The tumor metabolic marker Tumor M2-PK in stool: a new biomarker for colorectal cancer

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Introduction

According to the American Cancer Society colorectal cancer (CRC) is the third most common cancer in the US for both men and women. It is estimated that in 2005 about 145,290 people in the US will be newly diagnosed with CRC, and about 56,290 patients will die from CRC [1].

The development of CRCs takes place over several years. Early stages can easily be treated by endoscopic polypectomy or endoscopic resection of the mucosa. In this context effective screening strategies are of utmost importance. Although colonoscopy is the most sensitive and specific diagnostic tool, most patients will decline this investigation because of its inconvenience, invasiveness and cost. Therefore, more acceptable alternative markers are needed in order to detect patients at high risk.

One common alteration found during carcinogenesis is the isoenzyme shift of the glycolytic enzyme pyruvate kinase. The tissue specific isoenzymes, which have different metabolic tasks, are pyruvate kinase type L in the liver and kidney, type M1 in muscle and brain and type R in erythrocytes. All proliferating cells express the pyruvate kinase isoenzyme type M2 [http://www.metabolic-database.com].

In healthy tissues all isoenzymes of pyruvate kinase consist of four subunits. In all tumors investigated so far, including gastrointestinal tumors, only the type M2 is detectable and pyruvate kinase is mainly in the dimeric form [2]. Therefore, the dimeric form of M2-PK has been termed Tumor M2-PK.

M2-PK

Tumor M2-PK is up regulated in EDTA-plasma samples of patients with esophageal, gastric, colonic and rectal carcinomas [2, 3, 4, 5]. The quantification of Tumor M2-PK in feces provides a new sensitive screening tool for colorectal tumors [6, 7].

Conclusions

This study shows that the determination of Tumor M2-PK in the stool is a valuable tool for the early detection of colorectal cancer. The levels of Tumor M2-PK are significantly higher (p < 0.001) in patients with CRC than in the healthy control group and are correlated with tumor staging according to Dukes’ classification and TNM classification. Overall specificity is 79% and sensitivity is 80%. In comparison to a variety of indirect tests that detect blood in stool with a sensitivity less than 30% [8], Tumor M2-PK has a much higher sensitivity when a single spot stool sample is analyzed. The test directly detects a tumor specific enzyme that is released by the tumor itself.

Material and Methods

The present study includes 338 patients who underwent complete colonoscopy after providing a sample for the determination of Tumor M2-PK. Stool samples of patients with CRC and patients without pathological findings were tested. Histology was obtained from the routine biopsies and/or from surgery. Tumor M2-PK in stool extracts was determined immunologically with a quantitative ELISA which is based on two monoclonal antibodies (Scheffler + Biotech AG, Germany).

References:

5 Zhang et al. World J Gastroenterol 2004; 10: 1643-1646

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Table 1: Tumor M2-PK in Colorectal Carcinoma (CA) and Controls

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Mean [U/ml]</th>
<th>Median [U/ml]</th>
<th>Range [U/ml]</th>
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<tr>
<td>Colon CA</td>
<td>147</td>
<td>49.6 ± 8.0</td>
<td>16.5</td>
<td>0.24 – 800.0</td>
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<td>Rectal CA</td>
<td>88</td>
<td>57.1 ± 12.4</td>
<td>23.8</td>
<td>0.48 – 800.0</td>
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<tr>
<td>Controls</td>
<td>59</td>
<td>38.3 ± 7.5</td>
<td>11.7</td>
<td>0.24 – 270.4</td>
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<tr>
<td>Controls</td>
<td>191</td>
<td>3.5 ± 0.4</td>
<td>1.7</td>
<td>1.7 – 34.3</td>
</tr>
</tbody>
</table>

Figure 1: Fecal Tumor M2-PK in Colorectal Carcinoma (CA) and Controls

Figure 2: Correlation of fecal Tumor M2-PK levels and TNM staging in Colorectal Carcinoma patients (n = 88)

Figure 3: Correlation of fecal Tumor M2-PK levels and staging according to Dukes’ classification (n = 88)