Digital pathology: Discovering and verifying Barrett’s disease progression markers in LCM tissue samples using SRM assays.

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Overview

The incidence of esophageal adenocarcinoma (EAC) arising from Barrett’s esophagus (BE) has increased by 350% since 1970, and at the time of presentation, 50% of patients will have advanced disease with virtually no chance for cure. The prognosis for EAC arising from BE is poor with an overall 5-year survival rate and less than 15%, with no verified progression markers. Currently, risk for esophageal cancer is determined by the histologic appearance of BE; however, there is a large degree of intra- and inter-observer variability among pathologists. Using an LCM-SRM assay, and a novel software algorithm we hypothesize that coupling of objective SRM-based assay information with subjective histology-based information will increase the sensitivity and specificity for risk stratification for BE patients.

Introduction

The incidence rate of esophageal adenocarcinoma (EAC) has risen by 350% since 1970, with all other cancers (www.cancer.gov). There are approximately 15,000 new cases of esophageal cancer per year in the United States, half of which are EAC. The incidence of EAC is 4 cases per 100,000 person years. This cancer is associated with a dismal prognosis, with an overall 5-year survival rate of less than 15%. Although the survival rate depends on the stage of disease, more than 50% of patients present with dysphagia (difficulty swallowing) secondary to obstruction from the tumor and with inoperable disease. Upon review of the Surveillance, Epidemiology and End Results (SEER) database for the last 27 years, it is ominous that the incidence rate for esophageal cancer is mirrored precisely by the age-adjusted mortality for a given year (seer.cancer.gov).

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Conclusion

We employed internal standard peptides for monitoring of chromatographic and mass spectrometric performance parameters. 2. A number of known stage-specific proteins, along with a number of novel candidates, were identified whose relative abundances vary along the pathway of progression from Barrett’s metaplasia to esophageal carcinoma. 3. Using the SRM assays, we monitored the 6 proteins for the same tissue sections, and absolute abundances were calculated. The relative expression levels between the pathologies were the same as observed by LC-MS/MS Orbitrap work (Figure 4). A novel software algorithm was developed to link the LCM tissue images with the quantitative SRM data (Figure 5). We hypothesize that coupling of objective SRM-based assay information with subjective histology-based information will increase the sensitivity and specificity for risk stratification for BE patients.