Metabolic phenotyping by $^1$H-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
- Conclusion and future perspectives
Hallmarks of cancer

2000

- Self-sufficiency in growth signals
- Evading apoptosis
- Insensitivity to anti-growth signals
- Sustained angiogenesis
- Tissue invasion & metastasis
- Limitless replicative potential

Hanahan, 2000

2011

Emerging Hallmarks

- Deregulating cellular energetics
- Avoiding immune destruction
- Genome instability and mutation
- Tumor-promoting inflammation

Enabling Characteristics

Hanahan, 2011
Dysregulated cancer cell metabolism

Weinberg, 2009
Metabolomics

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

NMR tube containing blood plasma

$^1$H-NMR spectrometer

$^1$H-NMR spectrum
Research questions

Does the analysis of the metabolite composition of blood plasma by $^1$H-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

Controls

Lung cancer patients

Analysis by $^1$H-NMR spectroscopy

Valine (1mg/100µl plasma)

110 integration regions

Reference sample (600 µl D$_2$O + 200 µl plasma)

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Research methodology

Controls

Lung cancer patients

Metabolic interpretation

Analysis by \(^1\)H-NMR spectroscopy

\(^1\)H-NMR spectrum

Multivariate statistics

110 integration regions

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## Subject characteristics

<table>
<thead>
<tr>
<th></th>
<th>Training cohort</th>
<th>Validation cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lung cancer patients (LC)</strong></td>
<td><strong>Controls (C)</strong></td>
<td><strong>Lung cancer patients (LC)</strong></td>
</tr>
<tr>
<td>Number</td>
<td>190</td>
<td>182</td>
</tr>
<tr>
<td>Gender</td>
<td>M: 71%</td>
<td>M: 53%</td>
</tr>
<tr>
<td></td>
<td>F: 29%</td>
<td>F: 47%</td>
</tr>
<tr>
<td>Average age</td>
<td>68 ± 10</td>
<td>69 ± 11</td>
</tr>
<tr>
<td>Average BMI</td>
<td>25.8 ± 4.7</td>
<td>28.1 ± 4.8</td>
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- **Construct statistical classifier**
- **Examine predictive accuracy of statistical classifier**
Training cohort – 110 variables

OPLS-DA plot
 Discrimination

S-plot
 Biomarkers

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

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

\[ \downarrow \text{in } \text{LC} \]
- Alanine
- Lactate
- Lipids

\[ \uparrow \text{in } \text{LC} \]
- Glucose
- Threonine
- Myo-inositol

: C
: LC
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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