Background
Colorectal cancer (CRC) occurring in the setting of Inflammatory Bowel Disease (IBD) is relatively uncommon. Mutations in p53 have been found in these cancers, and have been proposed as a possible genetic marker with utility in detection of these cancers and their precursor dysplasias. We undertook this study to determine the frequency of p53 null alterations, a recently observed pattern that has not previously been described in colitis-associated neoplasia.

Methods
Patients with CRC were selected from the pathology database of Miraca Life Sciences. The database includes demographic and clinical information, summary of the endoscopic report, biopsy location, and the histopathologic report for each biopsy specimen. Cases of CRC with a report date from 11/1/2007 to 11/30/2011 were extracted from the database. From these cases, a database search was performed to extract patients with a history of Ulcerative Colitis (UC) and Crohn Disease (CD). p53 immunohistochemical staining was performed on the carcinomas and interpreted as wild-type (<20% 2-3+ nuclear positivity), point mutant (>50% 2-3+ nuclear positivity) or null (no nuclear positivity).

Results
Biopsies from 917,599 colonoscopies were interpreted on 878,835 patients (51% female, 49% male) during the study period. Of these, 16,631 unique patients (48% female, 52% male) had histological and clinical features of UC while 5,736 patients had histological and clinical features of CD. During this period, 6,211 CRCs were diagnosed (52% male, 48% female). Of these cancers, 22 occurred in patients with UC (prevalence of 22/16,631 = 0.13%), and 5 occurred in patients with CD (prevalence of 5/5,736 = 0.09%). 19 IBD patients were male (70.4%) and 8 were female (29.6%). The mean age was 58 years (median 56 years, standard deviation 13.5 years, range 33 to 84 years). Of these tumors, 14 (51.9%) were moderately differentiated (MD) and 13 (48.1%) were poorly differentiated (PD). Immunohistochemical staining for p53 showed abnormalities in 24/27 (89%), including 14 carcinomas with null pattern (51.9%), 10 with mutant pattern (37.0%) and 3 with wild-type pattern (11.1%). One MD carcinoma and 2 PD carcinomas showed wild-type p53 staining.

Conclusions
• The p53 null staining pattern is very common in colitis-associated carcinoma, and more than doubles the detectable frequency of p53 immunohistochemical alterations in these tumors.
• This finding indicates that p53 alterations are one of the most common genetic abnormalities in colitis-associated neoplasia, and has important implications for the potential use of p53 in screening and early detection programs.
• CRC occurring in the setting of IBD is rare, occurs predominantly in males and tends to be poorly differentiated.

References