PROJECT TITLE
HUMAN GENOME LIBRARIES

FINAL PROGRESS REPORT

for Period February 1, 1994 - August 31, 1997

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FINAL REPORT FOR PERIOD FEBRUARY 1, 1994 - AUGUST 31, 1997

This 3-year grant, entitled "Chromosome region-specific libraries for human genome analysis", was awarded for the period 3/1/94 to 1/31/97, with an unfunded extension to 8/31/97. This grant is a renewal of a preceeding grant for the period 3/1/91 to 2/28/94.

The overall goal of this grant is to use a novel technology of chromosome microdissection and microcloning, previously developed in this laboratory funded by DOE, to construct chromosome region-specific libraries as resources for various human genome program studies, including physical mapping, STS preparation, clone isolation, microsatellite probes for genetic linkage mapping, positional cloning of disease genes, and reagents for sequencing.

During the grant period, we have achieved the stated goal of applying the microdissection and linker-adaptor microcloning technology to the construction of region-specific libraries for the entire human chromosomes 2 and 18. These high quality libraries are available not only for the DOE National Laboratories for their genome projects, but also for the scientific community as resources for their genome and genetic studies. The libraries have been deposited to the ATCC (American Type Culture Collection) for permanent maintenance and distribution. The following describe these accomplishments.

1. Construction of 11 region-specific libraries for the entire human chromosome 2.

We have completed construction of all 11 region-specific microdissection libraries for the entire chromosome 2, including 4 libraries for the short arm, 6 libraries for the long arm, and one library for the centromeric region, as listed below:

Library	Chromosome Region	Size (Mb)
2P1	2p23-p25	25
2P2	2p21-p23	28
2P3	2p14-p16	22
2P4	2p11-p13	28
2CEN	2p11-q11	4
2Q6	2q11-q14	31
2Q5	2q21-q22	23
2Q4	2q23-q24	19
2Q3	2q31-q32	26
2Q2	2q33-q35	24
2Q1	2q35-q37	28

2. Characterization of 11 region-specific libraries of chromosome 2 for quality control

All microdissection libraries were carefully characterized to confirm their high quality. This quality control includes the following procedures:

- (1) Accurate microdissection of 20 chromosome fragments from the designated region of chromosome 2.
- (2) The chromosome fragments were treated with proteinase K, extracted with phenol, cleaved with MboI, and ligated to an MboI linker-adaptor. All were performed under the microscope.
- (3) The ligated sequences were amplified by PCR.
- (4) The amplified sequences were analyzed by gel electrophoresis to ensure that the library was in the right size range (100-800 bp).
- (5) Use of the PCR products in transformation to construct a pUC19 plasmid library.
- (6) Colony hybridization of microclones from the library using labeled total human DNA to ensure that the library contained the normal proportion (40-60%) of the microclones with highly repetitive sequences.
- (7) Isolation of a random sample of unique sequence microclones from the library for analysis by Southern blot hybridization using DNAs from human, human/CHO cell hybrid containing a single human chromosome 2, and CHO. A great majority of the microclones should be derived from chr. 2.
- (8) Library quality was confirmed to be excellent if the library met the above criteria.

3. Isolation and characterization of unique sequence microclones from each library for genomic uses.

For each library, between 26 and 66 unique sequence microclones were isolated and characterized to facilitate applications to genome analysis. These included 26 microclones for 2P1 Library, 60 microclones for 2P2, 66 microclones for 2P3, 35 microclones for 2P4, 37 microclones for 2CEN, 32 microclones for 2Q6, 26 microclones for 2Q5, 31 microclones for 2Q4, 33 microclones for 2Q3, 31 microclones for 2Q2, and 26 microclones for 2Q1.

These unique sequence microclones have been used as probes to isolate corresponding clones with large inserts, like YAC, P1, PAC, BAC, cosmid, and phage, to facilitate contigs assembly for the dissected region.

4. Detailed description of the production and characterization of the 11 libraries of chromosome 2 and the unique sequence microclones from the libraries.

The detailed characteristics of these libraries are summarized in Table 1. Details of the libraries have been described in the following publications:

(i) 2P1 Library (2p23-p25):

Yu, J., Qi, J., Tong, S. and Kao, F.T. (1994) A region-specific microdissection library for human chromosome 2p23-p25 and the analysis of an interstitial deletion of 2p23.3-p25.1. *Hum. Genet.* 93, 557-562.

(ii) 2P2 Library (2p21-p23):

Kao, F. T., Yu, J., Qi, J., Tong, S. and Muenke, M. (1995) A region-specific microdissection library for human chromosome 2p21-p23 and the analysis of an interstitial deletion of 2p21. *Cytogenet. Cell Genet.* 68, 17-18.

(iii) 2P3 Library (2p14-p16):

Yu, J., Tong, S., Qi, J. and Kao, F.T. (1994) Construction and characterization of region-specific microdissection libraries and single-copy microclones for the short arm of human chromosome 2. *Somat. Cell Mol. Genet.* 20, 353-357.

(iv) 2P4 Library (2p11-p13):

Yu, J., Qi, J. and Kao, F.T. (1994) Region-specific microdissection library and single-copy microclones for human chromosome 2p11-p13. *Somat. Cell Mol. Genet.* 20, 133-136.

(v) 2CEN Library (2p11.1-q11.1):

Kao, F.T., Tong, S., Whittier, A. and Yu, J. (1996) Complete set of eleven region-specific microdissection libraries for human chromosome 2. *Somat. Cell Mol. Genet.* 22, 57-66.

(vi) 2Q6 Library (2q11-q14):

Kao, F.T., Tong, S., Whittier, A. and Yu, J. (1996) Complete set of eleven region-specific microdissection libraries for human chromosome 2. *Somat. Cell Mol. Genet.* 22, 57-66.

(vii) 2Q5 Library (2q21-q22):

Kao, F.T., Tong, S., Whittier, A. and Yu, J. (1996) Complete set of eleven region-specific microdissection libraries for human chromosome 2. *Somat. Cell Mol. Genet.* 22, 57-66.

(viii) 2Q4 Library (2q23-q24):

Yu, J., Tong, S., Whittier, A. and Kao, F.T. (1995) Three region-specific microdissection libraries for the long arm of human chromosome 2, regions q33-q35, q31-q32 and q23-q24. *Somat. Cell Mol. Genet.* 21:335-343.

(ix) 2Q3 Library (2q31-q32):

Yu, J., Tong, S., Whittier, A. and Kao, F.T. (1995) Three region-specific microdissection libraries for the long arm of human chromosome 2, regions q33-q35, q31-q32 and q23-q24. *Somat. Cell Mol. Genet.* 21:335-343.

(x) 2Q2 Library (2q33-q35):

Yu, J., Tong, S., Whittier, A. and Kao, F.T. (1995) Three region-specific microdissection libraries for the long arm of human chromosome 2, regions q33-q35, q31-q32 and q23-q24. *Somat. Cell Mol. Genet.* 21:335-343.

(xi) 2Q1 Library (2q35-q37):

Yu, J., Tong, S., Yang-Feng, T. and Kao, F.T. (1992) Construction and characterization of a region-specific microdissection library from human chromosome 2q35-q37. *Genomics* 14, 769-774.

TABLE 1. Summary of characteristics of 11 region-specific libraries of chromosome 2

Library	Region	Size of Region (Mb)	Mean insert size (bp)	Potential library size*	Microclones derived from dissected region (%)	No. unique sequence microclones characterized	% clones conserved in rodents** (No.)
2P1	p23-p25	25	200	300,000	77	26	3.8 (1/26)
2P2	p21-p23	28	250	900,000	82	60	1.8 (5/28)
2P3	p14-p16	22	250	1,000,000	93	66	6.1 (4/66)
2P4	p11-p13	28	380	600,000	85	35	2.9 (1/35)
2CEN	p11.1-q11.1	4	180	200,000	90	37	2.7 (1/37)
2Q6	q11-q14	31	180	200,000	91	32	3.1 (1/32)
2Q5	q21-q22	23	180	200,000	85	26	0 (0/26)
2Q4	q23-q24	19	190	100,000	90	31	6.7 (2/30)
2Q3	q31-q32	26	190	200,000	85	33	3.3 (1/30)
2Q2	q33-q35	24	130	400,000	97	31	22.6 (7/31)
2Q1	q35-q37	28	270	20,000	77	26	7.7 (2/26)

*Estimated number of microclones that can be produced if the entire primary PCR products are used in transformation in DH5 bacterial host cells.

**Percentage of clones cross-hybridized to rodent species (CHO or mouse) by Southern blot hybridization.

5. Conversion of DNA (in PCR products) libraries to plasmid libraries for convenient use in genome research.

Initially, all of our region-specific libraries were prepared and stored as in the form of DNA after PCR amplification. In order to make the libraries more convenient to use by other investigators, we decided to convert the libraries into plasmid libraries. We took a subset of the DNA from the original PCR products in each library to clone into pUC19 to make a plasmid library. Each sub-library contained at least 20,000 independent, different species of microclones. Samples from each sub-library were analyzed to ensure excellent quality of the library, e.g. insert size, % of repetitive sequences, high percentage of microclones derived from dissected region,

etc. The titers of the libraries were generally maintained at approximately 1×10^8 microclones per ml.

6. Deposition of region-specific libraries to ATCC for permanent storage and general distribution.

We deposited all of the 11 region-specific libraries of chromosome 2 to ATCC. In order to facilitate the storage and distribution of these libraries by ATCC, we deposited the libraries to ATCC in plasmids, instead of DNA. This would eliminate the process of purification and transformation of DNA to make plasmid libraries by ATCC. Since the inserts of the microclones are short (mean length 200-300 bp), extreme care must be taken to reduce loss of the inserts during cloning, particularly in purification. Thus, we carried out this process in our lab because we have extensive experience dealing with these problems.

After we sent each plasmid sub-library to ATCC, their personnel expanded the library to large quantities and stored the aliquots in frozen vials for permanent maintenance and general distribution. They also sent us a vial to verify the authenticity of the expanded library before release. These chromosome region-specific libraries are listed in the ATCC's catalogue for general use. Thus, the libraries should have increased accessibility to a wider spectrum of the scientific community. The following ATCC Repository Numbers have been assigned to the 11 chromosome 2 libraries:

Library	ATCC Repository No.
2P1	#87188
2P2	#87189
2P3	#87103
2P4	#87104
2CEN	#87411
2Q6	#87410
2Q5	#87409
2Q4	#87310
2Q3	#87309
2Q2	#87308
2Q1	#77419

7. Construction of 3 region-specific libraries for the entire human chromosome 18

Three region-specific libraries for the entire human chromosome 18 have been constructed, including:

Library	Chromosome Region	Size (Mb)
18P	18p11.32-p11.1	22
18Q1	18q11.1-q12.3	25
18Q2	18q21.1-q23	34

All these libraries are large, potentially comprising hundreds of thousands of recombinant microclones. The insert sizes ranged between 50-600 bp (mean 180-200 bp). The libraries contained approximately 40-60% microclones with unique sequence inserts. More than 30 unique sequence microclones from each library were analyzed by Southern blot hybridization to show that they are human specific and were derived from chromosome 18. These libraries and the unique sequence microclones are useful reagents for (1) isolating highly polymorphic microsatellite markers for refined linkage analysis, (2) identifying corresponding YAC or other clones with large inserts for contig assembly, (3) isolating cDNA clones from the dissected region as candidate genes for positional cloning, and (4) convenient sequencing of the short insert microclones. Since chromosome 18 is one of the less-exploited chromosomes in the human genome, these resources should facilitate high resolution mapping and sequencing of this chromosome. Details describing the 3 libraries of chromosome 18 have been published in:

Kao, F.T., Tong, S., Shen, Y. and Yu, J. (1996) Construction and characterization of three region-specific microdissection libraries for human chromosome 18, *Somat. Cell Mol. Genet.* 22, 191-199.

8. Examples of applications of the chromosome region-specific microdissection libraries generated in this grant.

The grantee has made these resources available to many investigators for their genome-related and other genetic research. Some of the notable examples are summarized below.

(i) One of the most gratifying uses of our libraries was the contribution to the cloning of the gene responsible for hereditary nonpolyposis colorectal cancer (HNPCC). Right after the discovery of the location of this gene on the short arm of chromosome 2, region 2p15-p16, Dr. Bert Vogelstein of the Johns Hopkins Cancer Center contacted us about the use of our 2P3 Library (2p14-p16) to facilitate the gene search. We provided Dr. Vogelstein with the library and also supplied 66 unique sequence microclones from this region for use by his team. Through a world-wide collaboration, including our contribution of the library and the microclones, the first colon cancer gene hMSH2 was cloned which is a homolog of the bacterial mutS (and the yeast MSH2) mismatch repair gene. Our microclones from the region were also instrumental for isolating highly polymorphic markers for refined linkage analysis with the colon cancer gene. (Refer to publications in *Cell* 75, 1215-1225, 1993, and in *Hum. Mol. Genet.* 3, 2082, 1994.)

(ii) Another important application of the microdissection and microcloning technology developed in this grant was the collaboration between this lab and the biotech company BIOS in New Haven, CT. Since 1996, we have collaborated with BIOS to construct region-specific microdissection libraries from the most gene-rich regions (about 10 Mb per region) in the human genome. BIOS

would then convert these libraries into P1 libraries and make the P1 libraries commercially available (in the forms of individual P1 clones, DNAs from individual P1 clones, gridded P1 clones in plates, etc.) to investigators interested in these regions. These libraries can also be used as painting probes for FISH analysis involving the dissected regions. The collaboration has been funded by a Phase II SBIR grant (2 R44 GM50658) from NIH for two years (2/6/96-1/31/98), entitled "Band-specific libraries from microdissected chromosomes".

(iii) Dr. Max Muenke, Children's Hospital in Philadelphia and U. of Penn., used our 2P2 Library (2p21-p23) and unique sequence microclones in mapping and cloning of the gene for holoprocencephaly (HPE). HPE is an autosomal dominant disorder involving abnormal embryonic development in midbrain and midface. Some of the patients suffer an interstitial deletion in the 2p21 region. We sent Dr. Muenke unique sequence microclones from our 2P2 Library so he could use the microclones from this region to isolate corresponding YAC clones with large inserts for contig construction and physical mapping and cloning of the HPE gene. Details refer to the publication *Hum. Mol. Genet.* 5, 223-229, 1996.

(iv) Drs. Jeff Gingrich and Anthony Carrano of Lawrence Livermore National Laboratory used our 2Q1 and 2P1 libraries and the unique sequence microclones for their genome studies on chr. 2. In particular, this group sequenced microclones from 2Q1 library to prepare new STSs for the 2q35-q37 region. The unique sequence microclones were also used to screen genomic libraries with large inserts, such as cosmid, PAC, YAC and P1, for contig assembly and physical mapping.

(v) Dr. Eric Lai, University of North Carolina, used our 2P2 Library (2p21-p23) and 26 unique sequence microclones from the library to screen a chromosome 2-specific BAC library constructed in his lab. In one study, he used 20 microclones from 2P2 Library in the BAC screening and isolated 23 corresponding BAC clones. They were also developing methods to use the entire 2P2 library to screen the BAC library in order to make the screening highly efficient.

(vi) Professor Tom Strachan, University of Newcastle Upon Tyne, UK, used our 2P4 Library (2p11-p13) and 35 unique sequence microclones from the library to map and clone the gene underlying limb-girdle muscular dystrophy (LGMD). They established linkage of this gene to 2p13. They were sequencing our microclones to prepare primers for YAC library screening to isolate YACs from this region for refined physical mapping and the cloning of the disease gene.

(vii) Dr. Pudur Jagadeeswaran, University of Texas Health Sciences Center at San Antonio, used our 2Q1 Library to facilitate his development of a new technique for isolating coding sequences from genomic DNA by generating genomic-cDNA chimeras. He was interested in using our region-specific libraries in his search for cDNAs from defined genomic regions.

(viii) Dr. Nicholas Lemoine, Imperial Cancer Research Fund, Hammersmith Hospital, London, used our 2P2 Library to facilitate his search for a pancreatic cancer gene which was frequently rearranged near the 2p22 region.

(ix) Dr. Theodore Puck, Eleanor Roosevelt Institute for Cancer Research in Denver, used our 2Q1 Library in his studies of the genome structure and exposure in relation to gene expression and genome regulation.

(x) Because a number of genetic diseases have been mapped to specific regions of chromosome 2, the availability of our chr. 2 region-specific libraries should be valuable for the cloning of these disease genes. Fig. 1 presents some examples of the genetic diseases mapped to specific regions of chr. 2 but the genes responsible for these diseases have not yet been cloned.

Figure 1. Diagram showing examples of genetic diseases that mapped to specific regions in human chromosome 2 but the responsible genes have not yet been cloned.

9. Students and post-doctoral fellows trained on the project

(i) Jingwei Yu, M.D., Ph.D. - Dr. Yu received both graduate and post-doctoral training on this project. Dr. Yu has a medical doctor degree from Tongji University in China, with an M.S. degree in medical genetics from the same University. He recently completed his Ph.D. degree in Dr. Kao's lab in 1997, in the Department of Biochemistry and Molecular Genetics, University of Colorado Health Sciences Center in Denver. Dr. Yu had been a co-investigator of this grant since 1991. Dr. Yu is currently working at Yale University on a two-year Fellowship on the Clinical Genetics Training Program.

(ii) Suhong Tong, M.S. - Research Fellow trained on this project. Now working in Dr. Kao's lab.

(iii) Yiping Shen, M.S. - Research Fellow trained on this project. Now a Ph.D. student in the State University of New York at Syracuse.

(iv) Jianxin Qi, M.D. - Research Fellow trained on this project.

(v) Ben Tsai - Summer student trainee on this project. Now a pre-med student in the Northwestern University.

(vi) Amy Whittier, M.S. - Research Fellow trained on this project. Now working in a biotech company.

(vii) Patricia Way, B.S. - Research Fellow trained on this project. Now working in a biotech company.

(10) Publications resulted from this grant (a complete set of publications is enclosed in Appendix) —

(A) RESEARCH PAPERS — *all Reprints - removed for separate processing (1-05)*

- (1) Yu, J., Qi, J., Tong, S. and Kao, F.T. (1994) A region-specific microdissection library for human chromosome 2p23-p25 and the analysis of an interstitial deletion of 2p23.3-p25.1. Hum. Genet. 93, 557-562.
- (2) Yu, J., Qi, J. and Kao, F.T. (1994) Region-specific microdissection library and single-copy microclones for human chromosome 2p11-p13. Somat. Cell Mol. Genet. 20, 133-136.
- (3) Yu, J., Tong, S., Qi, J. and Kao, F.T. (1994) Construction and characterization of region-specific microdissection libraries and single-copy microclones for the short arm of human chromosome 2. Somat. Cell Mol. Genet. 20, 353-357.
- (4) Spurr, N. K., Barton, H., Bashir, R., Bryson, G. M., Bushby, K., Cox, S., Gringrich, J. C., Hentati, A., Hildebrandt, Kao, F. T., Kruse, T., Lai, E., Liu, J., Muenke, M., Naylor, S., Nicklin, M., Read, A., Reiner, O., Rocchi, M., and Summar, M. (1994) Report of the third international workshop on human chromosome 2 mapping 1994. Cytogenet. Cell Genet. 67, 215-244.

- (5) Leach, F. S., Nicolaides, N. C., Sistonen, P., Yu, J. W., Kao, F. T., de la Chapelle, A., Kinzler, K. W. and Vogelstein, B. (1994) Three dinucleotide repeat polymorphisms proximal to the D2S123 locus. *Hum. Mol. Genet.* 3, 2082.
- (6) Kao, F. T., Yu, J., Qi, J., Tong, S. and Muenke, M. (1995) A region-specific microdissection library for human chromosome 2p21-p23 and the analysis of an interstitial deletion of 2p21. *Cytogenet. Cell Genet.* 68, 17-18.
- (7) Kao, F.T. (1995) Chromosome microdissection and microcloning: Application to genome analysis. In "Classical and Molecular Cytogenetic Analysis of Cereal Genomes", Proc. US-Japan Joint Seminar, March 21-23, 1994, Kansas State University, Manhattan, Kansas, eds. Raupp, W.J. and Gill, B.S., published in Kansas Agricultural Experiment Station Report 95-352-D, Dec. 1995, pp. 104-109.
- (9) Yu, J., Tong, S., Whittier, A. and Kao, F.T. (1995) Three region-specific microdissection libraries for the long arm of human chromosome 2, regions q33-q35, q31-q32 and q23-q24. *Somat. Cell Mol. Genet.* 21:335-343.
- (10) Kao, F.T. (1996) Chromosome microdissection and microcloning: Application to genome analysis. In "Methods of Genome Analysis in Plants", ed. Prem P. Jauhar, CRC Press, pp. 329-343.
- (11) Schell, U., Wienberg, J., Kohler, A., Bray-Ward, P., Ward, D.E., Wilson, W.G., Allen, W.P., Lebel, R.R., Sawyer, J.R., Jacobs, P.A., Aughton, D.J., Punnett, H.H., Lammer, E.J., Kao, F.T., Ward, D.C. and Muenke, M. (1996) Molecular characterization of breakpoints in patients with holoprosencephaly and definition of the HPE2 critical region in 2p21. *Hum. Mol. Genet.* 5:223-229.
- (12) Kao, F.T., Tong, S., Whittier, A. and Yu, J. (1996) Complete set of eleven region-specific microdissection libraries for human chromosome 2. *Somat. Cell Mol. Genet.* 22, 57-66.
- (13) Spurr, N.K., Bashir, R., Bushby, K., Cox, A., Cox, S., Hildebrandt, F., Hill, N., Kao, F.T., Krols, L., Marzella, R., Miller, N., Nothwany, H.G., Rocchi, M., Sarfarazi, M., Stratakes, C.A., Wallgren-Pettersson, C. and Naylor, S. (1996) Report of the fourth international workshop on human chromosome 2 mapping 1996. *Cytogenet. Cell Genet.* 73:255-273.
- (14) Choi, J.Y., Li, W.L., Kouri, R.E., Yu, J., Kao, F.T. and Ruano, G. (1996) Assignment of the acute phase response factor (APRF) gene to 17q21 by microdissection clone sequencing and fluorescence in situ hybridization of a P1 clone. *Genomics* 37:264-265.
- (15) Kao, F.T., Tong, S., Shen, Y. and Yu, J. (1996) Construction and characterization of three region-specific microdissection libraries for human chromosome 18. *Somat. Cell. Mol. Genet.* 22:191-199.

(B) ABSTRACTS

- 1-15 - Removed for separate processing*
- (1) Kao, F. T. and Yu, J. (1994) Construction and characterization of 4 region-specific microdissection libraries and single-copy microclones for the short arm of chromosome 2. Abstract presented in the 3rd Chromosome 2 Single Chromosome Workshop, Aarhus, Denmark, June 24-26, 1994. (Published in *Cytogenet. Cell Genet.* 67, 242, 1994)
 - (2) Muenke, M., Schell, U., Wienberg, J., Bray-Ward, P., Hehr, A., Kao, F. T. and Ward, D. C. (1994) Physical mapping of the holoprosencephaly minimal critical region in 2p21.

- Abstract presented in the 3rd Chromosome 2 Single Chromosome Workshop, Aarhus, Denmark, June 24-26, 1994. (Published in *Cytogenet. Cell Genet.* 67, 242-243, 1994)
- (3) Yu, J., Cox, M., Patterson, D. and Kao, F. T. (1994) YAC contig and cell hybrid mapping of six expressed sequences encoded by human chromosome 21. Abstract presented in the 44th Annual Meeting of the American Society of Human Genetics, Montreal, Quebec, Canada, October 18-22, 1994. (Published in *Am. J. Hum. Genet.* 55, A375, 1994)
 - (4) Schell, U., Wienberg, J., Bray-Ward, P., Aughton, D. J., Punnett, H. H., Kao, F. T., Ward, D. C. and Muenke, M. (1994) Towards cloning the gene for holoprosencephaly on chromosome 2. Abstract presented in the 44th Annual Meeting of the American society of Human Genetics, Montreal, Quebec, Canada, October 18-22, 1994. (Published in *Am. J. Hum. Genet.* 55, A31, 1994)
 - (5) Kao, F. T. and Yu, J. (1994) Construction and characterization of region-specific microdissection libraries for human chromosome 2. Abstract presented in the 4th Department of Energy (DOE) Human Genome Contractor-Grantee Workshop, Santa Fe, New Mexico, November 13-17, 1994.
 - (6) Kao, F. T. and Yu, J. (1995) Construction of region-specific microdissection libraries and single-copy microclones for human chromosome 2. Abstract presented in the "Genome Mapping & Sequencing" Meeting, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, May 10-14, 1995.
 - (7) Choi, J. Y., Li, W. L., Tesla, C. I., Kouri, R. E., Yu, J., Kao, F. T. and Ruano, G. (1995) "Virtual Mapping": Homology searches of databases with clones from band-specific microdissection libraries. Abstract presented in the 7th International Genome Sequencing and Analysis Conference, Hilton Head, South Carolina, September 16-20, 1995.
 - (8) Yu, J., Tong, S., Whittier, A. and Kao, F. T. (1995) Region-specific microdissection libraries for human chromosome 2. Abstract presented in the 45th Annual Meeting of the American Society of Human Genetics, Minneapolis, Minnesota, October 24-28, 1995.
 - (9) Ruano, G., Li, W., Huckaby, C. S., Choi, J. Y., Yu, J., Kao, F., Zehetner, G., Lehrach, H. and Kouri, R. (1995) Reconstituting 17q21 with P1 clones isolated with microdissected DNA. Abstract presented in the 45th Annual Meeting of the American Society of Human Genetics, Minneapolis, Minnesota, October 24-28, 1995.
 - (10) Choi, J. Y., Li, W., Kouri, R. E., Kao, F., Yu, J. and Ruano, G. (1995) Localization of APRF to 17q21 by "Virtual Mapping" based on sequencing of locus-specific microdissected DNA clones and database homologies. Abstract presented in the 45th Annual Meeting of the American Society of Human Genetics, Minneapolis, Minnesota, October 24-28, 1995.
 - (11) Kao, F. and Yu, J. (1996) Region-specific libraries for the human genome. Abstract presented in the Fifth Contractor-Grantee Workshop, Department of Energy Human Genome Program, Santa Fe, NM, January 28-February 1, 1996.
 - (12) Kao, F. and Yu, J. (1996) Complete set of 11 region-specific microdissection libraries for human chromosome 2. Abstract presented in the Human Genome Meeting '96, March 22-24, 1996, Heidelberg, Germany.

- (13) Kao, F. and Yu, J. (1996) Complete set of 11 region-specific microdissection libraries for human chromosome 2. Abstract presented in the 4th International Workshop on Human Chromosome 2, April 10, 1996, London, UK.
- (14) Kao, F. and Yu, J. (1996) Chromosome region-specific libraries constructed by microdissection and MboI linker-adaptor microcloning. Abstract presented in the 9th International Congress of Human Genetics, August 18-23, 1996, Rio de Janeiro, Brazil.
- (15) Bentley, K.L., Kao, F.T., Weissman, S., Choi, J.Y., Tesla, C.T. and Ruano, G. (1996) "Virtual" mapping of genes based on sequence bioinformatics of microdissected DNA and of locus-specific cDNA clones. Abstract presented in the 46th Annual Meeting of the American Society of Human Genetics, Oct. 29-Nov. 2, 1996, San Francisco, CA.