monoclonal anti-COX-2-antibody, active and chronic inflammatory reactions were classified according to the Updated-Sydney-System.
Results: Within Barrett's sequence, a significant progressive increase in COX-2 expression was identified ($p < 0.0001$). The most significant differences were detected between squamous epithelium and Barrett's metaplasia ($p < 0.001$) and from low- to high-grade dysplasia ($p < 0.0001$). Active and chronic inflammation were significantly different between squamous epithelium and Barrett's metaplasia ($p < 0.0001$) but not during further progression in the MDC sequence.
Conclusion: There is a significant association between increasing COX-2 protein levels and the development and progression of Barrett's MDC sequence. Increasing COX-2 expression is associated with a change in type or degree of the associated morphological inflammation in Barrett's metaplasia but not during progression of MDC. Chemoprevention strategies aiming at a reduction of COX-2 expression can likely not be monitored by morphological analysis of the inflammatory reaction.

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P58. HIF-1α mRNA IS SIGNIFICANTLY OVEREXPRESSED IN ESOPHAGEAL SQUAMOUS CELL CANCER BUT NOT ASSOCIATED WITH HISTOPATHOLOGIC REGRESSION FOLLOWING NEOADJUVANT CHEMORADIATION

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Background: Hypoxia-inducible factor-1α (HIF-1α) expression was reported to be associated with tumor growth, progression and resistance to radio- and chemotherapy. We analyzed if HIF-1α mRNA or protein expression is associated with histomorphologic response or prognosis following neoadjuvant chemoradiation and surgery in locally advanced esophageal cancers.
Methods: Fifty-three patients with resectable, locally advanced esophageal cancers (cT2-4, N_x, M_0) received neoadjuvant chemoradiation (cisplatin, 5-FU, 36 Gy) followed by transthoracic en bloc esophagectomy. RNA was isolated from endoscopic biopsies (paired tumor and normal tissue) prior to neoadjuvant treatment and quantitative real-time reverse transcriptase PCR (RT-PCR, TaqMan™) assays were performed to determine HIF-1α mRNA expression. HIF-1α protein expression in pretreatment biopsies and posttherapeutic resection specimens was analyzed by immunostaining of tumor cells.
Results: In squamous cell cancer, HIF-1α mRNA expression was significantly higher in tumor tissue as in paired normal epithelium (Wilcoxon test: $p < 0.001$). Normal squamous epithelium showed significant elevated expression in adenocarcinomas suggesting a field effect (Mann–Whitney test: $p < 0.04$). HIF-1α protein expression showed a significant downregulation after chemoradiation.
Conclusion: However, neither HIF-1α mRNA nor protein expression was associated with histomorphologic regression or prognosis following neoadjuvant chemoradiation and surgery in locally advanced esophageal cancers. HIF-1α mRNA expression is differentially upregulated in esophageal squamous cell cancer compared to adenocarcinomas however does not predict tumor regression or prognosis.

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P59. TOWARDS THE MOLECULAR CHARACTERIZATION OF DISEASE: COMPARISON OF MOLECULAR AND HISTOLOGICAL ANALYSIS OF ESOPHAGEAL EPITHELIA

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Background: Reliable quantification of gene expression offers the possibility of more accurate and prognostically relevant characterization of tissues than potentially subjective interpretations of histopathologists. The aim of this study was to evaluate the feasibility of molecular characterization of normal and pathologic esophageal epithelia. Therefore we measured the expression of 18 selected genes and compared them to histological features in a spectrum of esophageal disease.
Methods: Esophageal tissue biopsies from patients with foregut symptoms were laser-capture microdissected and the expression levels of 18 selected genes were measured by QRT-PCR (Taqman®). Linear discriminant analysis, which uses combinations of genes to distinguish between histological groups, was performed to compare gene expression and the following 5 histological groups: (1) normal squamous epithelium, ($n = 32$); (2) reflux-esophagitis, ($n = 13$); (3) non-dysplastic Barrett's, ($n = 17$); (4) dysplastic Barrett's, ($n = 10$); (5) adenocarcinoma, ($n = 22$).
Results: A panel of 7 genes had 90–94% predictive power to distinguish non-dysplastic and dysplastic Barrett's esophagus. Clustering analysis revealed structure in gene expression values even in the absence of histology. Expression levels in 17 genes differed significantly across histological groups. Classification based on gene expression agreed with histopathological assessment in the following percentage of cases: normal squamous epithelium = 53%, reflux-esophagitis = 31%, non-dysplastic Barrett's = 76%, dysplastic Barrett's=40% and adenocarcinoma = 59%. Interestingly, predictive power improved markedly when inflammatory and dysplastic tissues were removed (77–94%).
Conclusion: Gene expression classification agrees well with histopathological examination. When differences occur, it is unclear whether this effect is due to intra-observer variability in pathological diagnosis or to a genuine difference between gene expression and histopathology.

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