Title: Collagen Hydroxyproline Analysis of Colon Cancer Polyps in Patients within the Appalachian Mountain Region.

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Abstract:

Emerging evidence suggests that collagen morphology may influence the prognosis and response to treatment of colorectal cancer (CRC). We sought to investigate the overarching differences in collagen posttranslational hydroxyl prolines as a predictive model of tumor stage and to investigate population differences in the American Appalachian population. Tissue microarrays (TMAs) comprising of matched benign and malignant tissue from 45 patients were constructed to evaluate the degree of collagen alpha-1(I) hydroxylation of proline. In total 86 samples were analyzed. 5 specific peaks were discovered to differ between benign and malignant polyps. ROC curve analysis indicated high sensitivity and specificity of these peaks to predict polyp malignancy. 17 individual peaks indicated differences between early-stage (Stage I+II) and late-stage (Stage III+IV) polyps with a high predictive power (Area; 0.7355, 95% CI: 0.7014-0.7696, $p=1.000x10^{-15}$). Analysis of late-stage malignant polyps showed the same 17 peaks were significantly increased in patients from the Appalachian region of the United States vs Non-Appalachian residents. This present study highlights the potential for utilizing TMA as a method for detecting with high predictive power the influence of collagen on overall tumor prognosis. Further, we provide evidence that TMA analysis can be utilized to detect differences between specific at-risk populations, a method that might improve diagnostic and prognostic outcomes. Taken together we provide evidence for the investigation of collagen proline hydroxylation in CRC as a prognostic and diagnostic marker which can have significant clinical outcomes.