northern blotting and (4) comparative genomic analysis with distant vertebrate species such as *Fugu rubripes* and *Tetraodon nigroviridis*. This transcript-mapping strategy has identified 32 potential transcription units, including 2 known genes, 5 new genes, 9 Unigene entries and 16 other expressed sequence tag clusters. The region also contains five pseudogenes. The map should facilitate subsequent efforts to characterize the candidate genes. This study illustrates how the integration of genome-based approaches facilitates the identification of genes in a large interval.

Sjögren, Helene [31]

Fusion of the NH_2-terminal domain of the bHLH protein TCF12 to TEC in extraskeletal myxoid chondrosarcoma with translocation t(9; 15)(q22; q21)

Helene Sjögren, Barbro Wedell, Jeanne M. Meis Kindblom, Lars-Gunnar Kindblom & Göran Stenman

Sahlgrenska University Hospital, Gula Stråket 8, SE-413 45 Gothenburg Bohuslän, Sweden

Extraskeletal myxoid chondrosarcomas (EMC) are characterized by recurrent t(9; 22) or t(9; 17) translocations resulting in fusions of the NH_2-terminal transactivation domains of EWS or TAF2N to the entire TEC protein. We report an EMC with a new translocation, t(9; 15)(q22; q21), and a third type of TEC-containing fusion gene. The chimeric transcript encodes a protein in which the first 108 amino acids of the NH_2 terminus of the basic helix-loop-helix (bHLH) protein TCF12 is linked to the entire TEC protein. The translocation separates the NH_2-terminal domain of TCF12 from the bHLH domain as well as from a potential leucine zipper domain located immediately downstream of the breakpoint. These results demonstrate that the NH_2-terminal transactivation domains of EWS or TAF2N are not essential for the oncogenic properties of fusion proteins in EMC, and that EWS or TAF2N may be replaced by a similar domain from a bHLH protein that presumably endows the fusion protein with similar functions.

Sjögren, Helene [32]

Fusion of the NH_2-terminal domain of the bHLH protein TCF12 to TEC in extraskeletal myxoid chondrosarcoma with translocation t(9; 15)(q22; q21)

Helene Sjögren, Barbro Wedell, Jeanne M. Meis Kindblom, Lars-Gunnar Kindblom & Göran Stenman

Sahlgrenska University Hospital, Gula Stråket 8, SE-413 45 Gothenburg Bohuslän, Sweden

Extraskeletal myxoid chondrosarcomas (EMC) are characterized by recurrent t(9; 22) or t(9; 17) translocations resulting in fusions of the NH_2-terminal transactivation domains of EWS or TAF2N to the entire TEC protein. We report an EMC with a new translocation, t(9; 15)(q22; q21), and a third type of TEC-containing fusion gene. The chimeric transcript encodes a protein in which the first 108 amino acids of the NH_2 terminus of the basic helix-loop-helix (bHLH) protein TCF12 is linked to the entire TEC protein. The translocation separates the NH_2-terminal domain of TCF12 from the bHLH domain as well as from a potential leucine zipper domain located immediately downstream of the breakpoint. These results demonstrate that the NH_2-terminal transactivation domains of EWS or TAF2N are not essential for the oncogenic properties of fusion proteins in EMC, and that EWS or TAF2N may be replaced by a similar domain from a bHLH protein that presumably endows the fusion protein with similar functions.

Smith, David I. [33]

Comprehensive analysis of genetic alterations in ovarian cancer

Viji Shridhar[1], Ajay Pandita[1], John Lee[2], Steve Iturria[1], Julie Staub[1], Raji Avula[1], Ami Sen[2], Eric Calhoun[1], Fergus Couch[1], David James [1], Lynn Hartmann[1], Jim Lillie [2] & David Smith [1]

[1]*Mayo Foundation, Rochester, Minnesota, USA*[2]*Millennium Predictive Medicine*

Ovarian cancer is the leading cause of death from gynecological malignancies among women in the United States. The 5-year survival for the patients with late stage tumors is 20%, compared to 50–90% in early stage tumors. The aim of this study is to use state-of-the-art molecular technologies to better understand the biology of ovarian cancer. We used cDNA microarrays to distinguish the variation in gene expression of approximately 20,000 genes among 10 early stage (stage I/II) and 10 late stage (stage III/IV) ovarian tumors against 5 pooled normal ovarian epithelial cell brushings. Subtracted cDNA libraries of several of these tumors versus normal ovarian epithelial cell brushings were generated to identify additional genes not present on the cDNA microarrays. Calculation of average fold induction (both up and down) revealed no statistically significant increase in the number of genes showing differential expression in the late stage tumors compared to early stage, and the differentially expressed genes in both the early and late stage tumors were very similar. The loss of expression of 20 of 30 top candidate down-regulated genes was confirmed in a panel of both early and late stage tumors (15 each) by semi-quantitative RT-PCR. To complement the gene expression profiles obtained, DNA from 35 ovarian tumors of various stages/grades were used for comparative genomic hybridization (CGH) and loss of heterozygosity (LOH) studies. Gains were commonly observed on chromosomes 1, 8, 17, 19 and 20, whereas losses were mainly observed on chromosomes 4q, 5q, 13q, and 18q. 13q14.1 and 19q13.4 were two regions that showed more loss in early stage than late stage tumors. Through these analyses we are developing a molecular signature for ovarian cancer and identifying important genes involved in early stage ovarian carcinogenesis.

Sood, Raman [34]

Use of experimentally constructed haplotypes in gene mapping studies of hereditary cancers

E. Gillanders[1], J.A. Douglas[2], S.B. Gruber[3], H. Yan[4], B. Vogelstein[4], R. Sood[1], J. Carpten[1], T. Dennis[1], M. Boehnke[2] & J.M. Trent[1]

[1]*Cancer Genetics Branch, National Human Genome Research Institute, Bethesda, Maryland, USA*
[2]*Department of Biostatistics, University of Michigan, Ann Arbor, Michigan, USA*
[3]*Department of Epidemiology and Internal Medicine, University of Michigan, Ann Arbor, Michigan, USA*
[4]*Howard Hughes Medical Institute and Johns Hopkins Oncology Center, Baltimore, Maryland, USA*

Conversion provides several advantages for gene mapping projects of complex diseases such as cancer. The approach takes advantage of selective retention of a subset of human chromosomes within somatic cell hybrids, isolating single copies of all