eported with a de novo balanced translocation involving chromosome
and Heterotaxia. Cytogenetic analysis of our patient revealed that the
eakpoints in both patients were found to be located in the same chromo-
al region on 6q21, spanning approximately 1Mb. These results strongly
est the existence of a locus for Heterotaxia on chromosome 6q21. Since
cidence at birth of balanced reciprocal translocations and Heterotaxia are
remely low, we believe that this presents a unique opportunity to positionaly
one or more genes, explaining the Heterotaxia.
present experimental data on the physical mapping of the two breakpoints
1Mb interval using publicly available contig and sequence data from the
romosome 6 sequencing project from the Sanger Centre (Cambridge, UK)
egrated with our own data. This study demonstrates the power of modern
nomics for efficient cloning of candidate disease genes utilizing rare cytoge-
ic aberrations.

019
nstruction of a BAC Map of Human Chromosome 16
S. Han, R.D. Sutherland, P.B. Jewett, M.L. Campbell, L.J. Meincke, J.G.
mer, M.O. Mundt, L.L. Deaven and N.A. Doggett.
OE Joint Genome Institute, Center for Human Genome Studies, Los Alamos
ational Laboratory, Los Alamos, NM 87545.

have used sequence-based markers from an integrated YAC STS-content/
matic cell hybrid breakpoint physical map and radiation hybrid maps of
man chromosome 16 to construct a new sequence-ready BAC map of this
romosome. The integrated physical map was previously generated in our
oratory and contains 1150 STSs, providing a marker on average every 78 Kb
the euchromatic arms of chromosome 16. The other two maps utilized for
s effort were the radiation hybrid maps of chromosome 16 from Whitehead
titute and Stanford University. To create large sequenceable targets of this
romosome we used a systematic approach to screen high density BAC fil-
s with probes generated from overlapping oligonucleotide probes (overgos).
first identified all available sequences in the three maps. These include
quences from genes, ESTs, STSs, and cosmid end sequences. We then used
LAST to identify 36 bp unique fragments of DNA for overgo probes. A total
906 overgos were selected from the long arm of chromosome 16. After a
al of 212 hybridizations we have constructed an initial probe-content BAC
p of chromosome 16q consisting of 828 overgo markers and 3363 BACs pro-
ing greater than 85% coverage of the long arm of this chromosome. Gaps
the map are being closed with the following methods: 1) PCR screening
RPCI-11 library with the BAC end sequence-derived STSs, 2) BAC end
quence database searches with draft sequences of BAC clones near the gaps.
Screening the RPCI-11 library with overgos generated from the BAC end
uences near the gaps. To date, 400 PCR screenings and 5 pooled overgo
bridizations have been completed for the gap closing effort, extending the
verage of the BAC map to over 90%. Supported by the US DOE, OBER
er contract W-7405-ENG-36.

320
e Effort to Map and Sequence Human Chromosome 7
Fulton, Mundeep Sekhon and the physical mapping group
nome Sequencing Centre, Washington University
ool of Medicine, St. Louis, MO, 63108

mapping and sequencing of Human Chromosome 7, approximately 170
in size, is nearing completion. The Genome Sequencing Center (GSC)
. Louis is responsible for 145 Mb of the chromosome, with a smaller
n being finished at the University of Washington. As of the beginning of
mber 1999, 106 Mb of chromosome 7 was at various stages of compltion
the GSC sequencing pipeline. This includes genomic clones which are
ntly being sequenced or finished (~35 mb) and clones which have been
itted to GenBank (~70 Mb). Our sequencing efforts are supported by
based physical mapping which has provided 169 clone contigs anchored
to chromosome 7 by hybrization to know markers. These contigs represent approximately 86% of te 145 Mb being sequenced by the GSC. Currently, the five largest contigs range in size from 3.0 to 8.4 Mb. Additional clone coverage will be provided by a whole-gneome BAC fingerprint database containg 275,00 BAC clones. In this presentation we will discuss our efforts to close the remaining gaps on chromosome 7, as well as to sort out the varous complex repeat structures at both the mapping and sequencing levels.

#321
A physical and transcription map of the candidate region 17q23q24 for a gene causing RussellSilver syndrome (ASS).
S. Dorr'; A.T. Midro ; I. J. Giannakudis ; I. Hansmannn .
Inst. f Humangenetik, Halle, Germany; Dept. of Clin. Genetics, Bialystok, Poland

RussellSilver syndrome is mainly (characterized by pre and postnatal growth retardation and some morphological abnormalities including lateral asymmetry, a small triangular face with prominent forehead and clinodactyly of the fifth fingers. The genetic etiology of the sAyndrome is unknown and seems to be heterogeneous. Most cases are sporadic although in a minority familial inheritance has been described. About 10% of patients show maternal uniparental disomy of chromosome 7. Furthermore, two autosomal truslocations involving band 17q25 were reported in association with RSS (RamirezDuenas et. al., 1992; Midro et. al., 1993). Molecular analysis of the breakpoint on chromosome 17 of the de novo translocsation previously described as t(1;17)(q31;q25) enabled us to refine the localization of the breakpoint to 17q23q24. In order to identify a gene for RSS in the region 17q23q24 a YAC/PAC/cosmid contig (5 Mb) for the RSandS critical region around the breakpoint was constructed. This contig comprises loci for 38 STSs and 30 genes / ESTs. Evidence is provided for a duplication/amplifemion of 8 loci on both sides of the translocation breakpoint. By sequence analysis the duplicated sequences share identity between 85 % and 98%, respectively. This observation has to be taken into account as a possible explanation for the generalogy of the disease: e.g. this region may be target by unequal crossing over between the duplicated regions on both sides of the breakpoint. By searching for expressed sequences within the breakpoint area we identified a gene of a multigene family in close proximity to the breakpoint. We determined the exonintron structure of thus gene and screened 30 RSSpatients for sequence variants by direct sequencing of the 11 exons of this gene and adjacent intron sequences. However, no disease related mutations were detected so far. Interestingly we identified a specific haplotype comprising 6 intragenic polymorphisms showing association to a RSSgene in the region 17q23q24.

#322
Exploring Chromosome 4q22-24 Hepatocellular Carcinoma Tumor Suppressor Gene Region by Genome Sequencing
K.-J. Hsiao , C.-Y. Chen, H.-M. Chang, K.-M. Wu, S.-H. Chiang, M.-Y. Chung, U.-C. Yang, C.-K. Chou, S.-F. Tsai. Institutes of Genetics and Biochem., National Yang-Ming University, and Dept. of Medical Res. & Edu., Veterans General Hospital-Taipei, Shih-Pai, Taipei, Taiwan 112, R.O.C.

Hepatocellular carcinoma (HCC) is a major cause of cancer deaths in Asia and Africa. Based on clinical and basic researches on HCC in many countries, we have focused our study on chromosomes 4q22-24 and 16q22 regions, previously identified by molecular cytogenetics and loss of heterozygosity (LOH) analysis of Chinese HCC samples. To investigate the putative tumor suppressor gene(s) that are relevant to HCC development, we have established the first large-scale genome sequencing center in Taiwan. As of January 29, 2000, we have sequenced thirty-five BAC clones for the chromosome 4 and 16 targets. These clones, together, have an added insert size of 4349 kb (4039 kb and 310 kb for the chromosome 4 and chromosome 16 targets, respectively). Three clones were abandoned during the course of physical mapping as we found that they have a large overlap with the adjacent clones. Of the thirty-two projects