Identification and distribution of thioredoxin-like 2 as the antigen for the monoclonal antibody MC3 specific to colorectal cancer
**Brief Introduction of MC3 Antigen**

Using a homogenate preparation of colon cancer tissues, Fan et al. [1] developed a series of colorectal cancer (CRC) specific monoclonal antibodies. Among a series of intestinal cancer specific antibodies, MC3 is a specific and sensitive antibody that reacts with an unknown antigen present in cancer tissues as well as the sera of CRC patients.

MC3 enabled detection of up to 90.2% (185/205) of CRC in pathological samples. In contrast, MC3 antigen (MC3-Ag) was not detectable in normal colorectal mucosa (0/40) [2]. Staining was observed in the cytoplasm of carcinoma cells, although the intensity varied between samples. MC3 antigen (MC3-Ag) positive tumors generally showed uniform staining without significant heterogeneity. Several separate studies also confirmed that the positive detection rate in CRC was around 90% [3-5]. Serological screening of CRC using the ConA-BSA-ELISA method obtained a positive detection rate of 62.07% (72/116) [3]. MC3-Ag was observed in CRC but not in normal colorectal mucosa, suggesting that MC3-Ag may play a role in the development of CRC. In cases of CRC, MC3-Ag was significantly positively correlated with depth of invasion and clinical stage [2] as well as tumor differentiation ($P<0.05$) [4]. However, its expression was not correlated with patient’s age, gender and tumor location.

It has been clinically observed that most cases of CRC arise from a sequence of adenoma to carcinoma. MC3-Ag was increased gradually with the development of polypoid CRC: from 37.5% (15/40) in adenoma, 47.62% (20/42) in adenoma accompanied with dysplasia, to 93.8% (45/48) in CRC ($P<0.05$) [4]. Another study also showed that MC3-Ag increased along with the dysplasia grade of colonic adenoma [6]. The dynamic changes in expression of MC3-Ag in normal colorectal mucosa, precancerous lesions and CRC implicated that MC3-Ag increased gradually with the development and progression of CRC, and could be possibly used as a marker for screening. Moreover, the colon adenoma patients whose MC3-Ag had
been positive later developed colon cancer. In 18 cases of MC3-Ag was positive, 66.7% (6/9) MC3-Ag ++~+++ staining patients developed CRC, 22.3% (2/9) MC3-Ag + staining patients developed CRC while none of the MC3-Ag negative patients (0/18) developed CRC 5 years after adenoma resection [7]. These results suggested MC3-Ag could be used as early predictor of CRC in patients with adenoma. Meanwhile, poorer prognosis was found in MC3-Ag positive CRC patients than in MC3-Ag negative patients [5], suggesting MC3-Ag might be used as a prognostic factor.

Although most cases of colorectal cancer are thought to arise from a sequence of adenoma to carcinoma, evidence from Asia suggests another mechanism. Clinicopathological studies have shown that there is another group of CRC—non-polypoid (superficial) tumours. They are flat lesions with a raised or depressed surface. In non-polypoid dysplasia which is generally thought to be the precancerous lesion of non-polypoid CRC, MC3-Ag was also increased along with dysplasia grade, from 69.4%, 80.0% to 86.4% [2]. This result suggested that MC3-Ag might also play a role in non-polypoid carcinogenesis.

Additionally, $^{131}$I-labeled MC3 antibody against CRC in tumor bearing nude mice was studied [8-9]. In nude mice bearing CRC xenografts, a clear image of tumor was obtained by ECT between 48~120h after injection of labeled MC3. The concentration of MC3 in tumor increased with time and the optimal imaging time was 96~120h after injection. Whereas injection of $^{131}$I-IgG resulted in an equal distribution in the whole body. At 120h after injection of $^{131}$I-MC3, the tumor/liver and tumor/normal colon distribution ratios were 3.61 and 9.81, and the localization index of tumor was 4.26. Histological examination showed that in the $^{131}$I-MC3 concentrated tumor there were large areas of necrosis and only a few round cancer cells remained near the capsule of the tumor. The results suggested potential clinical application of MC3-Ag as a diagnostic marker and a therapeutic target. Functional blockage of MC3-Ag may lead to a novel strategy for the treatment of CRC.
References


Voyager Spec #1 => BC => SM5 => Adv BC (32, 0.5, 0.1) [BP = 2915.5, 735]