ORIGINAL RESEARCH

72. Evaluating SLC11A2 Expression in Stage III Colon Adenocarcinoma: No Prognostic Signal but Coordinated Expression with SLC40A1

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Background: Colon cancer is characterized by the uncontrollable growth of abnormal epithelial cells and is a leading cause of cancer-related mortality worldwide. Stage 3 colon adenocarcinoma involves local lymph nodes and has a 5 year survival rate of about 65-75%. In diseases associated with marked inflammation, expression of iron regulating genes has been shown to experience significant alterations and predict worse prognosis in some patients. Notable genes involved in this pathway include SLC11A2, HAMP, FTH1, and SLC40A1.

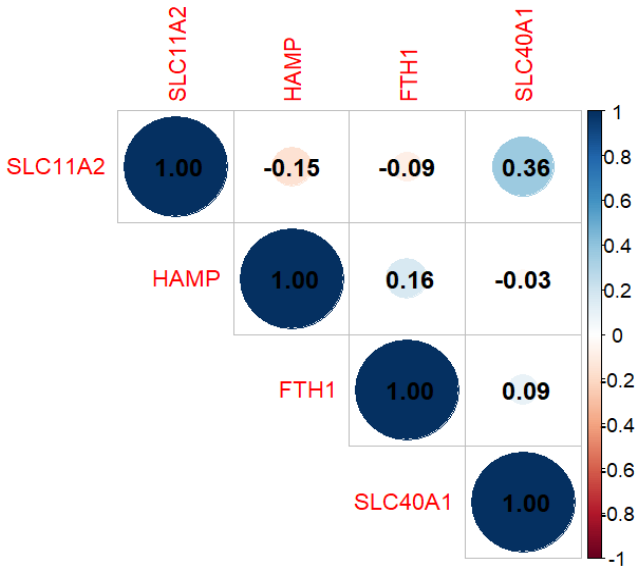
Aim: This study assessed SLC11A2's significance for predicting overall survival in stage 3 colon adenocarcinoma followed by a gene expression correlational analysis with other iron regulating genes in patients from The Cancer Genomic Atlas COAD database.

Methods: TCGA was queried for clinical and STAR counts RNA gene expression data within the TCGA-COAD project. 362 patients with AJCC stage 3 primary colon adenocarcinoma were selected. STAR RNA data was normalized using variance stabilizing transformation and patients were stratified by quartiles of expression into Q1, Q2, Q3, or Q4 groups. Additionally, patients were classified as early onset (EO) or late onset (LO) if age at diagnosis was before or after 50 years old, respectively. A Kaplan-Meier overall survival (OS) curve was created comparing survival across quartiles of SLC11A2 expression with log rank analysis assessing significance. Univariate and multivariate Cox Proportional Hazards Analysis was completed for SLC11A2 expression quartile, age, gender, and race. Linear regression testing was completed to assess colinearity of SLC11A2 expression with HAMP, FTH1, and SLC40A1.

Results: On Kaplan-Meier analysis, SLC11A2 expression was not a significant predictor of survival at any quartile. Q2 experienced the worst survival, with all other quartiles displaying similar survival. On univariate analysis, quartiles of SLC11A2 expression were nonsignificant for OS. LO patients experienced significantly worsened survival compared to EO (7.23 HR, 1.76-29.7 95% CI, p=0.006). On multivariate analysis, SLC11A2 expression remained a nonsignificant predictor of OS. However, LO age group remained a significant predictor of worsened survival, moreso than on univariate analysis (13.3 HR, 3.04-58.2 95% CI, p<0.001). Race became a significant survival predictor with African American patients surviving worse than white patients (2.07 HR, 1.15-3.70 95% CI, p=0.015). On correlational analysis, SLC11A2 and SLC40A1 showed a significant positive expression correlation with no other genes showing significance (r=0.36, p<0.001).

Conclusion: Regardless of SLC11A2 expression, overall survival in stage 3 colon adenocarcinoma is mediated by age and race. SLC11a2 does not appear to be a significant gene in predicting prognosis in stage 3 of this cancer. SLC40a1 and slc11a2 display a significant positive expression correlation. After accounting for SLC11A2 expression, age, and gender, African American and LO patients experience significantly worsened OS.

Figure 1. Linear Regression Testing of SLC11A2 Expression with HAMP, FTH1, and SLC40A1 Genes.



Legend: Numeric values are the Pearson's correlation coefficient with 1 being a perfect correlation.

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