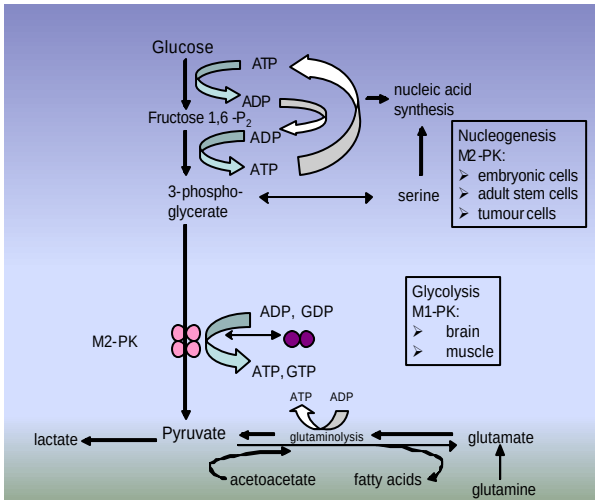
Tumour M2-PK, a novel screening tool for colorectal cancer.

R Mc Loughlin, E Shiel, S Sebastian, Ryan B, O'Connor HJ, O'Morain C.
Department of Gastroenterology, Adelaide & Meath Hospital, Dublin, Ireland.

INTRODUCTION

Colorectal cancer is the leading cause of mortality from cancer in Europe. In population-based studies the overall five-year survival from colorectal cancer is only sixty percent, a reflection of its frequent late presentation. If colorectal cancer can be detected at an early stage, the prognosis is excellent and early colonic cancer has a five year survival in excess of 97%. Colorectal cancer screening leads to earlier detection and a reduced mortality. The currently recommended screening options are FOBT, sigmoidoscopy, colonoscopy, barium enema, or a combination thereof. Newer screening tools for colorectal cancer are under evaluation and may take their place in current guidelines, or even supercede current screening options. A promising new screening tool is pyruvate kinase type M2, or M2-PK.

Tumour cells are capable of surviving and proliferating under unfavourable conditions, namely a poor supply of oxygen and nutrients. A key control enzyme regulating this is the glycolytic enzyme pyruvate kinase. This enzyme determines the relative amount of glucose that is channeled into synthetic processes or used for glycolytic ATP production. Pyruvate kinase is expressed as different isoenzymes depending on the metabolic requirements, and M2-PK is found in proliferating tissues with a high capacity for nucleic acid synthesis such as embryonic cells, adult stem cells, and tumour cells.



In tumour cells the dimeric form of M2-PK increases and this isoenzyme, called tumour M2-PK, leads to an accumulation of all phosphometabolites above pyruvate kinase which are then channeled towards synthetic processes such as nucleic acid, amino acid and phospholipid synthesis. Tumour cells then obtain energy from the amino acid glutamine via glutaminolysis, but this process is dependent on oxygen supply, unlike the glycolytic ATP production by pyruvate kinase which is independent of oxygen. Under conditions of reduced oxygen supply glutaminolysis becomes inhibited and M2-PK switches back to the tetramer form. This allows the tumour to switch between an anabolic or catabolic state depending on oxygen and nutrient supply.

AIM

To evaluate fecal tumour M2-PK as a screening tool for colorectal cancer.

METHOD

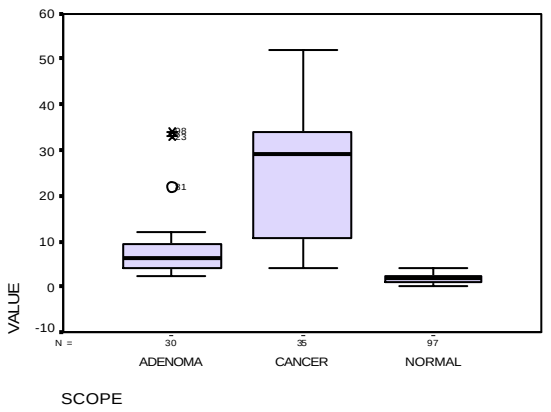
Ethical approval was obtained from our Ethics Committee.
Stool samples were collected from patients pre-colonoscopy and stored at – 80C.
Stool extraction was carried out using the commercially available ScheBo® Tumor M2-PK™ Quick-Prep™ dosing device. Tumour M2-PK was measured with a commercially available ScheBo® ELISA.

RESULTS

Our study included 162 patients, 97 patients with normal colonoscopy findings, 30 patients with adenomas at colonoscopy, and 35 patients with colorectal cancer.

	NORMAL	ADENOMA	CANCER
AGE	23-71 yrs	40-70 yrs	52-85 yrs
SEX (M:F)	42:58	50:50	60:40
COLON:			
RIGHT	Normal	8 adenomas	7 cancers
LEFT	Normal	22 adenomas	28 cancers
POLYPS:			
TA		85%	
TVA		14%	
HGD		1%	
CANCER:			
DUKES A			4
DUKES B			12
DUKES C			15
DUKES D			4

The tumour M2-PK values for those with a normal colonoscopy, adenoma, or cancer are as shown below:



SCOPE

The sensitivity of tumour M2-PK for colorectal cancer was 97% with a specificity of 98%.
For adenomas the sensitivity of tumour M2-PK was 76% with a specificity of 98%.

CONCLUSION

Tumour M2-PK has a high sensitivity and specificity for colorectal cancer. Its non-invasive nature makes it an ideal screening tool for average risk individuals, to identify those who need more invasive screening. Tumour M2-PK is detected by means of a simple ELISA test which can be automated, an advantage for large scale screening programmes. It is cost-effective in comparison with a multi-target DNA approach.

Poster from the NCRI Conference, 2.-5.10.2005, Birmingham, UK