Metabolomic characteristics in glioblastoma patients undergoing concurrent chemoradiation therapy.

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Objective: To illustrate changes of untargeted metabolomics in patients with glioblastoma IDH wildtype undergoing concurrent radiation therapy (RT) with temozolomide (TMZ). This study implemented machine learning (ML) algorithms to predict treatment phase: pre-surgery, post-surgery, pre-radiation, and post radiation based on untargeted metabolomics data.

Methods: Thirty-six patients with glioblastoma IDH wildtype (18 methylguanine methyltransferase [MGMT] methylated, 16 MGMT unmethylated, 2 MGMT status unknown) were enrolled into this study. Serum samples obtained from patients on the same day before surgery, 2 days after surgery, before starting their concurrent chemoradiation, and after concluding this phase of treatment. Blood samples were obtained via antecubital phlebotomy without regard for time of the day, diet, or fasting status. Untargeted metabolomics by GC-TOF mass spectrometry were obtained and compared. The proposed ML models analyzed 105 samples from 36 patients utilizing 157 structurally identified blood metabolites. Multinomial Logistic Regression (MLR) and GradientBoostingClassifier (GB Classifier) were used to classify patient samples based on detected changes in blood metabolites. The classification performance of these models was evaluated using performance metrics and AUC scores.

Results: Post radiation; significant increase in the following metabolites: glycine, serine, threonine, oxoproline, 6-deoxyglucose, gluconic acid, glycerol-alpha-phosphate, ethanolamine, propyleneglycol, triethanolamine, xylitol, and fumaric acid were noted while significant decrease in 3-aminopiperidine 2,6-dione was noted post radiation. MLR produced 78% accuracy, 75% precision, and AUC = 0.89, and GB Classifier produced 75% accuracy, 77% precision and AUC = 0.91. Finally, we presented a pattern of metabolites changes per clinical stage based on pairwise correlations.

Conclusions: This study represent the first serum metabolic signature associated with RT in patients with glioblastoma. The results from the classification algorithms and pairwise correlations showed that blood metabolites have the potential to predict phase of treatment and potentially enable to evaluate response to treatment in patients with glioblastoma in a relatively small cohort.