



Metabolic phenotyping by ^1H -NMR spectroscopy: A tool to detect lung cancer

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GSK Clinical Science Award
Presentation 3

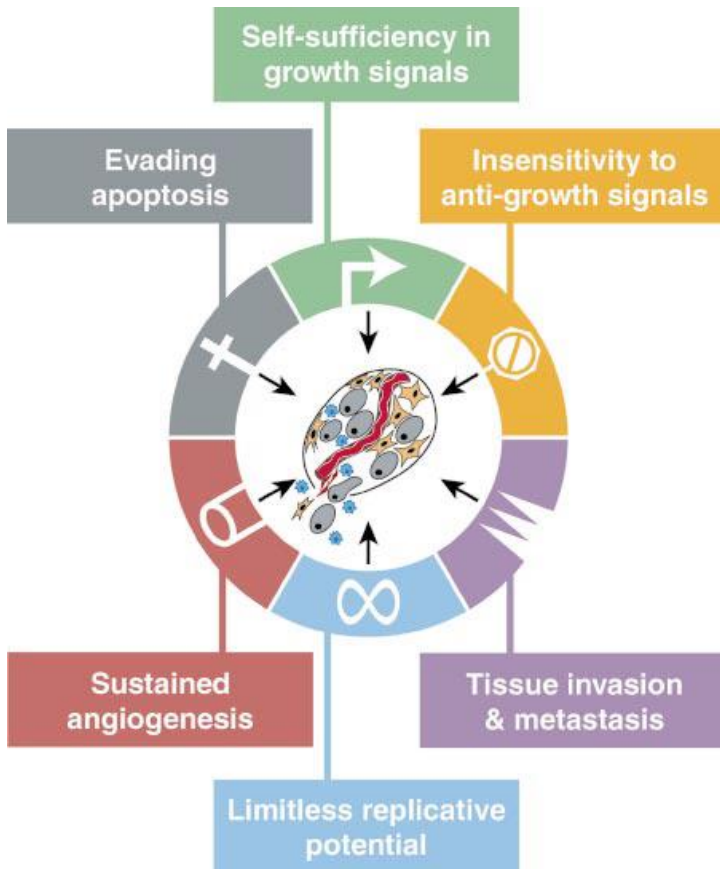


Content

- Introduction
- Research questions and methodology
- Results
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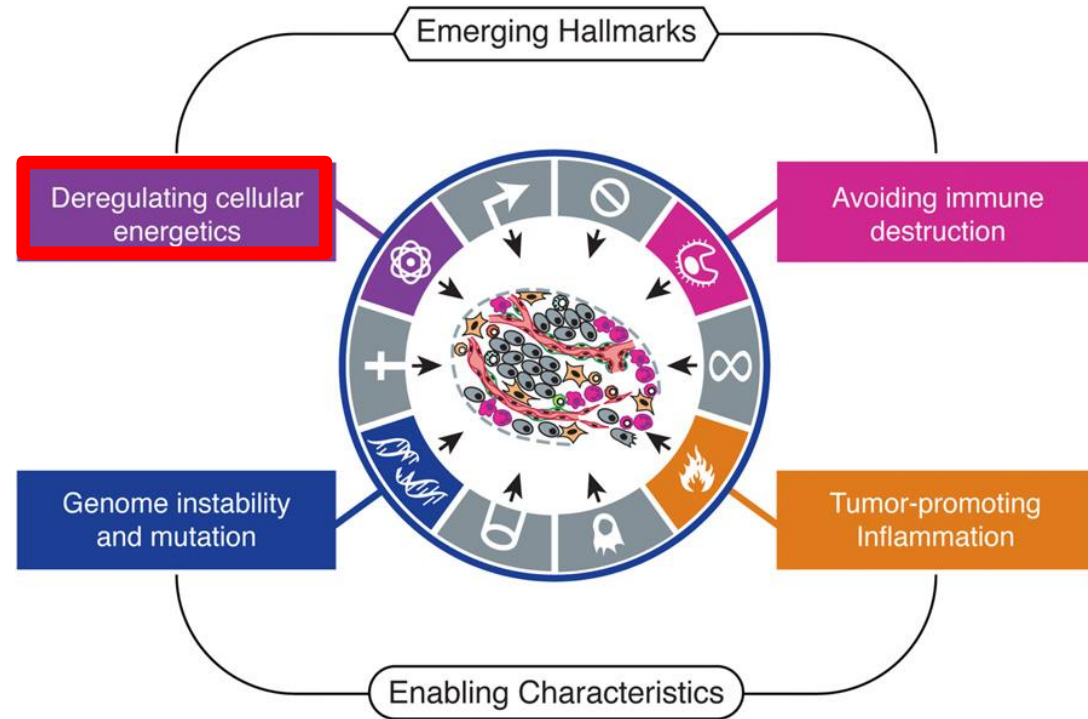
Hallmarks of cancer

2000



Hanahan, 2000

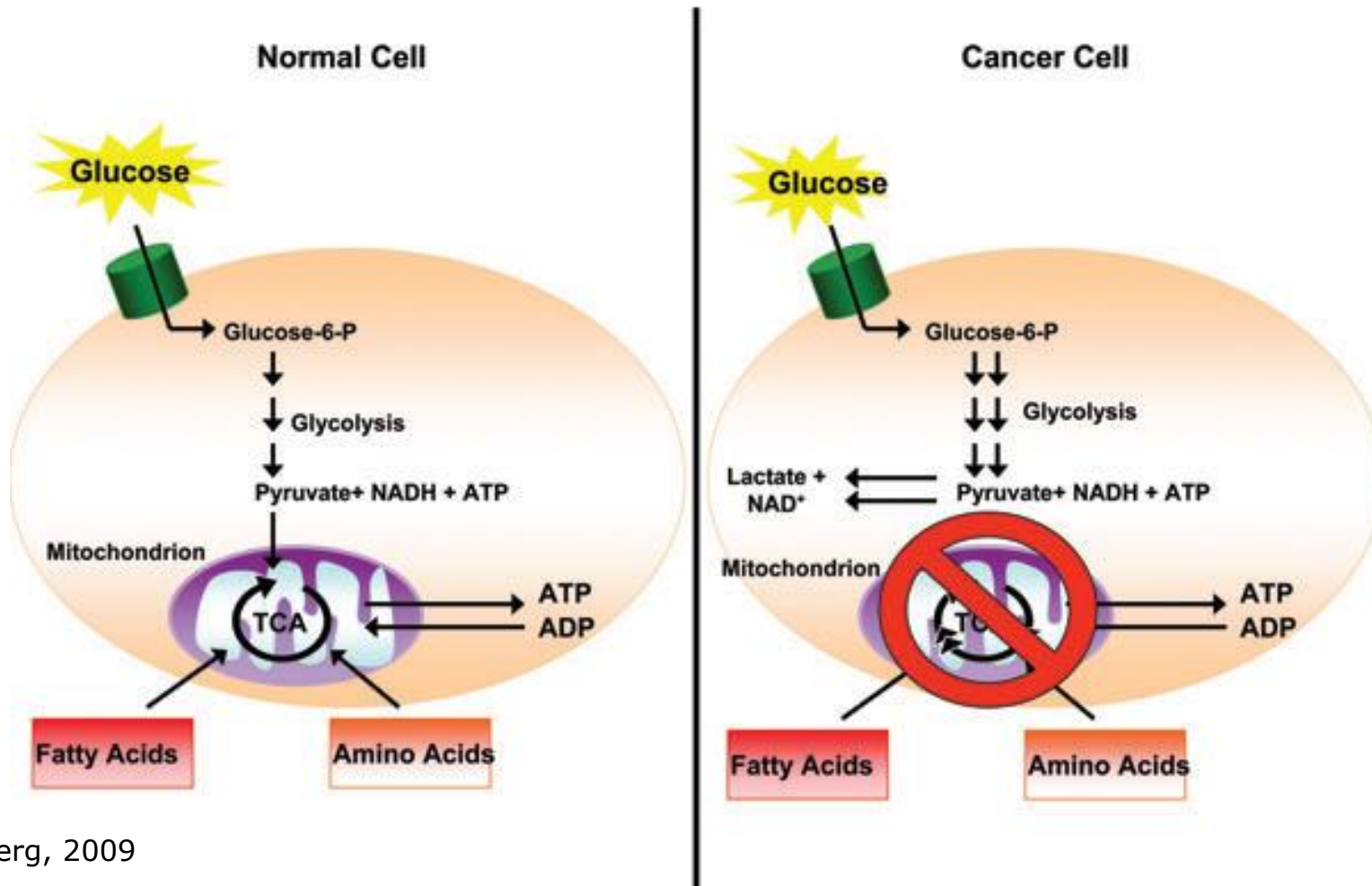
2011



Hanahan, 2011

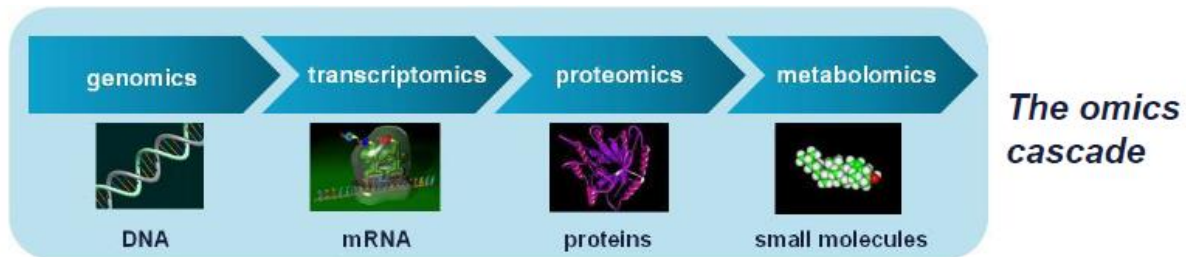
Dysregulated cancer cell metabolism

Warburg's Hypothesis for Origins of Cancer

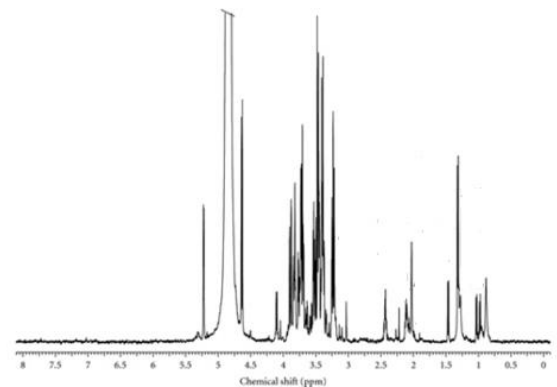


Weinberg, 2009

Metabolomics



- ^1H -NMR spectroscopy
 - Overview of protonated compounds in body fluids



NMR tube containing blood plasma

^1H -NMR spectrometer

^1H -NMR spectrum

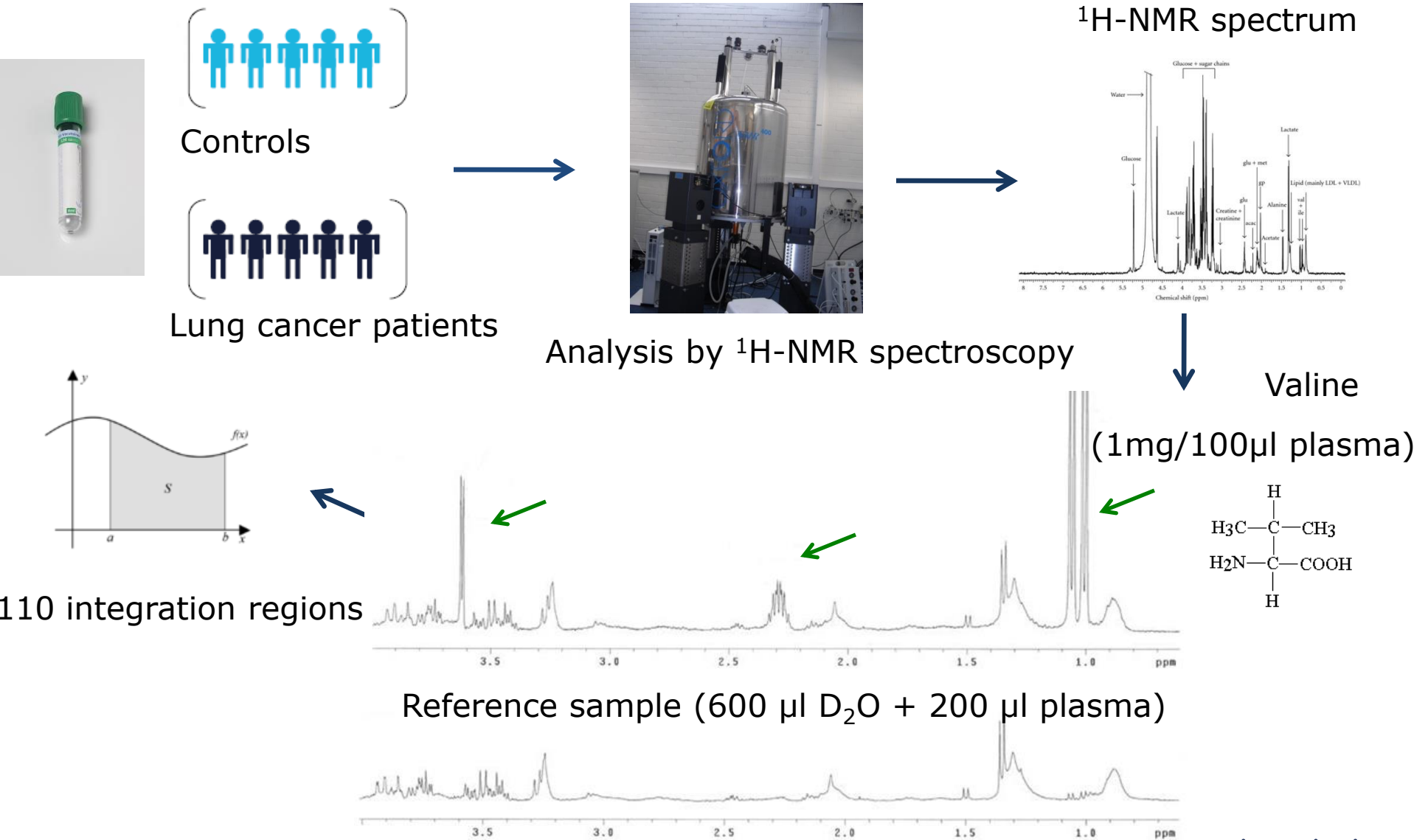
Research questions

Does the analysis of the metabolite composition of blood plasma by ^1H -NMR spectroscopy allows to detect lung cancer?

Can a statistical classifier be constructed by means of multivariate statistics?

Is it possible to validate this statistical classifier with an acceptable predictive accuracy?

Research methodology



Research methodology



Controls

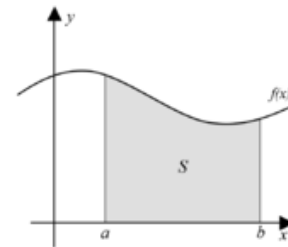
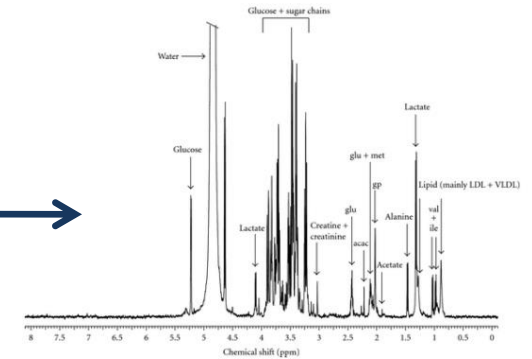


Lung cancer patients



Analysis by ¹H-NMR spectroscopy

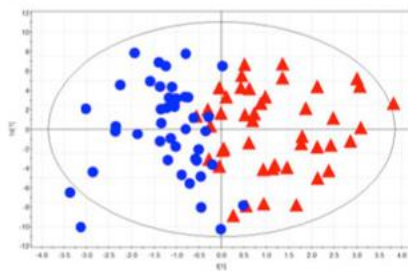
¹H-NMR spectrum



110 integration regions



	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10
IR Value 1										
IR Value 2										
IR Value 3										
IR Value 4										
IR Value 5										
IR Value 6										



Multivariate statistics



Metabolic interpretation

Subject characteristics

Training cohort

	Lung cancer patients (LC)	Controls (C)
Number	190	182
Gender	M: 71% F: 29%	M: 53% F: 47%
Average age	68 ± 10	69 ± 11
Average BMI	25.8 ± 4.7	28.1 ± 4.8

Validation cohort

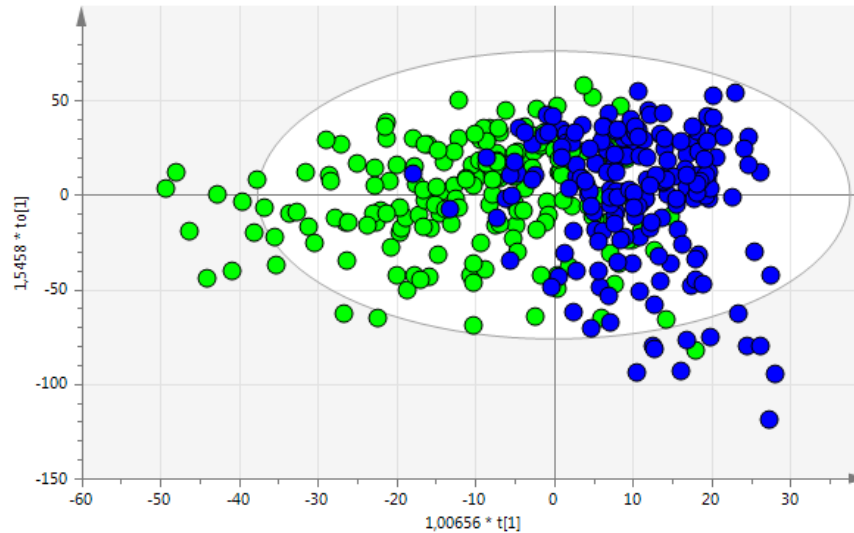
	Lung cancer patients (LC)	Controls (C)
Number	50	58
Gender	M: 60% F: 40%	M: 64% F: 36%
Average age	67 ± 9	63 ± 13
Average BMI	25.6 ± 4.3	26.9 ± 5.7

Construct statistical classifier

Examine predictive accuracy of statistical classifier

Training cohort – 110 variables

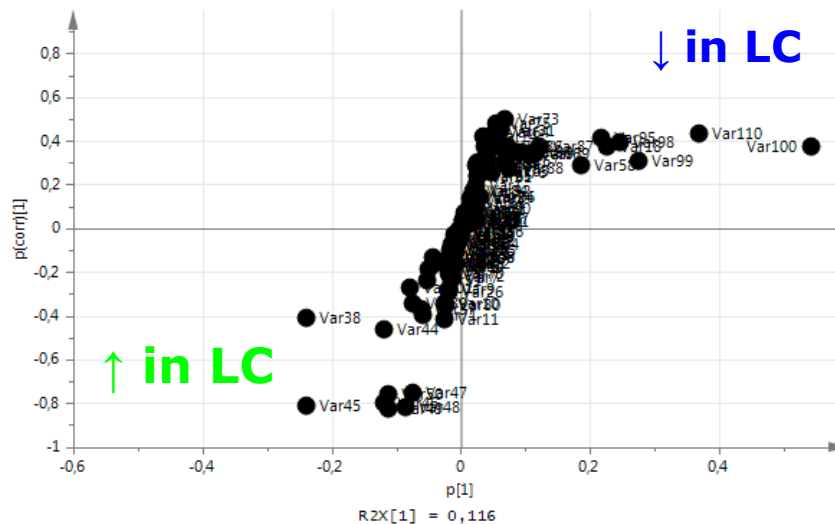
OPLS-DA plot
Discrimination



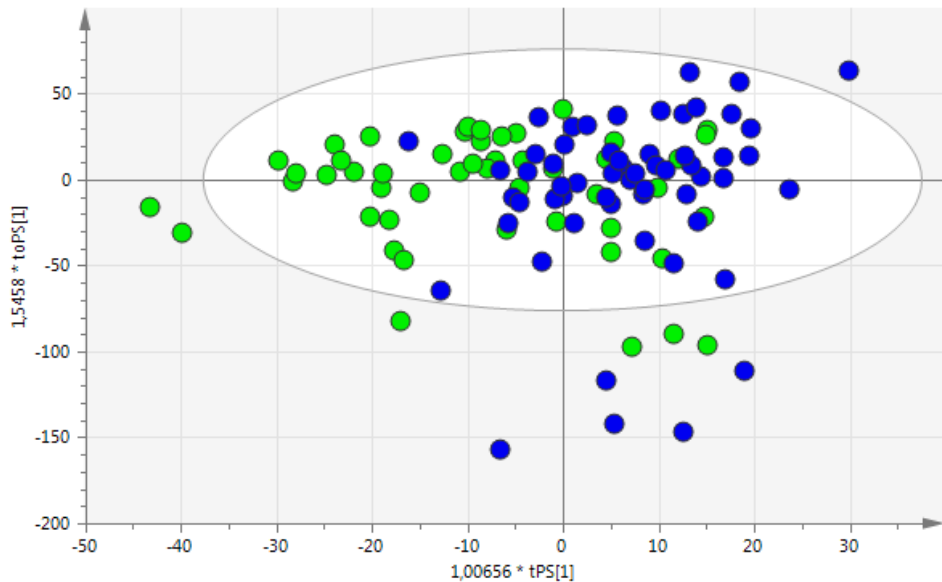
●: C
●: LC

162 out of 182 (89%)
correctly classified
145 out of 190 (76%)
correctly classified

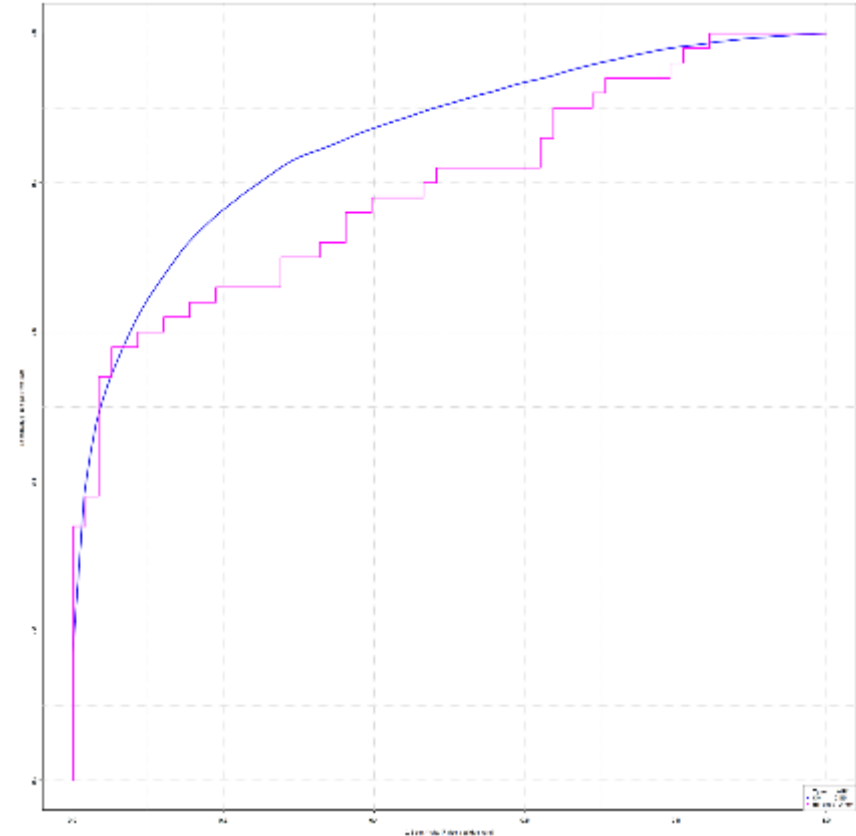
S-plot
Biomarkers



Validation cohort – 110 variables



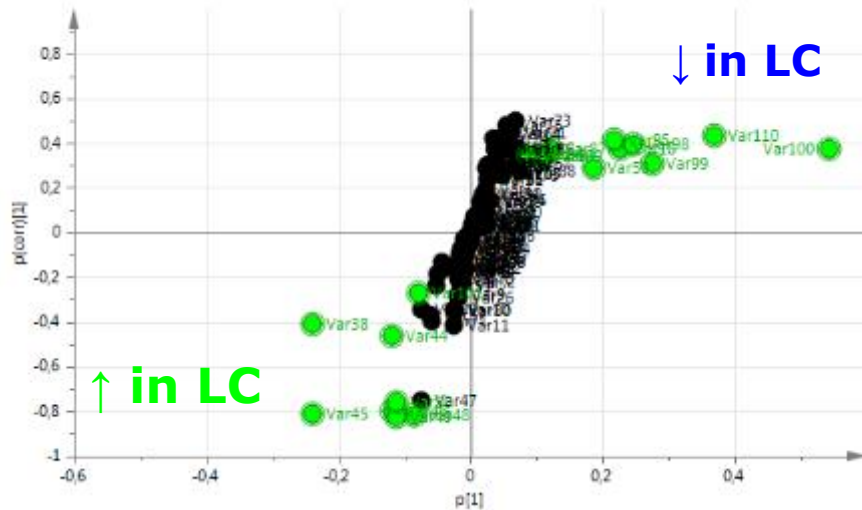
Specificity: 72% (42/58)
Sensitivity: 72% (36/50)



ROC-curve

AUC training cohort: **0.86**
AUC validation cohort: **0.79**

Training cohort – 19 variables

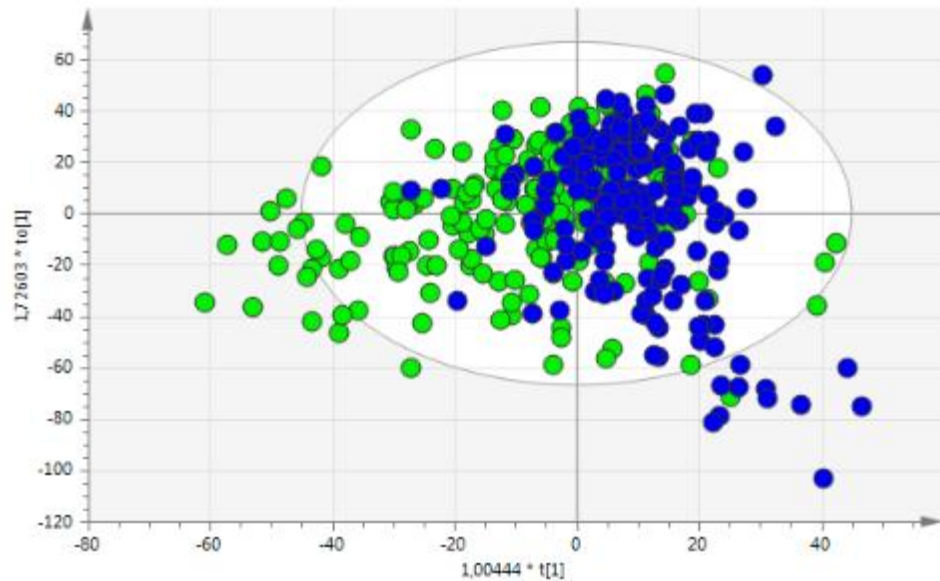


↓ **in LC**

Alanine Lactate
Lipids

↑ **in LC**

Glucose Threonine
Myo-inositol

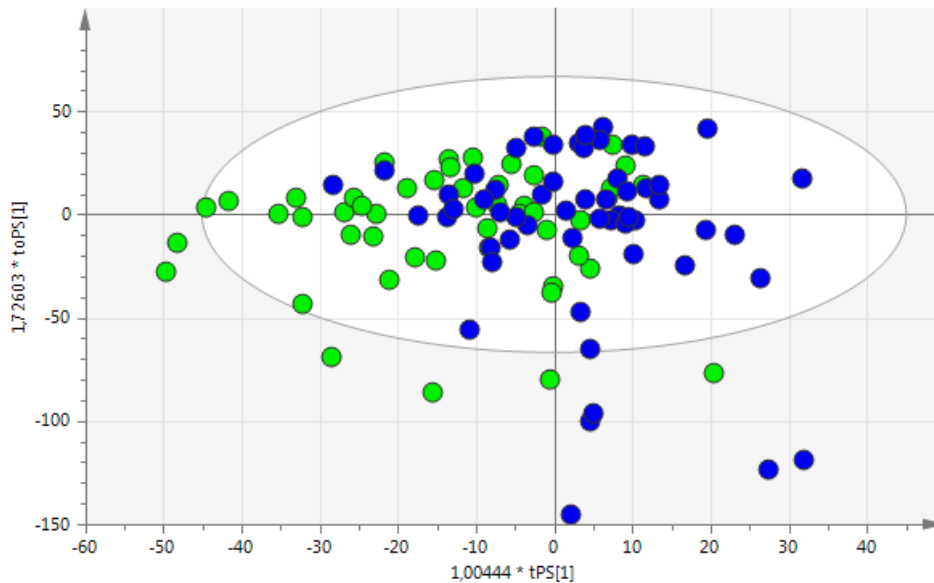


●: C

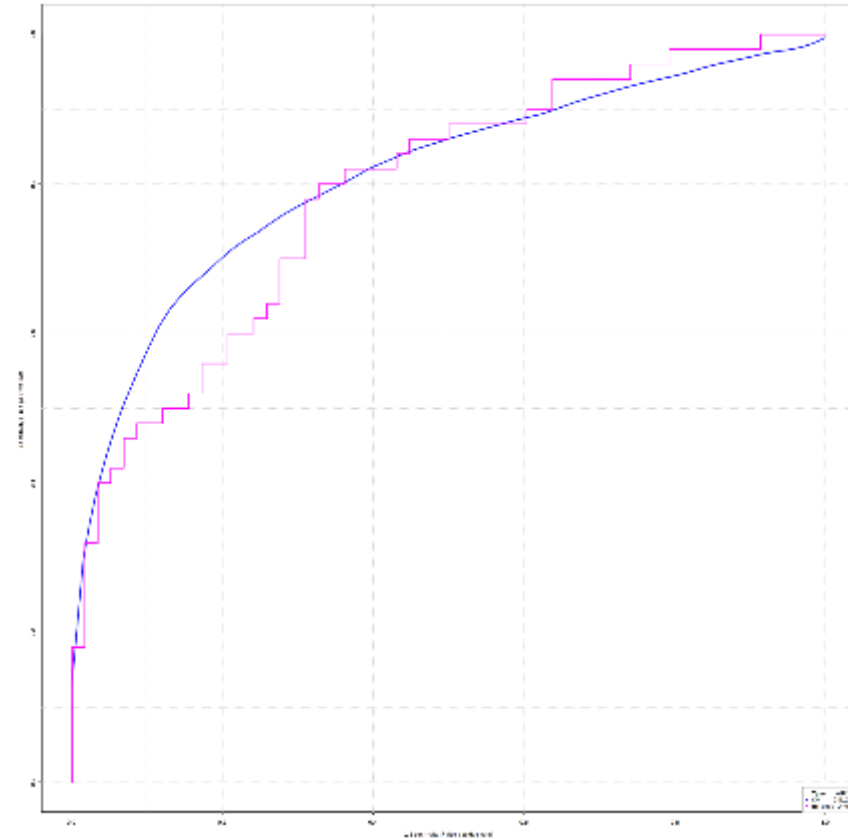
●: LC

151 out of 182 (83%)
correctly classified
132 out of 190 (69%)
correctly classified

Validation cohort – 19 variables



Specificity: 64% (37/58)
Sensitivity: 82% (41/50)



ROC-curve

AUC training cohort: **0.81**
AUC validation cohort: **0.79**

Conclusion and future perspectives

- A statistical classifier constructed with only the most discriminating variables has already an acceptable predictive accuracy
- Future experiments will investigate whether the constructed classifier can be used as a valid screening tool



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