Transcriptional Profiling of Intestinal Adenocarcinomas in $Apc^{+/Min}$ $Blm^{+/Cin}$ Mice

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Introduction: Colorectal cancer is a large health problem in the United States. It is the third most common cancer in men and women. Colorectal cancer begins as a benign polyp that grows on the endothelium lining the colon or rectum. If the polyp is identified and removed at this stage then the cancer can be avoided. However, if the polyp continues to grow it eventually develops into a malignant adenocarcinoma. A large percentage (95%) of colorectal cancers are adenocarcinomas and 85% of human colorectal tumors carry bi-allelic inactivating mutations of Apc which is a protein involved in the regulation of cell growth. The formation of polyps which progress into adenocarcinomas occurs very readily in the intestine of mice which are heterozygous for both the Apc and Blm genes. Blm is a protein involved in DNA repair. **Hypothesis:** The pattern of gene regulation that occurs in humans during the formation of colorectal cancer is poorly understood. We hoped to gain a better understanding of this process by studying the regulation of genes during the formation of adenocarcinomas in the mouse model for colorectal cancer ($Apc^{+/min}$ $Blm^{+/Cin}$). **Methods:** Intestinal tumors and normal intestinal tissue were obtained from $Apc^{+/min}$ $Blm^{+/Cin}$ mice and the grade of the tumor was established by histological examination. We then chose to compare an adenocarcinoma from the jejunum to normal tissue from the jejunum and also compare an adenocarcinoma from the duodenum to normal tissue form the duodenum. RNA from these tissues was isolated and reverse transcribed in vitro into cDNA which was then transcribed in vitro into RNA using biotinylated riboneuclotides. All steps were done using Affymetrix GeneChip® expression 3'-amplification one-cycle target labeling and control reagents. The biotinylated RNA form each tissue sample was then hybridized to a single Affymetrix UV74A2 mouse genome genechip and the intensity was measured using an Affymetrix GeneChip scanner. The data was analyzed and compared using Affymetrix GCOS software. **Results/Conclusions:** By comparing the adenocarcinomas from the duodenum and jejunum to normal tissue we identified around 1200 genes that were up-regulated or down-regulated by more then three fold in the adenocarcinomas. Further study must be done to give meaning to this number. The level of expression observed in the genechip can be confirmed using real-time PCR or Northern blots. Most importantly, many more samples must be run to identify genes that are consistently being regulated in the formation of adenocarcinomas.