Colorectal cancer (CRC) is the third most common cancer in both men and women. An estimated 103,170 cases of colon cancer and 40,290 cases of rectal cancer were expected to occur in 2012. Approximately 51,690 deaths from colorectal cancer were anticipated to occur in 2012, accounting for 9% of all cancer deaths.

Despite enormous advancement in diagnostic and therapeutic modalities in the management of this type of cancer, a steady increase in CRC incidence and mortality has been observed in Europe.

Immunohistochemistry (IHC) is now extensively utilized in refining cancer diagnosis and is applied to the study of biomarkers of clinical relevance across a broad range of human tumor types. IHC tests are known to be equal to or better than molecular testing in sensitivity and specificity therefore providing complimentary information. Recently, it has become feasible to identify individuals predisposed to this disease through genetic testing. IHC has the ability to identify the specific gene and therefore help in early detection and treatment. In a histo-diagnostic setting of carcinomas of unknown primary origin, clinico-pathological correlation and IHC staining with a panel of diagnostic antibodies facilitate the definition of the primary site, and direct appropriate treatment.

CDX2 is a master regulator of intestinal phenotype which has been shown to play a tumor-suppressive role in CRC. CDX2 is a caudal-type homeobox gene encoding a transcription factor that plays an important role in proliferation and differentiation of intestinal epithelial cells. The CDX2 protein is normally expressed throughout embryonic and postnatal life within nuclei of intestinal epithelial cells from the proximal duodenum to the distal rectum. CDX2 is also expressed in neoplastic intestinal epithelial cells with a relatively high sensitivity and specificity, and can be used as an IHC marker for neoplasms of intestinal origin. CDX2 expression is reported to be progressively reduced in gastric dysplasia and cancer. Hence, CDX2 may serve as a predictive marker for gastric cancer.

Cytokeratins (CKs) are a group of proteins that consist of a type of intermediate filament and are differentially expressed in epithelia of various organ sites. The cytokeratins most often used are CK7 and CK20 in Gastrointestinal (GI) tumors. CK7 is found in the glandular epithelium and epithelial tumors of lung, ovary, endometrium, and breast, but is not found in GI epithelium. On the other hand, CK20 is expressed mainly in the normal glands and epithelial tumors of the GI tract, urothelium, and Merkel cells. The cytokeratin 7/20 profile of a particular tumor has proven to be a useful aid in the differential diagnosis of carcinomas since primary and metastatic tumors tend to retain the cytokeratin profiles of the epithelium from which they arise. The CK7- / CK20+ expression pattern is known to be highly characteristic of colorectal carcinomas. However, not all colorectal carcinomas show the CK7- / CK20+ expression pattern. Occasionally, colorectal carcinomas may show significant CK7 expression, and expression of CK20 may be seen in a variety of non-colorectal adenocarcinomas.

The p53 tumor suppressor gene, perhaps the most well-known protein within the intrinsic pathways of apoptosis, encodes a transcription factor that regulates the expression of genes involved in the pathway of apoptosis, angiogenesis, cell cycle progression, and genomic maintenance. An acquired defect of p53 or loss of the wild-type allele generally tends to be a later event in colorectal carcinogenesis, probably occurring near the time of invasion. In 50% of human colorectal cancers, p53 is absent or mutated, which has major implications for the execution of apoptosis in colorectal cancer. Mutations in p53 can be determined using IHC since mutated proteins accumulate in the nucleus due to their increased half-life. Certain intracellular death signals mediated by the p53 protein that activate the apoptotic process provide important biomarkers that are directly involved in the apoptotic pathway in CRC. Expression of Bcl-2 in CRCs has also been demonstrated as a favorable prognostic factor. Therefore, IHC-based co-expression levels of p53 and Bcl-2 are an important indicator of the outcome in CRC patients.

Recently, the utility of IHC detection of DNA mismatch repair (MMR) gene proteins in screening colorectal tumors for hereditary non-polyposis colorectal cancer (HNPCC) syndrome has been the focal point of much comprehensive research. Defining tumor phenotype...
- microsatellite instability (MSI) or microsatellite stability (MSS) is desirable in standard therapy for CRC patients. Germline mutations in any of the mismatch repair (MMR) genes (MLH1, MSH2, and MSH6) are an underlying cause of CRC. Subjects carrying a mutation in one of the MMR genes may have a higher risk for developing colorectal cancer. Extra-colonic cancers are more often observed in MSH2 mutation families as compared to MLH1 mutation families. MSH6 mutation families seem more likely to have a milder clinical phenotype with a later onset of CRC. Therefore, MLH1, MSH2, and MSH6 mutations seem to cause distinguishable CRC risk profiles.

Cyclin D1 protein overexpression in 30–45% of CRCs has also been observed when compared with uninvolved epithelium.

The expression of Carcinoembryonic Antigen (CEA) is upregulated in many types of carcinoma. CEA is expressed in epithelial cell membranes and in the cytoplasm of the cells in almost all cases of colorectal adenocarcinoma. A relationship between CEA and CK20 expression and staging has also been reported for CRC.

IHC-based combinational prognostic biomarkers including CDX2, CK7/20, p53/Bcl-2, MLH1/MSH2/6, and Cyclin-1 in either multiplex platforms or individually are potentially important markers for differential tumor diagnosis and for the identification of high-risk subjects in CRC.

References:


Products

Continuing with our firm belief that high quality reagents can be produced and delivered at reasonable pricing. ScyTek Laboratories offers the following panel of markers for Colon Cancer. Each item is available in both Ready-To-Use and Concentrated format. All have undergone extensive in-house validation to provide consistent, high intensity results with virtually no lot-to-lot variability.

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**Product Reference Images**

*Note: All antibodies visualized using ScyTek’s UltraTek reagents and counterstained with hematoxylin*

**Antibody A00093**
- p53 ; Pab1801+DO-7
- Mouse Monoclonal
- Human Colorectal Carcinoma
- (Original Magnification x200)

**Antibody A00111**
- Cyclin D; Clone DCS
- Mouse Monoclonal
- Human Colorectal Carcinoma
- (Original Magnification x200)

**Antibody A00135**
- CEA; Clone COL-1
- Mouse Monoclonal
- Human Colorectal Carcinoma
- (Original Magnification x200)

**Antibody A00142**
- Cytokeratin 7 ; Clone OV-TL12/30
- Mouse Monoclonal
- Human Colorectal Carcinoma
- (Original Magnification x200)
Antibody A00146
Cytokeratin 20; Clone EP23
Rabbit Monoclonal
Human Colorectal Carcinoma
(Original Magnification x200)

Antibody A00147
CDX2; Clone EP25
Rabbit Monoclonal
Human Colorectal carcinoma
(Original Magnification x200)

Antibody A00148
CDX-2+CK-7; Multiplex Cocktail; Clones EP25+OV-TL12/30
Rabbit & Mouse Monoclonal Cocktail
Human Colorectal Carcinoma
(Original Magnification x400)

Antibody A00149
MSH-6; Clone EP49
Rabbit Monoclonal
Human Colorectal Carcinoma
(Original Magnification x200)

Antibody A00150
CDX-2 + CEA  Multiplex Cocktail; Clones EP25+COL-1
Rabbit & Mouse Monoclonal Cocktail
Human Colorectal Carcinoma
(Original Magnification x200)