Comprehensive metabolomic fingerprinting discriminates cancer from the non-transformed state in colonic tissue and cell lines

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1. Introduction

Colon cancer is the second and third most common cancer worldwide for women and men, respectively. Nevertheless, the underlying pathological mechanisms are not fully understood and need to be further explored, since they may serve as starting points for developing new prevention and therapeutic strategies. Moreover, colon (cancer) cell lines are frequently used in cancer research as models, although it is not known to what extent these cell cultures represent metabolic processes *in vivo*. Whilst several efforts have been made to map the genome and proteome of cells and tissue, the actual endpoints that truly reflect the cellular phenotype, i.e. the metabolites and lipids, have received less attention.

2. Approach

In this study, a comprehensive untargeted polar metabolomics (1) and lipidomics method (2) using Ultra High Performance Liquid Chromatography coupled to hybrid High Resolution Mass Spectrometry (UHPLC-HRMS) and multivariate statistics was applied to discriminate the non-transformed (NT) and transformed (T) state in colonic cell lines (CCD CON 841, FHC, Caco-2, HT29, HCT116, SW948, SW480) and human tissue samples obtained from 10 cancer patients.

3. Results and discussion

More then 15,000 components with CV < 30% were detected in the quality control samples and validated OPLS-DA models (R_2Y > 0.719 and Q_2 > 0.713) could be constructed (Figure 1). In total, 196 and 721 unique discriminating components for NT and T colonic tissue were retained, respectively, with VIP-value > 1.0. Of these components, 151 and 165 were significantly differently regulated between NT and T colonic cell lines, respectively. Hierarchical clustering of cell lines revealed two distinct classes, i.e. NT and T, and 3 subclusters in the T class (cluster 1: HT29 and Caco-2, cluster 2: HCT116, cluster 3: SW480 and SW948).

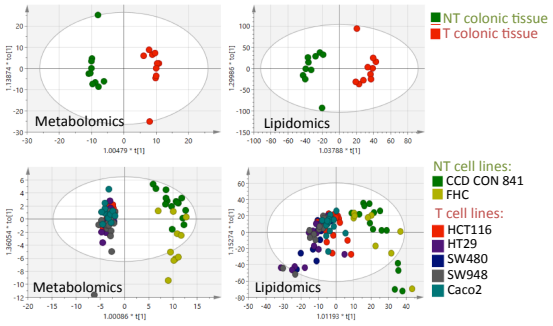

Figure 1. OPLS-DA models discriminating between the non-transformed (NT) and transformed (T) state in colonic tissue and cell lines

Identification of the retained components revealed enhanced glutaminolysis, pyrimidine and lipid synthesis in T as opposed to NT state in both sample matrices. Especially, glutaminolysis, whereby glutamine is incorporated in the building blocks of cells during high cell proliferation, has gained much interest in cancer research (3).

4. Conclusion

The applied comprehensive polar metabolomics and lipidomics platform enabled to discriminate between the NT and T state in colonic tissue and in cell lines. Moreover, interesting cancer-associated pathways were elucidated that could be further exploited as targets in prevention and drug discovery.

References

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