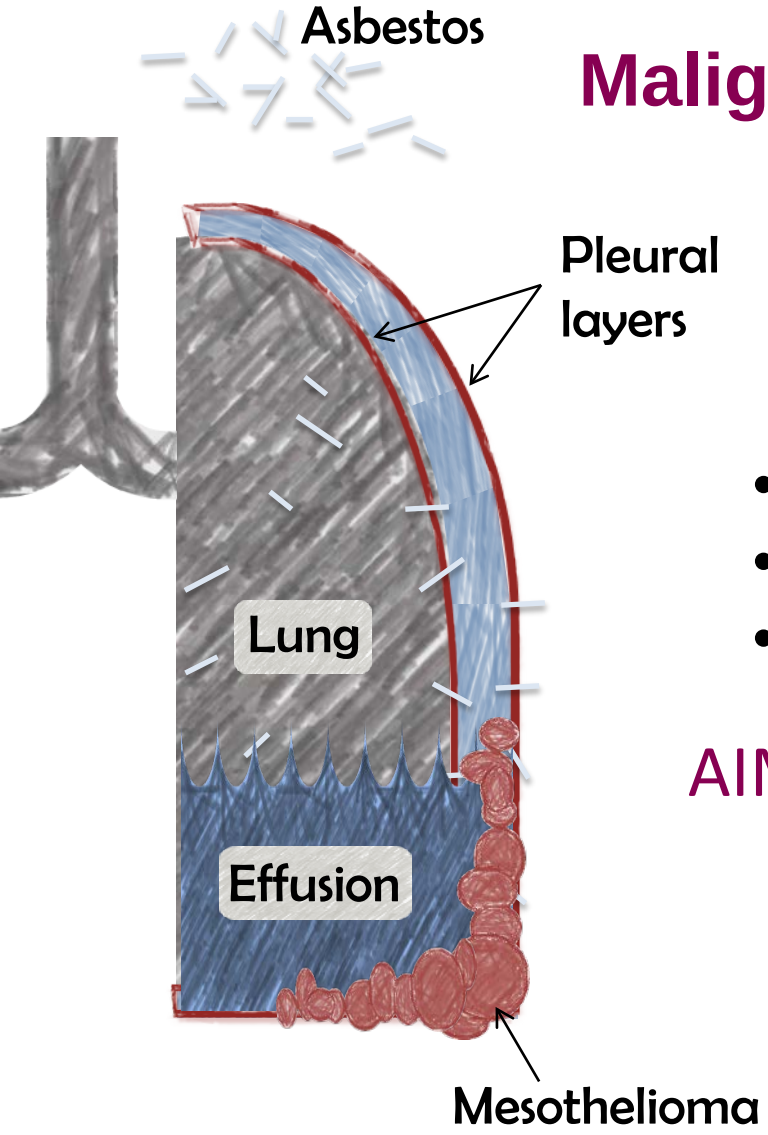
Proteome screening identifies galectin-1 as a negative predictor for malignant mesothelioma in pleural effusions

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Katalin Dobra's research group
Huddinge

Malignant Mesothelioma



- Median survival ~1 year
- Incurable
- Hard to diagnose

AIM: To find new biomarkers to aid diagnosis

Present study:

→ Pleural effusions
- Pre-processing (to reduce variance and complexity)

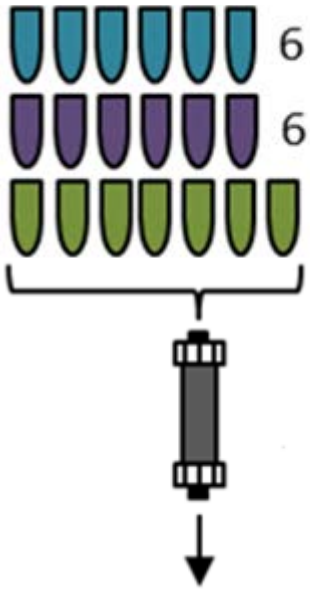
→ Mass spectrometry

→ Biostatistics & bioinformatics
- Identifying biomarker candidates

→ Validation
- ELISA

Present study: work-flow (1/4)

Pleural effusions



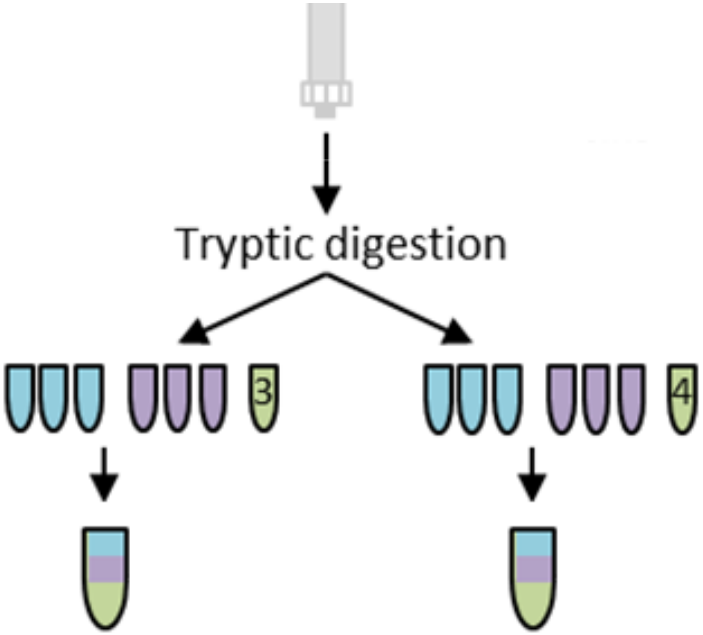
Malignant mesotheliomas

Lung adenocarcinomas

Benign conditions

- MARS-14 removal of abundant proteins

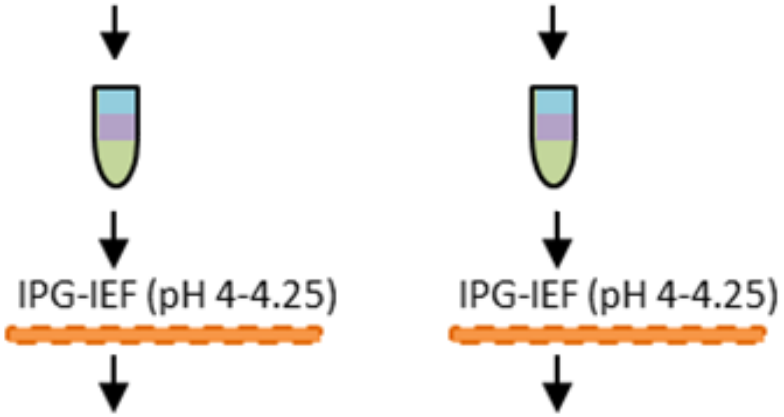
Present study: work-flow (2/4)



- MARS-14 removal of abundant proteins
- iTRAQ mass tags (2 x 8 labels)

  → Pooling = reduced variance

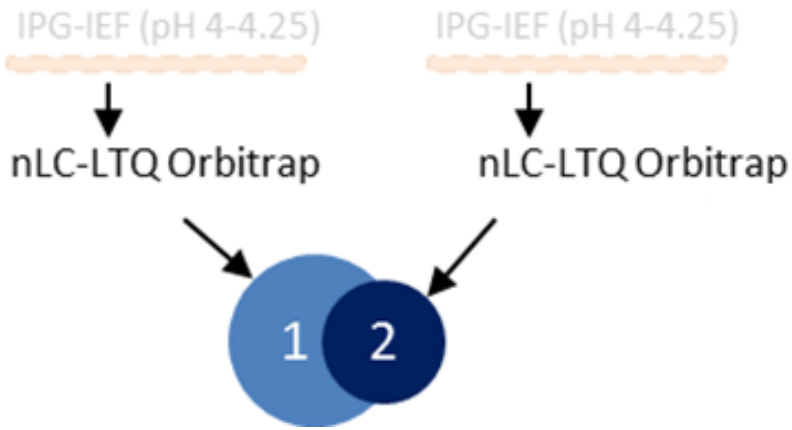
Present study: work-flow (3/4)



- MARS-14 removal of abundant proteins
- iTRAQ mass tags (2 x 8 labels)
  → Pooling = reduced variance
- Immobilized pH gradient/ isoelectric focusing (IPG-IEF)
  → Fractionation = reduced complexity

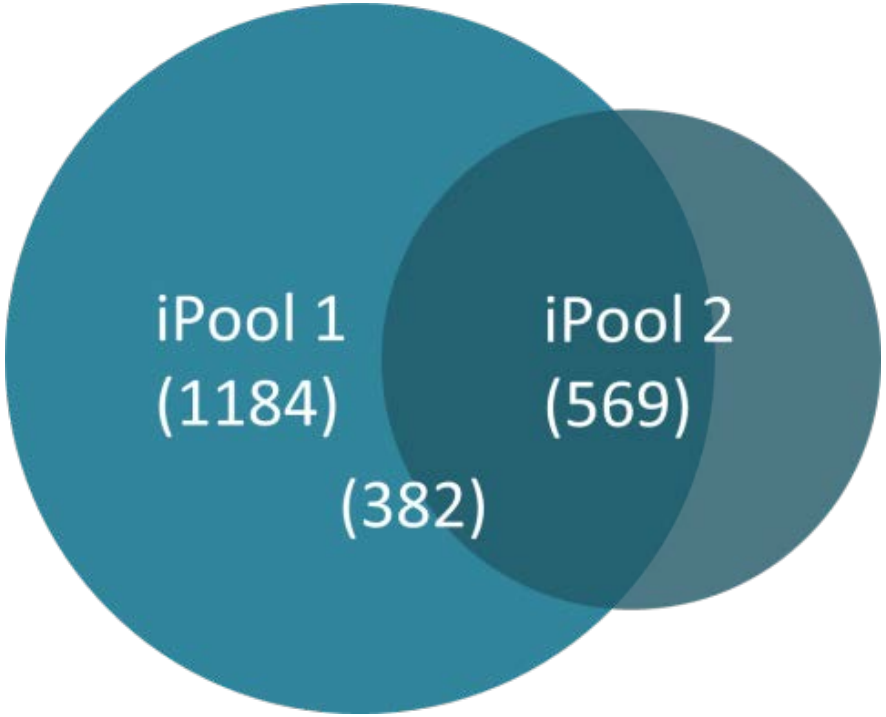
Pernemalm et al., Use of narrow-range peptide IEF. *Proteomics* 2009, *9*, 3414–3424

Present study: work-flow (4/4)



- MARS-14 removal of abundant proteins
- iTRAQ mass tags (2 x 8 labels)
  → Pooling = reduced variance
- Immobilized pH gradient/ isoelectric focusing (IPG-IEF)
  → Fractionation = reduced complexity
- Mass spectrometry

Results: number of identified proteins

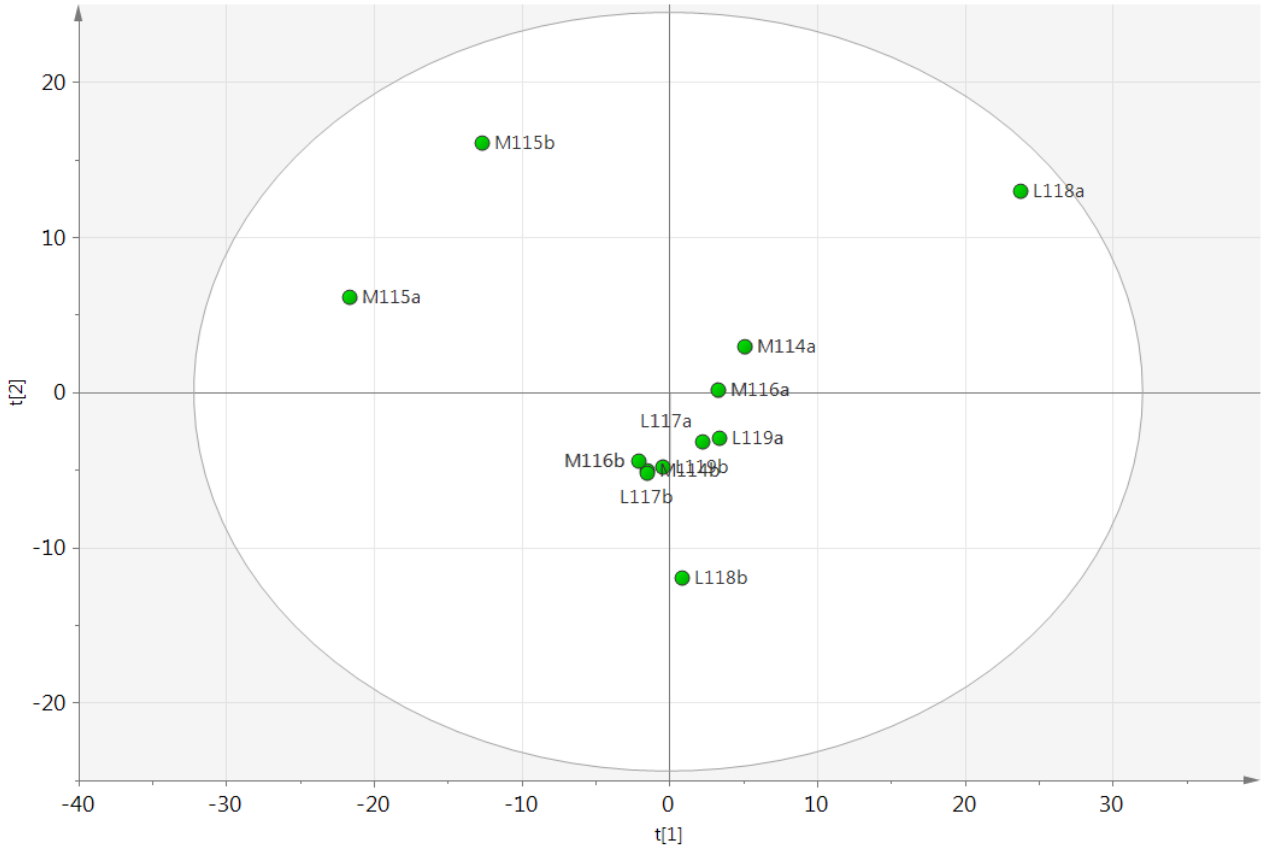


Candidate selection

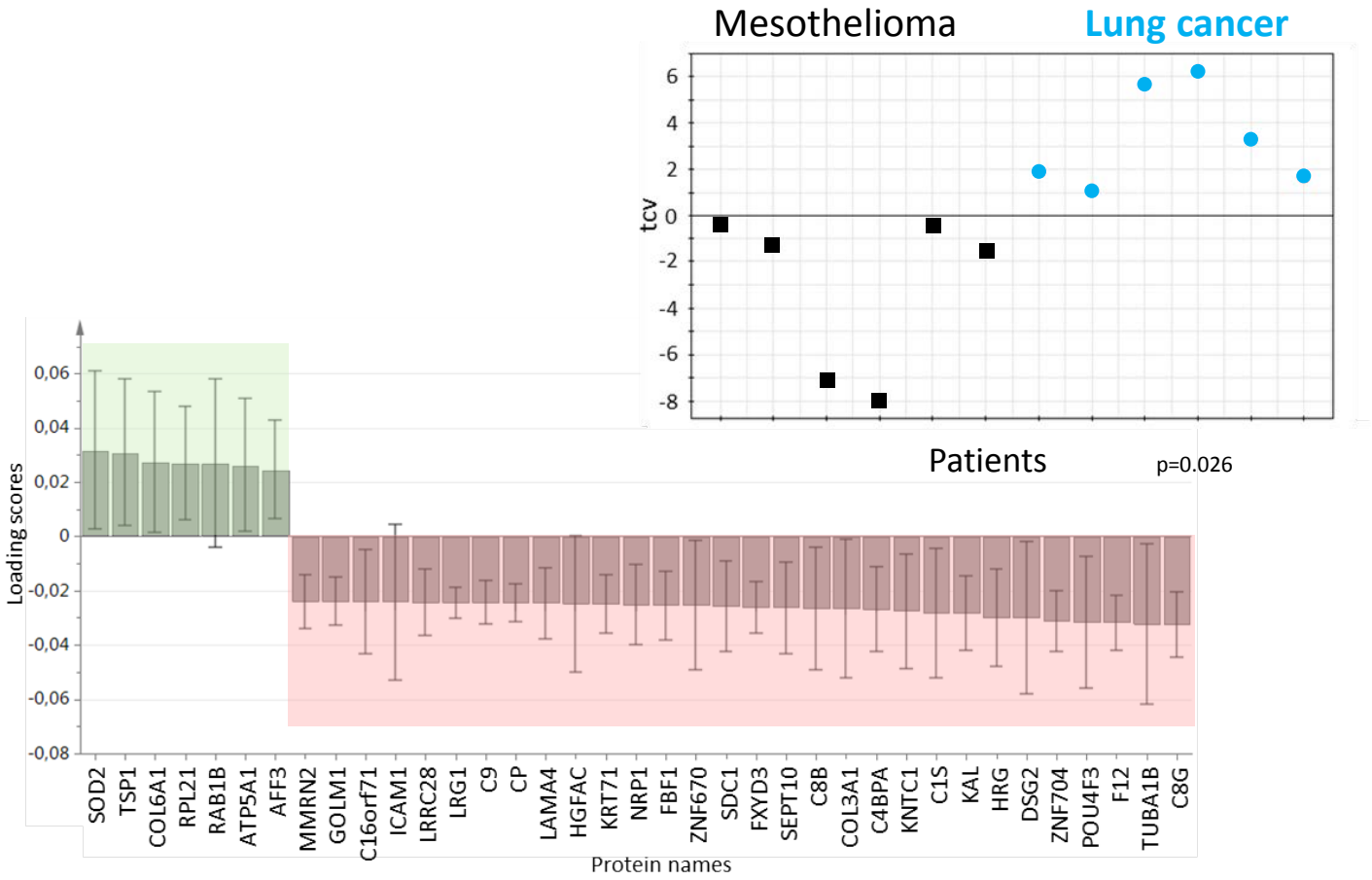
- Several identified proteins are already known mesothelioma biomarkers

- Multivariate analyses:
  → Principal Component Analysis **(PCA)**: distribution & possible outliers
  → Partial Least Squares **(OPLS-DA)**: supervised model building
- Bioinformatics:
  → Biological links between proteins
    - Ingenuity pathway analyser, BioCarta & KEGG

Results: PCA


M115b
L118a
M115a
M114a
M116a
L117a
L119a
M116b
L117b
L118b
t[1]
t[2]
20
10
0
-10
-20
-40
-30
-20
-10
0
10
20
30

Results: OPLS-DA



Candidate selection

- Candidates: ***1)*** differentially expressed,
  2) included in the OPLS-DA model &/or
  3) had interesting biological implications

Validation

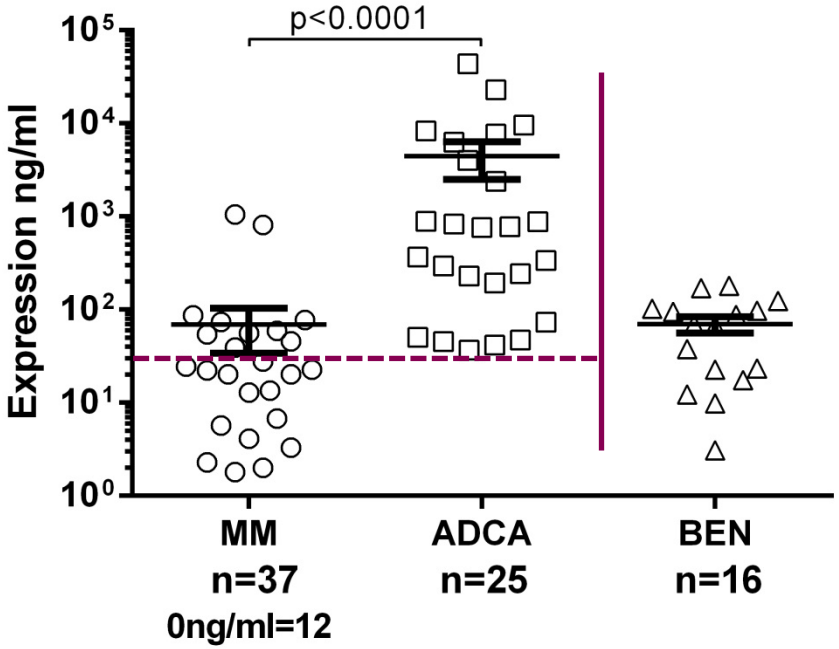
- ELISA based
  - Galectin-1
  - Aldo-keto reductase 1B10
  - Apolipoprotein-CI
  - Superoxide dismutase-2
  - Thrombospondin-1
  - Tenascin-1
  - Myosin-VIIb

Validation population	N
Mesothelioma	***37***
Metastatic cancers	***25***
Lung ADCA	20
Breast ADCA	4
Renal cell carcinoma	1
Benign diseases	***16***
Benign asbestos pleuritis	9
Pleuritis	3
TBC	2
CHF (transudate)	2

Results: candidate validation

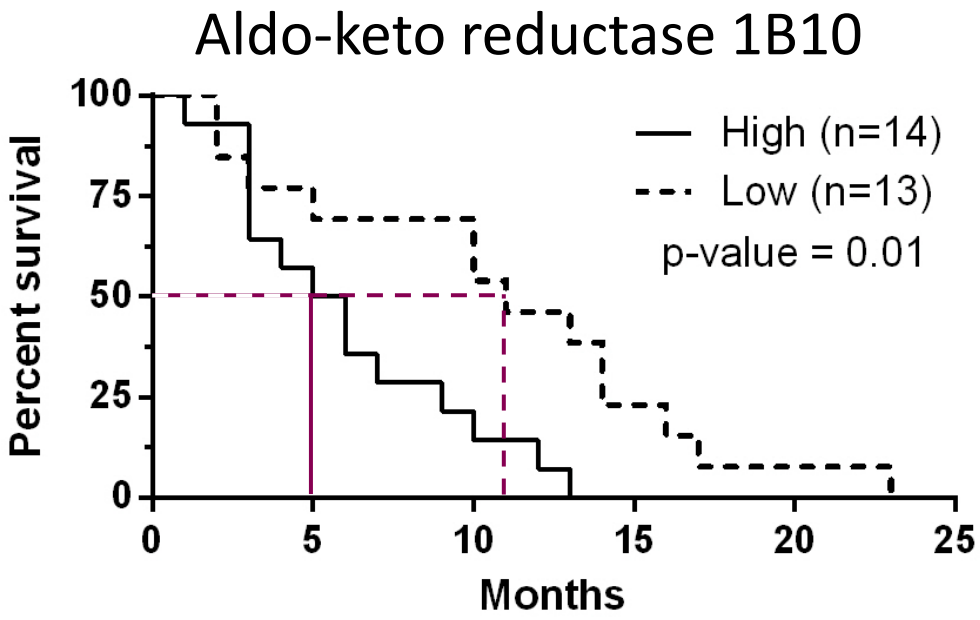
Galectin-1

Spec. = 100 %
Sens. = 73 %



MM=malignant mesothelioma, ADCA = adenocarcinoma, BEN = benign condition

Validation: Results



- Kaplan-Meier survival (mesothelioma patients)

Conclusions & future perspectives

- Galectin-1 is a possible negative predictor for mesothelioma
  → **Combination** with other biomarkers
- Aldo-keto reductase 1B10 show prognostic value
  → As a *predictive* marker?
- Follow-up on benign asbestos pleuritis patients
  → Identify **early markers**

Acknowledgments

- Katalin Dobra & Anders Hjerpe group
  Filip Mundt
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