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Research Letter

Serum lipidomic study reveals potential early biomarkers for predicting response to chemoradiation therapy in advanced rectal cancer: A pilot study

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Abstract

Purpose: Prospective detection of patients with advanced rectal cancer (LARC) who have a higher probability of responding to preoperative chemoradiotherapy (CRT) may provide individualized therapy. Lipidomics is an emerging science dedicated to the characterization of lipid fingerprint involved in different pato-physiological conditions. The purpose of this study is to highlight a typical lipid signature able to predict the tumor response to CRT.

Experimental Design: A prospective global analysis of lipids in 54 sera from 18 LARC patients treated with preoperative CRT was performed. Samples were collected at 3 time points: before (T0), at 14th day and at 28th day of CRT. An open LC-MS/MS analysis was performed to characterize lipid expression at T0. Differential lipids were validated by an independent approach and studied during treatment.

Results: From 65 differential lipids highlighted between responder (RP) vs not responder (NRP) patients, five lipids were validated to predict response at T0: SM(d18:2/18:1), LysoPC (16:0/0:0), LysoPC (15:1(9z)/0:0), Lyso PE (22:5/0:0) and m/z = 842.90 corresponding to a PC containing 2 fatty acids of 40 carbons totally. The levels of these lipids were lower in NRP before treatment. The ROC curve obtained by combining these five lipid signals showed an AUC of 0.95, evidence of good sensitivity and specificity in discriminating groups.

Conflicts of interest: None.

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Conclusion: Our results are in agreement with previous evidences about the role of lipids in determining the tumor response to therapy and suggest that the study of serum lipid could represent a useful tool in prediction of CRT response and in personalizing treatment.

Introduction

Colorectal cancer (CRC) is the third most frequently occurring cancer globally.[1] Preoperative fluoropyrimidine-based chemoradiation therapy (CRT) or short-course radiation therapy followed by total mesorectal excision are the standard treatments for CRC.[2-4] In the effort to personalize treatments, there is increasing interest in predicting which patients will respond to neoadjuvant CRT,[5] especially via investigating easily accessible biological fluids,[6] and in improving response rate and survival outcomes. Several biomarkers have been investigated for their ability to predict outcome in locally advanced rectal cancer (LARC) treated with CRT, but few works have investigated lipids.[7-9] Bioactive lipids are fundamental mediators of a number of biological processes,[10-12] and the implication of lipids in cancer growth and diffusion have already been demonstrated.[13] In this work, we aimed to study serum polar lipids in a prospective cohort of LARC patients before CRT (t0 group), including patients naïve to chemotherapy and radiation therapy. Samples were also collected during CRT (t14 and t28 days), in the effort to correlate the global lipid signature to response to treatment.

Methods

See Appendix E1, available as supplementary material online only at www.practicalradon.org.

Results

Lipidomics biomarker discovery

The serum from 18 patients with LARC (7 women, 11 men)—8 of whom were classified as responders (RPs) and 10 as not responders (NRPs) according to Mandard's tumor regression grading—treated with preoperative CRT was analyzed by liquid chromatography electrospray ionization tandem mass spectometry. Data were converted into a matrix containing m/z signals coupled with

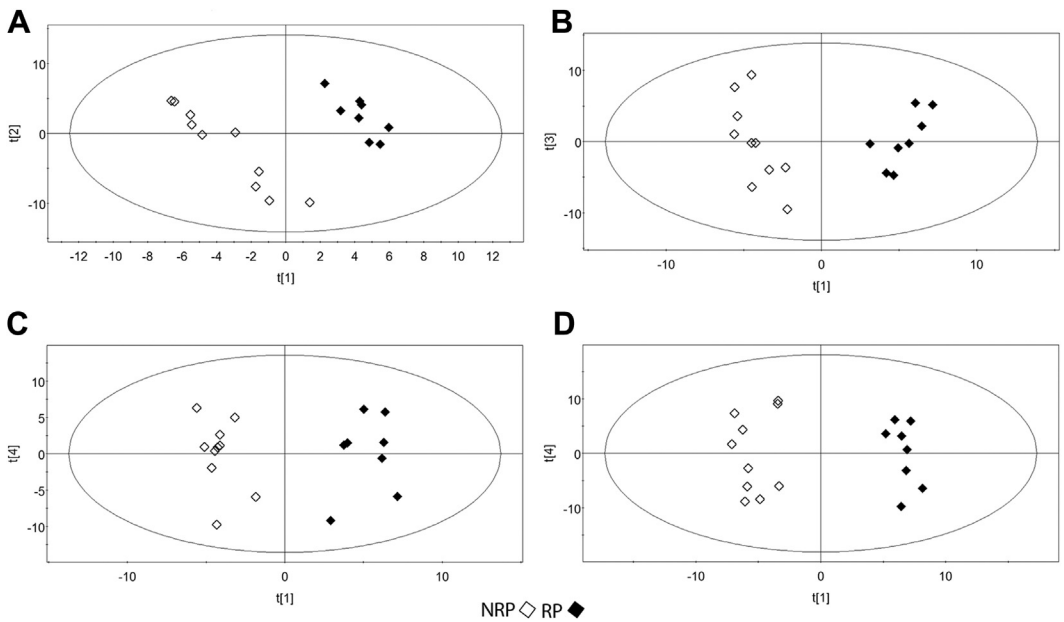

Figure 1 Partial least squares discriminant analysis score plots based on the lipidomics data. Responders (RPs) (represented as full diamonds) and not responders (NRPs; represented as open diamonds) before treatment (t0). The panels show partial least squares discriminant analysis score plots for the analyzed lipids, in particular the phosphatidylcholine/sphingomyelin class (A), phosphatidylethanolamine class (B), phosphatidylglycerol class (C), and phosphatidylserine class (D).