

ORAL PRESENTATION

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# Colorectal adenomas and cancer link to chromosome 13q22.1-13q31.3 in a large family with excess colorectal cancer

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## Background

Colorectal cancer is the fourth most common type of cancer and the second most common cause of cancer death. Approximately 5% of colon cancers arise in the presence of a clear hereditary cancer condition; however, current estimates suggest that an additional 15-25% of colorectal cancers arise on the basis of unknown inherited factors. Association studies report several low-penetrance genetic variants associated with colon cancer risk. Large families, whereby precise inheritance can be correlated with phenotype, offer another approach to identify moderately penetrant genes and to isolate responsible genetic loci and mutations. The aim of this study was to identify additional genetic factors responsible for colon cancer using large multigenerational pedigrees with excess colorectal cancer.

## Methods

A large 4-generation kindred with statistical excess colorectal cancer was identified through the Utah Population Database. 47 family members were enrolled and evaluated clinically by colonoscopy. Genome-wide genotyping was done using two sets of genetic markers: 325 short tandem repeat (STR) and the 10K Affymetrix SNP array, as well as fine mapping with 5 additional STR markers. Parametric and nonparametric linkage was analyzed using MLINK and GENEHUNTER.

## Results

A major genetic locus segregating with colonic polyps and cancer in this kindred was identified on chromosome

13q with a nonparametric linkage score of 26.39 (LOD score of 2.99 and  $p=0.0006$ ). The nonrecombinant region spans 21 Mbp and contains 27 RefSeq genes. Sequencing of 7 candidate genes in this region failed to identify a clearly deleterious mutation; however, polymorphisms segregating with the phenotype were identified. Chromosome 13q is commonly gained and over expressed in colon cancers and is correlated with metastasis suggesting the presence of an oncogene. Evaluation of a tumor from a kindred member revealed a gain of 13q as well.

## Conclusions

This identified region may contain a novel oncogene responsible for colon cancer in a yet to be determined fraction of the colon cancer population. Identification of the precise gene and causative genetic change will be an important next step to understand cancer progression and metastasis.

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