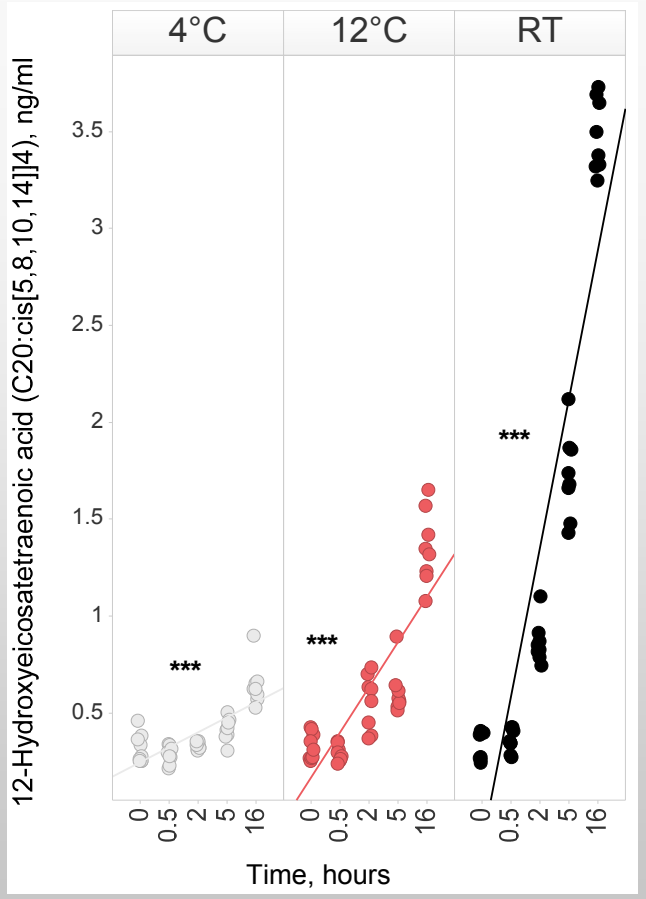
ANOVA, versus control group, FDR<0.2
* p-value<0.05
** p-value<0.001
*** p-value<0.0001

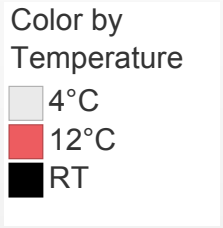
onin concentration in plasma is dependent on pre-analytics [Brand and Anderson, 2011, Clin Chem 57:10, 1376-86]
pecial regard to platelet metabolism

gosine-1-phosphate changes are probably related to platelet metabolism [Hammad et al. 2010, J Lip

esults: Examples of Plasma Processing







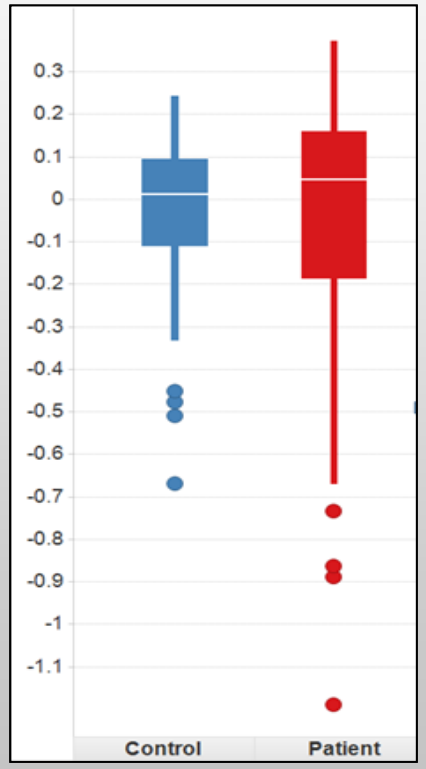
ANOVA, time as numerical fixed effect
FDR<0.2
* p-value<0.05
** p-value<0.001
*** p-value<0.0001

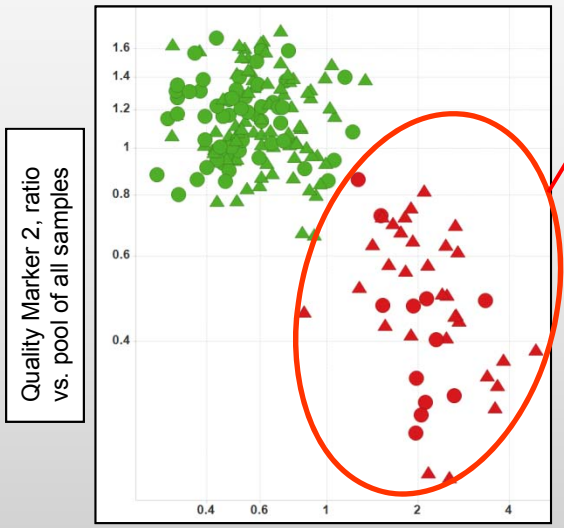
of plasma processing on the metabolome is different from that of blood processing
ical-oxidative processes and remaining enzyme activities in plasma change the plasma

enefit of Quality Control

rker identification study (human serum samples from an academic partner)

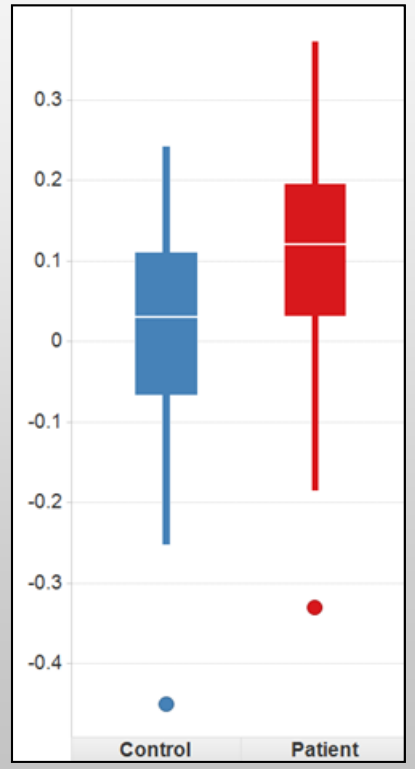
all samples
p-value: **0.68**





Quality Marker based data cut

w/o samples of poor quality
p-value: **0.00073**



P™ QC Assay Developed by Metanomics Health GmbH[13]

ality Control of Clinical Trial and Biobank Samples

Clinical trial

Medical need

↓

High $ resources

↓

Pre-analytical sample quality

↓

State-of-the-Art analyses

↓

Expert interpretation

- Biomedical research demands high-quality samples (QA, QC)
- Pre-analytical processes impact plasma sample quality
- MxP™ quality control assay currently developed by Metanomics Health GmbH
  - Checks sample type (EDTA -, citrate-, heparin-plasma; serum)
  - Controls for blood processing
  - Controls for plasma processing, storage and shipping
- Clinical use cases
  - Monitoring clinical sample quality
  - Selection of high quality samples from biobanks

Sincere thanks to ….

- Our academic and clinical partners
- Our pharma and nutrition partners
- Our dedicated and enthusiastic staff at Metanomics Health and metanomics

metanomics
new dimensions in discovery

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