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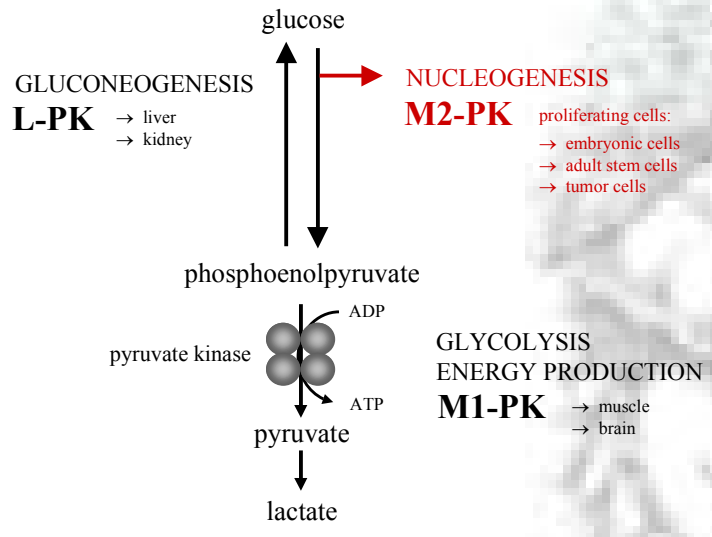
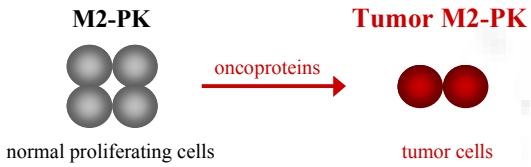
Introduction

The development of colorectal carcinomas (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 may be the most sensitive and specific screening tool, most patients will decline to participate in this program because of its inconvenience and invasiveness. Therefore, there is still a need for more acceptable alternative markers 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 [1]. Therefore, the dimeric form of M2-PK has been termed *Tumor M2-PK*.



Determinations of *Tumor M2-PK* in EDTA-plasma samples of patients with gastrointestinal tumors revealed an upregulation of Tumor M2-PK in oesophageal, gastric, colonic and rectal carcinomas [2, 3, 4].
Recently it could be shown that Tumor M2-PK can be quantified in feces of patients with colorectal tumors.[5].

Material and Methods

Stool samples of patients with colorectal cancer and patients without pathological findings were tested. Endoscopies were carried out as standard investigations. Histology was obtained from the routine biopsies and/or from surgery. Tumor M2-PK in stool extracts was determined immunologically with a new quantitative sandwich-type enzyme immunoassay which is based on two monoclonal antibodies (ScheBo® • Biotech AG, Germany).

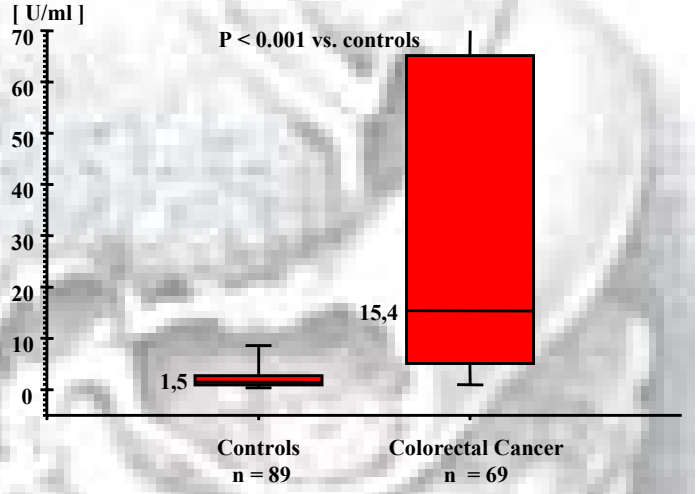


Figure 1: **Ranges of fecal Tumor M2-PK levels in colorectal cancer patients and controls**

	Controls	Colorectal Cancer
Median	**1.5**	**15.4**
Mean	**3.2**	**66.4**
Min	**0.1**	**0.2**
Max	**30.7**	**800**
SE	**0.6**	**16.2**
n	**89**	**69**

Table 1: **Fecal Tumor M2-PK levels in colorectal cancer patients and controls** (Min = minimum ; Max = maximum ; SE = Standard error of the mean; n = number of cases)

Results

Data from 89 controls and 69 patients with colorectal cancer have been evaluated to date (Figure 1 and Table 1). There is a highly significant ($P < 0.001$) difference between tumor patients and controls. At a cut off point of 4 U/ml, the sensitivity was calculated to be 78% for colorectal cancer and the specificity as 82%. The intra-assay variance was evaluated by 18-fold determination of five samples (5 – 66 U/ml), giving an average coefficient of variance (CV) of 7.9% (3.5 - 13.6%). The inter-assay variance was calculated with five samples 4 - 73 U/ml, tested on ten different days. The mean CV was 7.3 % (3.8 - 12.6%).
Preliminary results suggest that fecal Tumor M2-PK levels are correlated with tumor size and inversely correlated with tumor differentiation (data not shown).
In comparison to a variety of indirect tests that detect blood in stool with a sensitivity less than 30% Tumor M2-PK has a much higher sensitivity. The test directly detects a tumor-specific enzyme that is released by the tumor itself. Tumor M2-PK has the potential as a screening tool for the early detection of colorectal cancer.

Conclusions

The fecal levels of Tumor M2-PK are significantly higher in patients with colorectal cancer than in the healthy control group, and suggest that Tumor M2-PK levels are correlated with tumor size and histology. Overall specificity is 82 % and sensitivity is 78%.
The present study shows that the determination of Tumor M2-PK in the stool is a valuable tool for the detection of colorectal cancer in individuals without prior endoscopic evidence of colorectal neoplasms.

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