Post-translational modifications of albumin in cancer – a rich source for diagnostic and monitoring of treatment.

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Aim

The aim of this study is to develop cancer markers on basis of post-translational modifications in serum albumin.

Rationale

Albumin is in contact with all cells in a body.
This major protein in a plasma accesses all tissues and organs and has a number of different roles. Albumin was found to have more than 50 post-translational modifications (PTMs). Some of the albumin PTMs showed correlation with tumorigenesis. Examples of PTMs of albumin are reported at www.phosphosite.org.
Modifications like glycation of patients with breast cancer is seen higher as compared to healthy control.
Figure below shows an example of described PTMs of albumin. Note that every dot is a detected PTM.

Legend: PTM sites
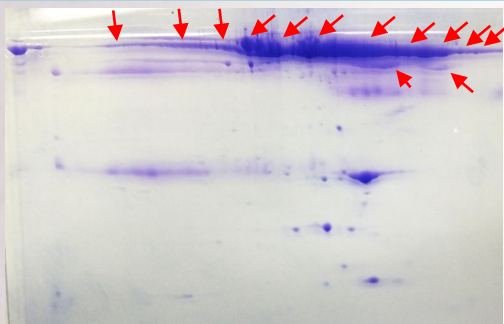- Phosphorylation
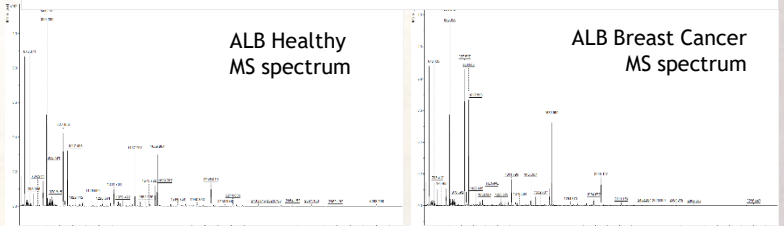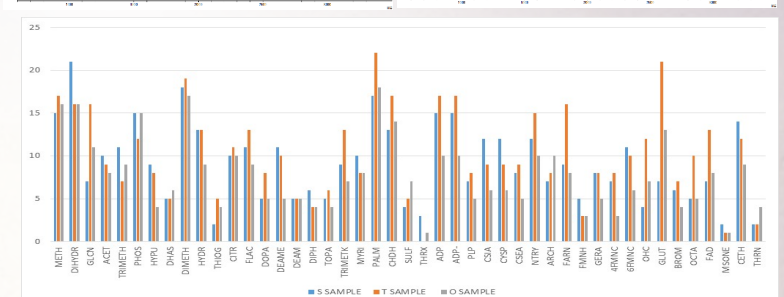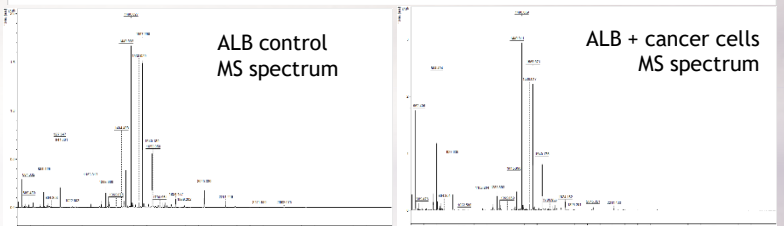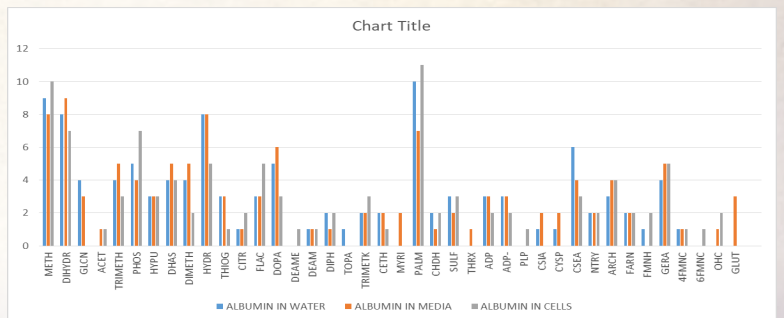- Acetylation
- Ubiquitylation
- Other
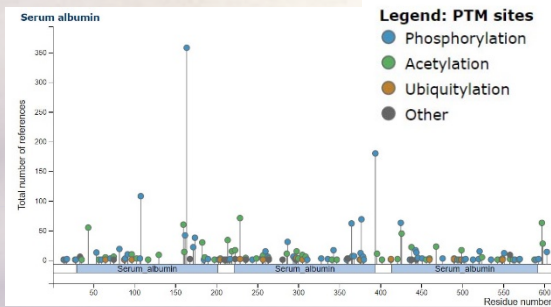
Results (2D-GE)

Image above shows a 2-dimensional gel with separated proteins of human serum. Arrows show main and some minor isoforms of Albumin.
The isoforms are results of PTMs.

Conclusion

We detected more than 30 PTMs in albumin.
We identified PTMs of albumin which change upon exposure to cancer cells and in breast cancer patient.

Results (mass spectrometry)

PTMs were detected by using MALDI TOF/TOF mass spectrometry.
Images below show 2 tables with listed PTMs identified in albumin as result of exposure to the human breast cancer cells and compared to non-exposed albumin (upper table).
Lower table shows albumin PTMs differentially present in albumin from serum of a breast cancer patient (O) as compared to a healthy individual (S).

ALB control MS spectrum

ALB + cancer cells MS spectrum

ALB Healthy MS spectrum

ALB Breast Cancer MS spectrum

We hypothesize that several novel post-translational modification in albumin could be related to cancer and can be used as biomarkers. We performed mass spectrometry and 2D gel electrophoresis analysis of serum albumin for 32 most common PTMs. We identified most of these PTMs in albumin. We observed that human cancer cells affected PTMs profile of albumin. Examples of affected PTMs are phosphorylation, palmitolylation, geranyl- geranylation etc. We observed also differences in PTMs profiles of albumin from serum of a healthy person and cancer patient. O - GlcNAcylation, farnesylation, glutathionylation , S- nitrosylation were found to differ.