Biomarker discovery by automatic annotation of N-glycan species in MALDI-TOF-TOF spectra

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Overview

We present Multi N-Glycan, a software can annotate different N-glycans by examining mass spectra automatically.

- User- or Pre-defined[1] N-glycan list will be tested for each potential isotopic envelope.
- Each envelope will have a correlation score in overlap and non-overlap scenarios.
- Multiple groups of spectra can be used to discover the significant different glycans between groups.

Software Link: http://mendel.informatics.indiana.edu/~chuyu/MultiNGlycan/

Introduction

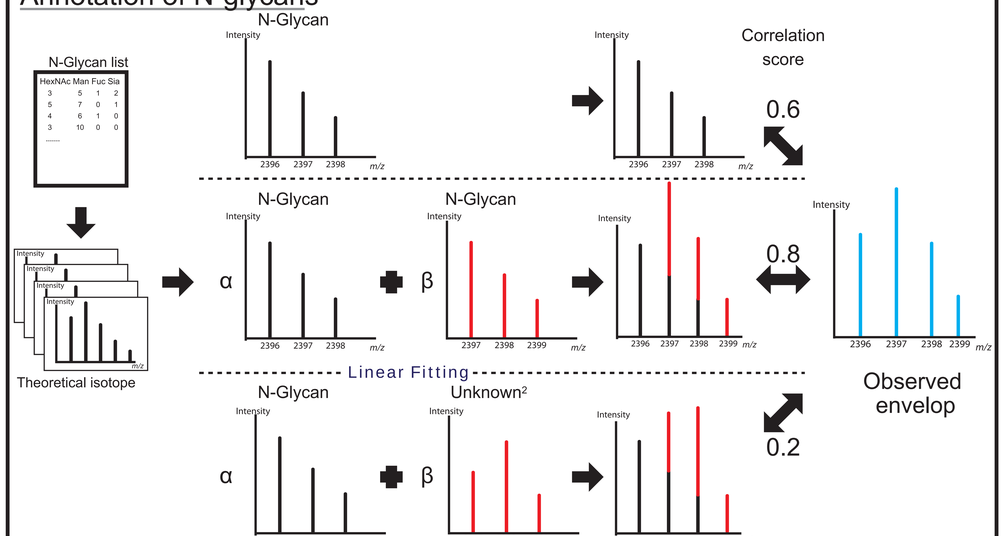
Mass Spectrometry (MS) is a high-throughput and high sensitive technology for the analysis of complex biological samples. The glycoproteins are more complex than proteins with other post-translational modifications, because of the microheterogeneity and diverse tree structure of the glycosylations. As a result, glycans are often cleaved from the glycoproteins and then analyzed separately by MS (e.g. MALDI-TOF-TOF). We combined machine learning, statistical and signal processing techniques to automatically annotate MALDI-TOF-TOF spectra of N-glycans. Our tool can detect the overlapping isotopic envelopes resulted from N-glycans of similar masses, and can also identify N-glycans of significantly different abundances across multiple spectra. Our program can be used in the biomarker discovery by comparing N-glycan profiles from two (or more) groups of samples (e.g. disease vs. normal).

Conclusions

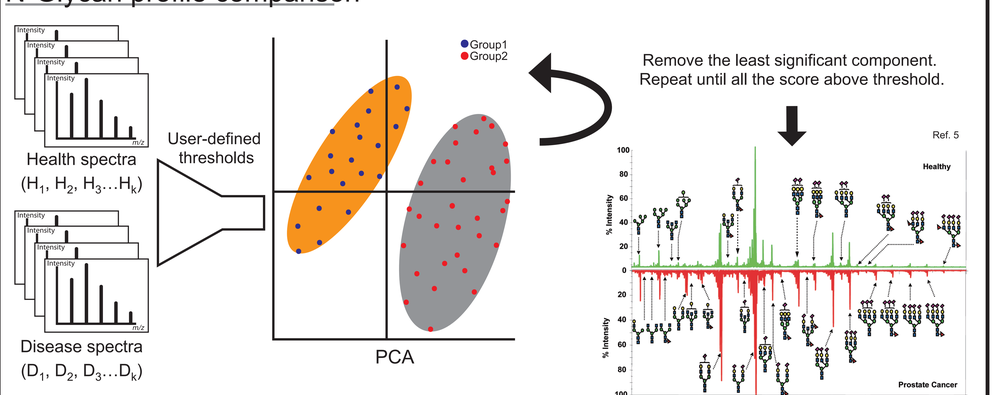
Our tool, Multi N-Glycan, can rapidly annotate and compare N-Glycan in MALDI-TOF spectra. It uses traditional biomarker discovery protocol with pre-annotated spectra; and comes out a high-quality and reliable result for preliminary screening.

Methods

Annotation of N-glycans



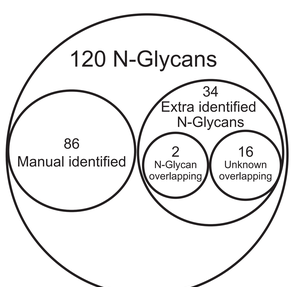
N-Glycan profile comparison

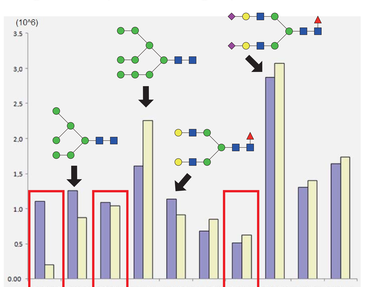


Results

In a MALDI-TOF-TOF experiment, we only can identify 86 N-glycans in manual inspection, but the software can identify an extra 34 N-glycans. Among these 120 N-glycans, 40 N-glycans received fitting scores above 0.7; 16 N-glycans were detected to have the isotopic envelope overlapping with that of another unknown molecule; and two N-glycans were detected to have overlapping isotopic envelopes with each other.(Buttom left)

We also compare our result with previous study[3]. Three out of ten N-glycans have the similar trend. Four out of seven the rest N-glycans found structures in the CFG database. These glycans might be considerable potential biomarkers for in addition investigation. (Buttom right)





Future work

We would like to extend this approach on O-glycan profiling, and also perform *de novo* glycan sequencing on reported glycan if the data contain MS/MS spectrum. This can help to differentiate microheterogeneity of the glycosylation.

References

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Acknowledgements

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