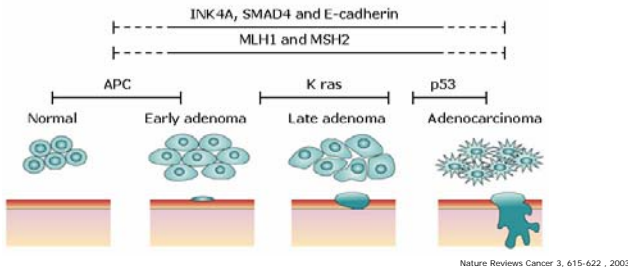


## Colorectal cancer (CRC) a dominant disease in the ageing population



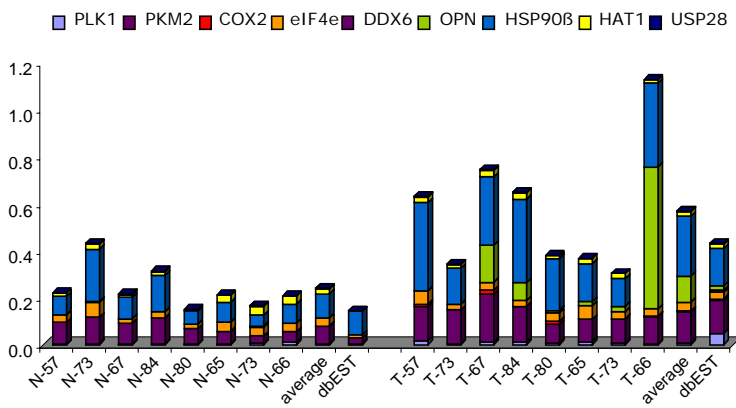
- Sequence of mutational events, including activation of oncogenes and inactivation of tumour suppressor genes are base for the transition from normal colon epithelium to premalignant adenoma and then invasive adenocarcinoma.

- The correlation between mRNA expression and protein abundance is complex and not always consistent.

- By using a quantitative approach, we have analyzed the expression profile of combination of selected genes and their corresponding proteins in paired normal and tumor colon tissue from patients with colorectal cancer.

## Diagnostic of colorectal cancer using the expression profiles of 9 genes

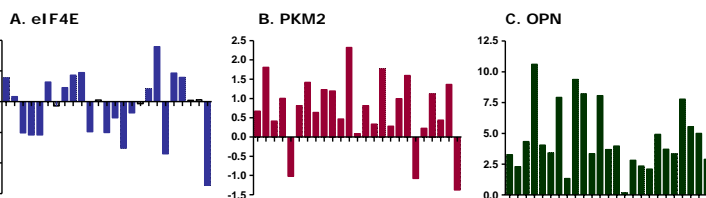
Barcode representation of 9 genes in 8 patients, the average over these patients and the prediction by dbEST data. The left group of columns represents the values in normal tissues (N), the right ones in paired tumor tissues (T).



- Distinct similarity in the expression pattern of the 9 genes in normal colon tissues.
- Drastic variations of expression levels in cancer tissue.
- Paired normal and tumor tissue from 12 additional patients have been used for evaluation in blinded study => 21 out of 24 or 87.5% were correctly predicted.
- Mining in the dbEST data base correctly predicts the gene expression levels in the 8 patients.

## Some of the genes are up-regulated in the cancer of all patients, some not!

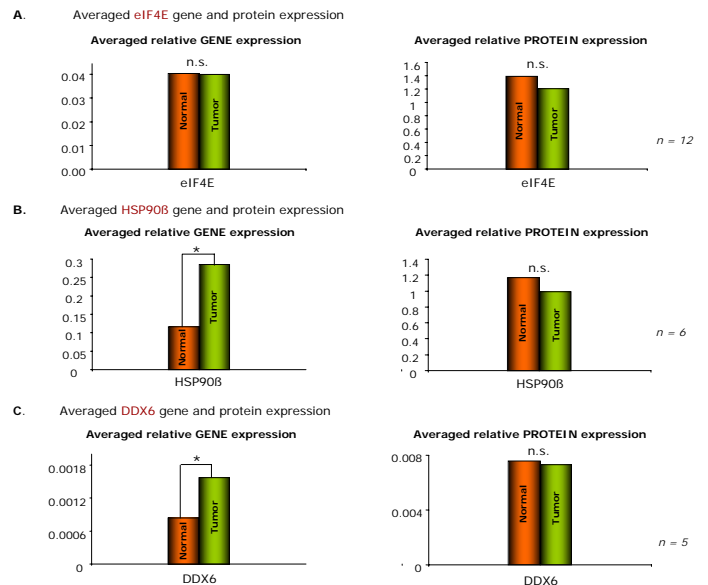
Log of expression ratio Tumor vs Normal for eIF4E (A), PKM2 (B) and OPN (C) across 25 patients



- eIF4E, DDX6, HAT1, USP28 and PLK1 genes are not showing any systematics in their regulation in CRC, see A.
- HSP90B, PKM2 genes are systematically although insignificant up-regulated in CRC, see B.
- Significant upregulation in CRC for OPN and COX2 genes, see C.

## Changes at the mRNA level do not always result in changes in protein expression!

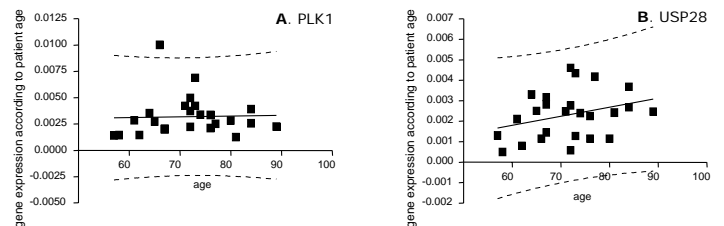
Comparison of the gene – and protein expression of eIF4E (A), HSP90B (B) and DDX6 (C) averaged over all investigated patients, n indicates the number of analyzed patients



- In case of DDX6 and HSP90B there is amplification of the gene in tumor, but the effect is leveled out on the protein side.
- Obviously for DDX6 and HSP90B, gene expression does not predict the protein expression.

## Does the expression of the selected genes depend on the age?

A linear regression analysis was performed in order to study whether the expression profile of the 9 genes depend on the patient age. The expression in normal tissue was taken into consideration.



- PLK1 gene expression profile was not showing any dependency on the age ( $p=0.89$ ), see A.
- Increase with age (moderate significance confirmed by  $p=0.12$ ) for USP28, see B
- Moderate increase in the expression of eIF4E ( $p=0.55$ ), DDX6 ( $p=0.46$ ), HAT1 ( $p=0.58$ ), HSP90B ( $p=0.41$ ) and PKM2 ( $p=0.4$ ) genes with age.
- The statistic is still poor, none of the selected genes showed slope with significant deviation from zero therefore a wider cohort of patients is needed to be analyzed