Detection of colorectal dysplasia using fluorescently-labeled lectins

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Introduction: Early detection of colorectal cancer is based currently on white light colonoscopy. However, diminutive and flat lesions may be frequently missed, particularly in the proximal colon where these lesions are typically advanced and require a more effective screening tool. We describe here the use of fluorescently labeled lectins targeting glycosylated biomarkers of dysplasia on the luminal surface epithelium, which may enable automated histological assessment of biopsies and fluorescence-guided resection at colonoscopy.

Methods: Colonoscopy identified 99 colorectal lesions in 48 patients. Biopsy and/or polypectomy, or partial colon resection were performed for suspected neoplastic lesions. Formalin-fixed-paraffin-embedded materials derived from these lesions were studied. Binding of fluorescently-labeled lectins to the luminal surface epithelium observable in colonoscopy was compared with histological assessment. Fluorescence intensity and chemical stains for mucins were analysed quantitatively, allowing consistent and standardised quantitative comparisons across samples.

Results: Normal epithelium (NE) occupied 40.1% of the area of the tissue sections, with hyperplastic polyps (HP) occupying 10.2%, low-grade (LGD) dysplasia 25.6%, high-grade (HGD) dysplasia 13.9%, and carcinoma (C) 10.2%. Fluorescent lectin histochemistry showed that wheat germ agglutinin (WGA) and Helix pomatia agglutinin (HPA) decreased their binding in the progression to cancer (P < 0.001, Jonckheere’s trend analysis) and could distinguish epithelial regions containing NE from regions containing LGD, HGD or C (sensitivity and specificity: 81% and 79% for WGA; 85% and 89% for HPA, respectively). The same pattern was observed previously in our lab using fluorescent lectins to aid the endoscopic identification of dysplasia in Barrett’s oesophagus (Bird-Lieberman, E.L., et al., Nat Med, 2012. 18(2): p. 315-21). Remarkably, WGA can distinguish hyperplasia from regions containing LGD, HGD or C with 100% sensitivity and specificity in our dataset. A strong linear correlation was observed between WGA binding and alcian blue staining (R = 0.79, P < 0.0001), consistent with the specificity of WGA for acidic glycans.

Conclusion: Analysis of fluorescently-labeled lectin binding, in particular WGA, to the luminal surface epithelium of excised colorectal tissue sections may be automated for improved assessment of colonic dysplasia. Fluorescently-labeled WGA may also be a useful tool for improving detection of dysplasia using fluorescence colonoscopy.

Figure: P-222