Tropomyosin Isoform and Diagnostic and Therapeutic Uses Therefor

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Technology description

Invention Summary:Tropomyosins are microfilament-associated proteins found in all eukaryotes and have been implicated in autoimmune diseases such as ulcerative colitis. To date, eight different isoforms (hTM1, hTM2, hTM3, hTMsmα, hTM5a, hTM5b, hTM4, and hTM5) have been identified. Although anti-tropomyosin autoantibodies have been detected in the sera of patients with ulcerative colitis, the autoantigen triggering the autoantibody response has not been definitively identified. Previous studies at Rutgers have identified hTM5 as the predominant immunogen in ulcerative colitis patients. Ulcerative colitis is difficult to diagnose because its symptoms are similar to other intestinal disorders. Furthermore, about 5% of patients with ulcerative colitis develop colon cancer.Thus, the identification of the autoantigen(s), in particular, the specific isoform of Tropomysoin and the specific epitope(s) that trigger ulcerative colitis and colon related diseases and dysfunction would be therapeutically beneficial.A new isoform of tropomyosin, named TC22, that predominates in human colon carcinoma has been identified and completely sequenced. Monoclonal antibodies, TC22-2, TC22-4, TC22-6 and TC22-7, specific for this distinctive protein have been generated. A significantly large percentage (83%) of colon cancer tissues obtained from colon cancer patients showed strong reactivity with TC22-4 monoclonal antibody compared with normal colon epithelial cells or normal colonic mucosa tissue from patients with Crohn’ s disease. Further, the amount of the TC22 protein was also elevated in ulcerative colitis tissues. Studies with GFP-TC22 revealed a weak interaction of the TC22 protein with actin filaments. During mitosis, the alignment of mitotic spindle is guided by strength of the actin filament-tropomysoin interaction thereby influencing cellular proliferation. The elevated expression of TC22 isoform in colon cancer cells and its abnormal interaction with actin filaments implicate a role for TC22 protein in cellular proliferation and cancer. Thus, this novel biomarker can be used for screening and detection of patients at risk of developing colon cancer and other colon related diseases, and ulcerative colitis.

Additional Data:

TC22 clones, GFP-TC22 constructs, and eukaryotic expression systems

TC22-2 (IgM), TC22-4 (IgG1), TC22-6 (IgM) and TC22-7 (IgM) monoclonal antibodies

Application area

To develop in vitro diagnostics for ulcerative colitis and colon cancer.
To develop assays for the screening of novel agents capable of modulating the activity of TC22 for therapeutic applications.
For research use to further the scientific advancement in the area of colon cancer and ulcerative colitis.
For selecting patients for enrolment in clinical trials.

Advantages

Surgery is the only cure for ulcerative colitis. The availability of a monoclonal antibody enables the design of simple and inexpensive diagnostic tests for the early detection and prevention of colon dysfunction and diseases.
Current diagnostic methods involve endoscopic or colonoscopic procedures that are expensive and painful. Patients with inflammatory bowel disease for a prolonged period of time are recommended for colonoscopic identification of precancerous dysplasia.

Institution

Rutgers University

Inventors

Kiron Das
Professor Emeritus
Gastroenterology

联系我们

叶先生

电 话：021-65679356

手 机：13414935137

邮 箱：yeyingsheng@zf-ym.com