Plenary session

Targeted Blood Lipidomics of Colorectal Cancer

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Being the third most frequently diagnosed cancer colorectal cancer (CRC) is also the third leading cause of cancer-related deaths. Additionally CRC early-onset incidence has been rising at a significant rate for the last 25 years further urging the need for population-based screening not only for individuals presenting red flag signs and symptoms. Current invasive and resource-demanding diagnosis methods such as colonoscopy need to be supported by a triage strategy that would allow to rule out non-CRC patients. Fecal immunochemical tests have high potential but lack sufficient sensitivity and would benefit from additional rapid chemical tests. In that context developing chemical methods to identify CRC markers with high specificity sensitivity robustness low level of invasiveness and cost effectiveness is of high interest.

We conducted a study on 64 human serum samples from different groups (adenocarcinoma adenoma and control) using cutting-edge GC×GC–LR/HR-TOFMS techniques. We analyzed samples with two different sample preparation approaches for targeted lipidomics12 (fatty acids) (25 µL serum) and metabolomics34 (50 µL serum). Samples were randomized with a QC sample (pooled human plasma) and NIST SRM 1950 for QA/QC requirements.

Highly structured 2D chromatograms facilitated the identification of chemical families and structures (e.g. structuration of fatty acid methyl esters (FAMEs) based on C numbers and number of double bonds). Before applying the statistical tools median normalization cubic root transformation and autoscaling of the data were applied. A chemometric screening including unsupervised (PCA HCA) and supervised analysis (PLS-DA) univariate analysis (volcano plot) and random forest (RF) classification algorithm was performed on both metabolomics and targeted lipidomics data sets. Out of the 354 compounds isolated in the metabolomics data set 52 were identified: 20 were amino acid derivatives 14 were lipids 8 were organic acids and 10 other compounds not belonging to a specific family.

In the targeted lipidomics data set 36 compounds were identified: 13 saturated fatty acids (SFA) 8 monounsaturated fatty acids (MUFA) 14 polyunsaturated fatty acids (PUFA; 6 ω-3 7 ω-6 1 ω-9) and 1 cholesterol derivative. Amongst them 8 features (MSI confidence levels of 1 or 2) were identified as significant (VIP score >1 MDA cut-off >0008). It revealed that specific PUFA (ω-3) molecules were inversely associated with increased odds of CRC while some PUFA (ω-6) analytes shown a positive correlation. Additionally a tendency to sub-categorization of the adenocarcinoma samples based of cancer stages appeared and is currently under deeper investigation. Random forest cross-validation also demonstrated the ability of the approach to predict sample classes with low-class error rates (OOB error 0015).