

AD\_\_\_\_\_

AWARD NUMBER: W81XWH-05-1-0282

TITLE: Do Structural Missense Variants in the ATM Gene Found in Women with Breast Cancer Cause Breast Cancer in "Knock-in" Mouse Strains?

PRINCIPAL INVESTIGATOR: Steve S. Sommer, M.D., Ph.D.

CONTRACTING ORGANIZATION: Beckman Research Institute  
Durate, California 91010-3000

REPORT DATE: April 2006

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command  
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;  
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

# REPORT DOCUMENTATION PAGE

*Form Approved*  
*OMB No. 0704-0188*

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. **PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.**

<b>1. REPORT DATE (DD-MM-YYYY)</b> 01-04-2006			<b>2. REPORT TYPE</b> Annual		<b>3. DATES COVERED (From - To)</b> 1 Apr 2005 – 31 Mar 2006	
<b>4. TITLE AND SUBTITLE</b>  Do Structural Missense Variants in the ATM Gene Found in Women with Breast Cancer Cause Breast Cancer in "Knock-in" Mouse Strains?					<b>5a. CONTRACT NUMBER</b>	
					<b>5b. GRANT NUMBER</b> W81XWH-05-1-0282	
					<b>5c. PROGRAM ELEMENT NUMBER</b>	
<b>6. AUTHOR(S)</b>  Steve S. Sommer, M.D., Ph.D.  E-Mail: <a href="mailto:sommeradmin@coh.org">sommeradmin@coh.org</a>					<b>5d. PROJECT NUMBER</b>	
					<b>5e. TASK NUMBER</b>	
					<b>5f. WORK UNIT NUMBER</b>	
<b>7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)</b>  Beckman Research Institute Durate, California 91010-3000					<b>8. PERFORMING ORGANIZATION REPORT NUMBER</b>	
<b>9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)</b> U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012						
<b>10. SPONSOR/MONITOR'S ACRONYM(S)</b>					<b>11. SPONSOR/MONITOR'S REPORT NUMBER(S)</b>	
<b>13. SUPPLEMENTARY NOTES</b>						
<b>14. ABSTRACT</b> The central hypothesis is that knock-in mice lines are made for two human cohort-specific missense mutations will develop breast cancer with dominant inheritance in a subset of animals. It also is hypothesized that other cancers will be more frequent as well. If correct, it follows that the ATM gene is the first known example of a "sup-oncogene", i.e., a tumor suppressor gene for lymphoma /leukemia and an oncogene for breast cancer. More generally, it is hypothesized that an increased risk for breast cancer due to ATM mutations most commonly derives from cohort-specific missense mutation, that do not cause A-T in a homozygous state and occasionally from a subset of A-T carriers that have non-truncating mutations. Two in human cohort-specific missense variants from our previous case-control analysis will be generated in mice using mouse knock-in technology. The rate and time course of cancer incidence will be determined in these mice in comparison to wild type littermates and an A-T- causing non-truncating structural variant. Since the mouse Atm gene is extremely close to the human gene in structure and function, mouse models with only a single alteration in the gene can be used to assess the effects of this alteration on tumor formation, especially mammary tumors, in mice. If a variety of uncommon missense variants are shown to predispose to breast cancer, there are important diagnostic, preventive, and therapeutic implications for women at risk for breast cancer.						
<b>15. SUBJECT TERMS</b> ATM mutation, breast cancer, prognosis						
<b>16. SECURITY CLASSIFICATION OF:</b>				<b>17. LIMITATION OF ABSTRACT</b>	<b>18. NUMBER OF PAGES</b>	<b>19a. NAME OF RESPONSIBLE PERSON</b> USAMRMC
<b>a. REPORT</b> U	<b>b. ABSTRACT</b> U	<b>c. THIS PAGE</b> U	<b>19b. TELEPHONE NUMBER (include area code)</b>			

## Table of Contents

<b>Table of Contents.....</b>	<b>3</b>
<b>Introduction.....</b>	<b>4</b>
<b>Body.....</b>	<b>5</b>
<b>Key Research Accomplishments.....</b>	<b>6</b>
<b>Reportable Outcomes.....</b>	<b>6</b>
<b>Conclusion.....</b>	<b>6</b>
<b>References.....</b>	<b>6</b>
<b>Appendices.....</b>	<b>6</b>

**Proposal Title:** Do Structural Missense Variants In The ATM Gene Found In Women With Breast Cancer Cause Breast Cancer in "Knock-in" Mouse Strains?

## **Introduction**

The recessive neurological disease ataxia telangiectasia (A-T), which has pleiotropic effects including an increased susceptibility to cancer, is known to be caused by homozygous or compound heterozygous mutations in the ATM gene. In a number of epidemiological studies of A-T families, heterozygous carriers have been shown to be at increased risk of breast cancer. However, a number of early studies of breast cancer patients in non-A-T families did not detect a significant number of ATM truncating mutations. Our laboratory has conducted a case control analysis of 90 women with stage 1 or 2 breast cancer who were referred for adjuvant radiation therapy. We determined that uncommon *missense* mutations, predominately at evolutionarily conserved amino acids, are associated with a 3.2 fold relative risk of developing breast cancer in individuals with such mutations relative to the breast cancer risk in normal population. From these data it is estimated that 13% of breast cancer cases in the population are due to these types of ATM missense mutations. Most disturbing is preliminary evidence that such individuals may harbor a much greater likelihood of recurrence relative to those individuals without such mutations.

These results can perhaps be integrated by testing the following hypothesis: in heterozygotes, truncating mutations causing total disruption of ATM function do not predispose to breast cancer, whereas missense mutations that alter ATM function do predispose to breast cancer. Therefore, increased risk of breast cancer in ataxia telangiectasia heterozygotes may be due to the missense mutations in approximately 30% of patients. Preliminary data suggest that women with ATM-mediated breast cancer have poor prognosis.

There is an overriding need to unequivocally determine the magnitude of breast cancer risk associated with ATM missense mutations. A second, more robust, approach would involve the murine model of the *Atm* locus, in which targeted mutations are introduced into the *Atm* gene to determine whether certain *missense* variants (rather than truncating mutations causing total disruption of ATM function) predispose to breast cancer in mice. The importance of the mouse model cannot be over-emphasized, since mouse genes are similar to their human counterparts, serve the same purpose, and mutations often mimic the corresponding human phenotype. The entire coding sequence of the mouse homolog of the human ATM gene has been cloned, cytogenetically mapped, molecularly characterized and was found to be remarkably similar to the human gene. Furthermore, mouse studies of the *Atm* locus indicate that absence of *Atm* activity in heterozygotes produces an ataxia-telangiectasia phenotype, whereas heterozygotes containing a small in-frame deletion for a mutant, but expressed, form of *Atm* exhibit a greater susceptibility to breast cancer.

We propose an innovative and as yet untried series of experiments to construct and analyze selected murine missense and truncating *Atm* mutations which, in combination with our ongoing human ATM mutation studies, has the potential to clearly and cleanly demonstrate a major role of certain ATM structural variants in the predisposition to breast cancer.



## Body

*Task 1.* To construct two vectors containing specific missense variants found in the ATM gene of breast cancer patients in a mouse Atm clone.

- a. This work is being initiated before the start of this grant by inGenious Targeting Laboratory (iTL).
- b. A BAC library will be screened for mouse Atm clones.
- c. Two subclones will be isolated for the regions of interest.
- d. Two knock-in targeting vectors containing the variants of interest will be constructed.

*Task 2.* To produce two mouse knock-in Atm lines. Production of the second line will be staggered by about two months (Months 1-8).

- a. Vector DNA will be transfected into 129/S6 embryonic stem (ES) cell lines and about 300 clones will be produced (Months 1-4).
- b. Clones will be screened by Southern blotting to determine those that carry the targeted mutation (Months 3-5).
- c. Clones positive for the targeted mutation will be expanded and injected into C57BL/6 blastocysts to produce chimeras for germline transmission. Tail biopsies of mice potentially heterozygous for the targeted mutation will be genotyped (Months 4-8).

Constructing the vectors has produced unanticipated challenges.

After a false start with a commercial entity, we are generating the two vectors in house. Although we are a technically oriented laboratory (see CV), we have not had previous experience in vector construction. I anticipate that Task 1 will be complete in two months and Task 2 will be complete within six months. We are in the queue with the transgenic mouse core facility to inject oocytes when the vectors are complete.

Meanwhile in relevant work not funded by this grant, we have generated more evidence in support of the central hypothesis underlying the transgenic knock-in mice being created with these funds.

The current analysis expands upon case control epidemiological analyses of the ATM gene in women with overwhelming Stage I or Stage II breast cancer vs. ethnically similar controls (Singh et al.) *Submitted*

We find that women with cohort-specific ATM mutations have substantially poorer prognosis than those who do not have ATM cohort specific structural variants.

The following is an abstract from our submitted publication.

Ataxia-Telangiectasia A-T is an autosomal recessive disorder characterized by progressive cerebellar degeneration, telangiectasias, radiosensitivity, immunodeficiency, and a predisposition to cancer development. Epidemiologic studies of families of A-T patients have demonstrated an increased risk of breast cancer in females. Furthermore, in a recently reported series, we observed a significant elevation of cohort-specific missense ATM mutations insufficient to cause A-T in 90 breast cancer patients as compared to ethnically matched controls.

We retrospectively reviewed the records of breast cancer cases for correlation with clinical features including age at diagnosis, histology, tumor size, axillary nodal metastases, disease control, acute toxicity of radiation therapy, and long-term sequelae. Freedom from relapse (FFR) was determined by the method of Kaplan & Meier and analyzed by the generalized Wilcoxon test.

FFR was significantly shorter in patients with cohort-specific mutations in the ATM gene relative to those without cohort-specific mutations ( $p = 0.0001$ ). With the exception of cohort-specific ATM mutations in women under 40, we found no significant differences in pre-treatment characteristics or treatment related toxicity between patients with and without mutations.

In this retrospective correlation of cohort-specific mutations of the ATM gene, we observed a negative prognosis. Larger studies are needed to conclusively determine if specific ATM missense mutations predict a worse outcome in breast cancer.

### **Key Research Accomplishments**

Construction of knock-in mice is in progress.

### **Reportable Outcomes**

None in this first year.

### **Conclusion**

Construction of the knock-in mice is in progress.

### **References**

Singh A, Jung M, Feng J, Buzin C, Moulds J, Zhang Y, Gehan E, Dritschilo A, Sommer SS (2006): Clinical prognosis of breast cancer patients with ATM missense mutations. *Submitted*

### **Appendices**

Steve S. Sommer, M.D., Ph.D. (CV)

# CURRICULUM VITAE

**Name:** Steve S. Sommer, M.D., Ph.D.

**Address:** City of Hope National Medical Center  
Beckman Research Institute  
Departments of Molecular Genetics and Molecular Diagnosis  
1500 East Duarte Road  
Duarte, CA 91010-3000  
Telephone: (626) 930-5497  
Telefax: (626) 301-8142  
E-mail: [sommeradmin@coh.org](mailto:sommeradmin@coh.org)

## **Education:**

1968-1972 B.A., University of Pennsylvania, Philadelphia, PA  
1972-1979 Cornell-Rockefeller, M.D., Ph.D. Fellowship  
1978 Ph.D. - Rockefeller University, New York, NY (Molecular Biology)  
1979 M.D. - Cornell University Medical College, New York, NY

## **Postdoctoral Training**

### **Residencies and Clinical Fellowships**

7/79-6/80 Resident, Surgical Pathology and Postmortem Section, Dr. Jose Costa, Chief; Laboratory of Pathology, Dr. Alan S. Rabson, Chief; National Cancer Institute, National Institutes of Health, Bethesda, MD  
7/82-7/84 Multicenter Individual Fellowship in Clinical Genetics; sponsors, Dr. James Sidbury, Jr., Chief, Section on Developmental Biology and Human Nutrition, National Institute of Child Health and Human Development and Dr. Kenneth Rosenbaum, Director, Clinical Genetics, Children's Hospital National Medical Center, Washington, DC

### **Research Fellowships**

7/80-7/85 Medical Staff Fellow, Section of the Genetics of Simple Eukaryotes, Dr. Reed Wickner, Chief; Laboratory of Biochemical Pharmacology, Dr. Herbert Tabor, Chief; National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD. Research area: molecular genetics of virus-like particles in yeast.

### **Academic Appointments:**

7/85-6/90 Assistant Professor of Molecular Biology, Department of Biochemistry and Molecular Biology, Mayo Foundation School of Medicine, Rochester, MN; Mayo Clinic ranks: Senior Associate Consultant, 7/85-11/89; Consultant, 11/89-present.  
7/90-6/94 Associate Professor of Molecular Biology, Department of Biochemistry and Molecular Biology, Mayo Foundation School of Medicine, Rochester, MN  
7/94-8/96 Professor of Molecular Biology, Department of Biochemistry and Molecular Biology, Mayo Foundation School of Medicine, Rochester, MN  
8/95-8/96 Director, Thrombosis and Haemostasis Molecular Diagnostic Laboratory, Division of Hematology, Mayo Foundation School of Medicine, Rochester, MN  
8/96 Director, Department of Molecular Genetics, Beckman Research Institute, City of Hope, Duarte, CA  
8/96 Director, Department of Molecular Diagnostics and Acting Chair, Division of Human Genetics, City of Hope National Medical Center, City of Hope, Duarte, CA

### **Licensure and Certifications:**

Medical Licenses in Minnesota and California  
American College of Medical Genetics  
Diplomat in Clinical Genetics, 1984  
Diplomat in Clinical Molecular Genetics, 1993 (97<sup>th</sup> percentile on certification exam)

### **Honors:**

Cornell-Rockefeller Biomedical Fellowship, 1972-1979  
Elected, American Society of Clinical Investigation (ASCI), 1992  
Elected, Association of American Physicians (AAP), 1996

### **Editorships/Editorial Boards:**

Editorial Board, PCR Methods and Applications, 1991-1993  
Communicating Editor, Human Mutation, 1991-present  
Editorial Board, BioTechniques, 1992-present  
Editorial Board, Mutation Research Genomics, 1997-present

## Patents

- No. 5194600 (3/16/93): Genes, which participate in beta-glucan assembly and use thereof  
No. 6207425 (3/27/01): Bidirectional PCR amplification of specific alleles  
No. 6312905 (11/29/01): Method for detecting mutations in nucleic acids  
No. 6376193 (4/23/02): Method for detecting mutations in nucleic acids  
No. 6287441 (9/11/01): Multi Conditional SSCP (SSCP<sub>3</sub>): A rapid method for mutation scanning with virtually 100% sensitivity.  
No. 6534269B2 (3/18/03): Pyrophosphorolysis activated polymerization (PAP): application to allele-specific amplification and nucleic acid sequence determination  
No. 6582574 (6/24/03): PK-matched running buffers for gel electrophoresis.  
No. 6,355,422 (3/12/02): Single tube PCR assay for detection of chromosomal mutations: application to the inversion hotspot in the factor VIII gene including optional use of subcycling PCR.  
No. 6,027,913 (2/22/00): Nucleic acid amplification with direct sequencing.  
No. 6,361,949(3/26/02): Nucleic acid amplification with direct sequencing.

## Current and Past Extramural Support:

Source: U.S. Army BC990386  
Title: **p53 Gene Mutagenesis in Breast Cancer** (Active) No Overlap  
Dates: Total Project Period: 08/01/2000-02/01/2005

Major Goals: To compare patterns of p53 mutations occurring in the Midwest in the 1960's, to present day patterns.

Source: U.S. Army BC000761  
Title: **Lipophilic Mutagens, Fat Consumption and Breast Cancer** (Active) No Overlap  
Dates: Total Project Period: 03/31/2001-07/31/2005

Major Goals: To test the central hypothesis that mammary epithelial cells are susceptible to lipophilic mutagens concentrated in adjacent mammary adipocytes and originating in the diet.

Source: NIH-RO1 AG19784-01  
Title: **Tissue-Specific Antioxidant Antimutagenesis** (Active) No Overlap  
Dates: Total Project Period: 07/01/2001-06/30/2006

Major Goals: The Big Blue<sup>®</sup> Transgenic Mouse Mutation Detection System is utilized to examine the antimutagenic effect of lifetime administration of mega doses of antioxidants.

Source: National Hemophilia Foundation  
Title: **Restoration of Factor VII/IX Function in Hemophilia A/B Patients** (Active) No Overlap  
Dates: Total Project Period: 09/01/2001-08/31/2002

Major Goals: A pilot study to investigate aminoglycoside therapy in hemophilia

Source: NIH-1 R21 CA94408-01  
Title: **Carbon Nanotubes: Artificial Gels for Mutation Detection** (Active) No Overlap  
Total Project Period: 04/01/2002-07/01/2006

Major Goals: Artificial gels generated by carbon nanotubes will be utilized to miniaturize DOVAM-S, a mutation scanning method that detects virtually all mutations.

Source: NIH-1 R21 CA94334-01  
Title: **PAP: A Platform Technology** (Active) No Overlap  
Total Project Period: 07/01/2002-06/30/2006

Major Goals: Pyrophosphorolysis activated polymerization (PAP) offers a novel approach for retrieving multiple types of information from nucleic acids.

Source: NIA-1 R03 AG 20756-01

Title: **Aging and Mutation Load in Transgenic Medaka Fish**  
Total Project Period: 06/01/2002-05/31/2005

(Active) No Overlap

Major Goals: Medaka fish (*Oryzias latipes*) transgenic for the Big Blue mutation detection system are an excellent model for *in vivo* analysis of age and mutation load (mutation frequency and pattern) with consideration of associated parameters such as tissue type and certain environmental conditions, including temperature

Source: NIH-1 R01 HL70147-03

Title: **Translational Bypass in Patient with Hemophilia**  
Total Project Period: 09/15/2002-08/31/2005

(Active) No Overlap

Major Goals: We hypothesize that small molecules that readily enter cells can induce nonsense suppression by the protein synthetic apparatus such, that nonsense mutations are translationally bypassed at levels up to 20%. Evaluation of efficacy will be performed with the prototype drug gentamicin, an aminoglycoside antibiotic.

Source: DOD U.S. Army BC0440-16-01

Title: **Do Structural Missense Variants in the ATM Gene Found in Women with Breast Cancer Cause Breast Cancer in Knock-in Mouse Strains?**  
Total Project Period: 12/01/04-11/30/2007

(Active) No Overlap

Major Goals: Test the hypothesis that the risk of breast cancer in ATM heterozygotes is due to a dominant negative effect of certain missense mutations in the gene by studying the effects in knock-in mouse models of ATM variants found in patients with breast cancer.

## BIOGRAPHICAL SKETCH A: Methodology Development

Name Steve S. Sommer, M.D., Ph.D.	Position Title Professor of Molecular Biology
--------------------------------------	--

### EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREES	YEAR(s)	FIELD OF STUDY
Rockefeller University, New York, NY	B.A.	1972-1978	Molecular Biology
Cornell University Med. College, New York, NY	Ph.D.	1972-1979	Medicine
NIH, Multicenter Indiv. Fellowship, Bethesda, Maryland	M.D.	1982-1984	Genetics
NIADDK, NIH, Medical Staff Fellow, Bethesda, Maryland		1980-1985	Genetics

**Medical Specialties:** ABMG Diplomate in Clinical Genetics (1984) and Clinical Molecular Genetics (1993)

### Experience:

- 1980-1985: Medical Staff Fellow, Killer System of Yeast; with Dr. Reed Wickner, NIADDK, NIH  
1982-1984: Multicenter Individual Fellowship in Clinical Genetics  
7/85-8/96: Assistant Associate and Full Professor of Molecular Biology, Department of Biochemistry and Molecular Biology, Mayo Foundation School of Medicine, Rochester, MN  
8/96-Present: Director, Departments of Molecular Genetics and Molecular Diagnosis, City of Hope, Duarte, CA

**Selected papers emphasizing the development, validation, and extension of novel methods: 43 of 251 publications (206 published or in press original papers and 45 reviews, letters...)**

### PCR Decontamination

36. Sarkar, G., and Sommer, S.S.: **Shedding light on PCR contamination.** *Nature* 343:27, 1990.
41. Sarkar, G., and Sommer, S.S.: **More light on PCR contamination.** *Nature* 347:340-341, 1990.
51. Sarkar, G., and Sommer, S.S.: **Parameters affecting susceptibility of PCR contamination to UV inactivation.** *Biotechniques* 10:590-593, 1991.

### SELECTED CORE METHODS

15. Stoflet, E.S., Koeberl, D.D., Sarkar, G. and Sommer, S.S.: **Genomic amplification with transcript sequencing.** *Science* 239:491-494, 1988.
23. Sarkar, G., and Sommer, S.S.: **Access to a messenger RNA sequence or its protein product is not limited by tissue or species specificity.** *Science* 244:331-334, 1989.
55. Kovach, J.S., McGovern, R.M., Cassady, J.D., Swanson, S.K., Wold, L.E., Vogelstein, B., and Sommer, S.S.: **Direct sequencing from touch preparations of human carcinomas: analysis of p53 mutations in breast carcinomas. I.** *Natl. Cancer Inst.* 83:1004-1009, 1991.
80. Dutton, C.M., Paynton, C., and Sommer, S.S.: **General method for amplifying regions of very high G + C content.** *Nucleic Acids Res.* 21:2953-2954, 1993.
157. Liu, Q., Nozari, G., and Sommer, S.S.: **Single-tube polymerase chain reaction for rapid diagnosis of the inversion of mutation in hemophilia A.** *Blood* 92: 1458-1459, 1998.
160. Liu, Q., and Sommer, S.S.: **Subcycling-PCR for multiplex long distance amplification of regions with high and low GC content: application to the inversion hotspot in the factor VIII gene.** *BioTechniques* 25:1022-1028, 1998.
159. Liu, Q., Weinshenker, B.G., Wingerchuk, D.M., and Sommer, S.S.: **Denaturation fingerprinting: two related mutation detection methods especially advantageous for high G+C regions.** *BioTechniques* 24:140-147, 1998.
184. Liu, Q., and Sommer, S.S.: **Pyrophosphorolysis Activated Polymerization (PAP): Application to Allele-Specific Amplification.** *BioTechniques* 29: 1072-1083, 2000.
198. Liu, Q., and Sommer, S.S.: **Pyrophosphorolysis-activatable oligonucleotides may facilitate detection of rare alleles, mutation scanning and analysis of chromatin structures.** *Nucleic Acids Res.* 15:30(2): 598-604, 1992, 2002.
200. Liu, Q., Swiderski, P., and Sommer, S.S.: **Truncated Amplification: A method for High Fidelity Template-Drive Nucleic Acid Amplification.** *Biotechniques* 33, 129-138, 2002.



195. Heinmoller, E., Liu, Q., Sun, Y., Schlake, G., Hill, K.A., Weiss, L.M., Sommer, S.S.: Toward efficient analysis of mutations in single cells from ethanol-fixed paraffin-embedded and immunohistochemically-stained tissue. Laboratory Investigation 82(4): 443-53, 2002.
216. Liu, Q. and Sommer, S.S.: Detection of extremely rare alleles by bidirectional pyrophosphorolysis-activated polymerization allele-specific amplification (Bi-PAP-A): measurement of mutation load in mammalian tissue. BioTechniques 36: 156-166, 2004.

#### Megaprimers

37. Sarkar, G., and Sommer, S.S.: The "megaprimer" method of site-directed mutagenesis. BioTechniques 8:404-407, 1990.
65. Sarkar, G., and Sommer, S.S.: Double-stranded DNA segments can efficiently prime the amplification of human genomic DNA. Nucleic Acids Res. 20:4937-4938, 1992.

#### Allele-Specific PCR and Variants Thereof

25. Sommer, S.S., Cassady, J., Sobell, J.L., and Bottema, C.D.K.: A novel method of detecting point mutations or polymorphisms and its application to population screening for carriers of phenylketonuria. Mayo Clinic Proceedings 64:1361-1372, 1989.
38. Sarkar, G., Cassady, J., Bottema, C.D.K., and Sommer, S.S.: Characterization of polymerase chain reaction amplification of specific alleles. Anal. Biochem. 186:64-68, 1990.
52. Sarkar, G., and Sommer, S.S.: Haplotyping by double PCR amplification of specific alleles. BioTech 10:436-440, 1991.
54. Dutton, C., and Sommer, S.S.: Simultaneous detection of multiple single-base alleles at a polymorphic site. Biotechniques 11:700-702, 1991.
62. Sommer, S.S., Groszbach, A., and Bottema, C.D.K.: PCR Amplification of Specific Alleles (PASA) is a general method for rapidly detecting known single-base changes. Biotechniques 12:82-87, 1992.
147. Liu, Q., Thorland E.C., Heit J.A., Sommer S.S.: Overlapping PCR for Bidirectional PCR Amplification of Specific Alleles: A Rapid One-Tube Method for Simultaneously Differentiating Homozygotes and Heterozygotes. Genome Research 7: 389-398, 1997.

#### SSCP Hybrid Scanning Methods That Detect Virtually All Mutations

64. Sarkar, G., Yoon, H-S., and Sommer, S.S.: Dideoxy fingerprinting (ddF): a rapid and efficient screen for the presence of mutations. Genomics 13:441-443, 1992.
114. Blaszyk, H., Hartmann, A., Schroeder, J.J., McGovern, R.M., Sommer, S.S., and Kovach, J.S.: Rapid and efficient screening for p53 gene mutations by dideoxy fingerprinting. BioTechniques 18:256-260, 1995.
134. Liu, Q., Feng, J., and Sommer, S.S.: Bi-directional dideoxy fingerprinting (Bi-ddF): a rapid method for quantitative detection of mutations in genomic regions of 300-600 bp. Hum. Mol. Genet. 5:107-114, 1996.
146. Kukita Y., Tahira T., Sommer, S.S.: Hayashi K: SSCP Analysis of Long DNA Fragments in Low pH Gel. Human Mutation 10:400-407, 1997.
113. Liu, Q., and Sommer, S.S.: Restriction endonuclease fingerprinting (REF): A sensitive method for screening mutations in long, contiguous segments of DNA. BioTechniques 18:470-477, 1995.
148. Liu, Q., Feng, J., Sommer, S.S.: In a blinded analysis, restriction endonuclease fingerprinting (REF) detects all the mutations in a 1.9 kb segment. BioTechniques 23: 836-839, 1997.
171. Feng, J.F., Buzin, C.H., Tang, S-H.E., Scaringe, W.A., and Sommer, S.S.: Highly sensitive mutation screening by REF with low concentrations of urea: a blinded analysis of a 2 kb region of the p53 gene reveals two common haplotypes. Human Mutation 14:175-180, 1999.
174. Scaringe, W.A., Liao, D., Liu, Q., and Sommer, S.S.: REF Select: Expert system software for selecting restriction endonucleases for restriction endonucleases fingerprinting (REF). BioTechniques 27:1188-12017, 1999.
159. Liu, Q., Weinshenker, B.G., Wingerchuk, D.M., and Sommer, S.S.: Denaturation fingerprinting: two related mutation detection methods especially advantageous for high G+C regions. BioTechniques 24:140-147, 1998.
170. Liu, Q., Feng, J., Buzin, C., Wen, C., Nozari, G., Mengos, A., Nguyen, V., Liu, J-Z., Crawford, L., Fujimura, F.K., and Sommer, S.S.: [Detection Of Virtually All Mutations] - SSCP (DOVAM-S): A rapid method for mutation scanning with virtually 100% sensitivity. BioTechniques 26:932-942, 1999.
182. Buzin, C., Wen, C., Nguyen, V., Nozari, G., Mengos, A., Li X., Chen, J., Liu, Q., Gatti, R.A., Fujimura, F.K. and Sommer, S.S.: Scanning by DOVAM-S detects all unique sequence changes in blinded analyses: Evidence that the scanning conditions are generic. BioTechniques 28:746-753, 2000.

**Molecular Epidemiology of Human Disease: Approaches and Statistical Methods**

34. Sommer, S.S.: Mutagen test. *Nature* 346:22-23, 1990.
127. Blaszyk, H., Hartmann, A., Liao, D-z., Kovach, J.S., and Sommer, S.S.: Evidence for diverse mutagens in breast cancer. *Lancet* 348: 683-684, 1996.
66. Sobell, J.L., Heston, L., and Sommer, S.S.: Delineation of genetic predisposition to multifactorial disease: A general approach on the threshold of feasibility. *Genomics* 12:1-6, 1992
81. Schaid, D.J., and Sommer, S.S.: Genotype relative risks: methods for design and analysis of candidate gene association studies. *Am. J. Hum. Genet.* 53:1114-1126, 1993.
101. Schaid, D.J., and Sommer, S.S.: Need to confirm promising case-control association studies. *Am. J. Med. Genet. (Neuropsychiatric Genetics)* 54:156-157, 1994.
102. Schaid, D.J., and Sommer, S.S.: Comparison of statistics for candidate-gene association studies with case and parents. *Am. J. Hum. Genet.* 55:402-409, 1994.
- R26 Sommer, S.S.: Recent human germ-line mutation: Inferences from patients with hemophilia B. *Trends in Genetics* 11:141-147, 1995.
176. Drost, J.B., Scaringe, W.A., Jaloma-Cruz, A.R., Li, X., Ossa, D.F., Kaspar, C.K., and Sommer, S.S.: Novel hotspot detector software reveals a non-CpG hotspot of germline mutation in the factor IX gene (F9) in Latin Americans. *Human Mutation* 16:203-210, 2000.
191. Weinshenker BG, Sommer S.S.: VAPSE-based Analysis: a two-phased candidate gene approach for elucidating genetic predisposition to complex disorders. *Mutation Research Genomics* 458:7-17, 2001.



**BIOGRAPHICAL SKETCH B: Spontaneous Mutagenesis**

Name Steve S. Sommer, M.D., Ph.D.	Position Title Professor of Molecular Biology
--------------------------------------	--

**EDUCATION/TRAINING**

INSTITUTION AND LOCATION	DEGREES	YEAR(s)	FIELD OF STUDY
Rockefeller University, New York, NY	B.A.	1972-1978	Molecular Biology
Cornell University Med. College, New York, NY	Ph.D.	1972-1979	Medicine
NIH, Multicenter Indiv. Fellowship, Bethesda, Maryland	M.D.	1982-1984	Genetics
NIADDK, NIH, Med.Staff Fellow Bethesda, Maryland		1980-1985	Genetics

**Medical Specialties:** ABMG Diplomate in Clinical Genetics (1984) and Clinical Molecular Genetics (1993)

**Experience:**

- 1980-1985: Medical Staff Fellow, Killer System of Yeast; with Dr. Reed Wickner, NIADOX, NIH  
 1982-1984: Multicenter Individual Fellowship in Clinical Genetics  
 7/85-8/96: Assistant Associate and Full Professor of Molecular Biology, Department of Biochemistry and Molecular Biology, Mayo Foundation School of Medicine, Rochester, MN  
 8/96-Present: Director, Departments of Molecular Genetics and Molecular Diagnosis, City of Hope, Duarte, CA  
 8/96-Present: Medical Director, City of Hope Clinical Molecular Diagnostic Laboratory

**Selected Papers: 23 of 251 publications (206 published or in press original papers and 45 reviews, letters...)****Human Germline Mutation: Lessons from the Factor IX gene**

32. Koeberl, D.D., Bottema, C.D.K., Ketterling, R.P., Bridges, P.J., Lillicrap, D.P., and Sommer, S.S.: **Mutations causing hemophilia B: direct estimate of the underlying rates of spontaneous germline transitions, transversions, and deletions in a human gene.** *Am. J. Hum. Genet.* 47:202-217, 1990.
153. Heit, J.A., Thorland, E.C., Ketterling, R.P., Lind, T.J., Daniels, T.M., Zapata, R.E., Ordonez, S.M., Kasper, C.K., and Sommer, S.S.: **Germline mutations in Peruvian patients with hemophilia B: pattern of mutation in AmerIndians is similar to the putative endogenous germline pattern.** *Human Mutation* 11: 372-376, 1998.
167. Ketterling, R.P., Vielhaber, E., Li, X., Drost, J., Schaid, D.J., Kasper, C.K., Phillips, J.A., Koerper, M.A., Kim, H., Sexauer, C., Gruppo, R., Ambriz, R., Paredes, R., Sommer, S.S.: **Germline origins in the human F9 gene: frequent G:C → A:T mosaicism and increased mutations with advanced maternal age.** *Human Genetics* 105: 629-640, 1999.
163. Ketterling, R.P., Drost, J.B., Scaringe, W.A., Laio, D-z., Liu, J-z., Kasper, C.K., Sommer, S.S.: **Reported in vivo splice site mutations in the factor IX gene – severity of splicing defects and a hypothesis for predicting deleterious splice donor mutations.** *Human Mutation* 13:221-231, 1999.
164. Thorland, E.C., Drost, J.B., Lusher, J.M., Warriar, I., Shapiro, A., Koerper, M.A., DiMichele, D., Westman, J., Key, N.S., and Sommer, S.S.: **Anaphylactic response to factor IX replacement therapy in hemophilia B patients: complete gene deletions confer the highest risk.** *Haemophilia* 5(2):101-105, 1999.
187. Li, X., Scaringe, W.A., Hill, K.A., Roberts, S., Careri, D., Pinto, M., Kasper, C.K., and Sommer, S.S.: **Frequency of Retrotransposition Events in the Human Factor IX Gene.** *Human Mutation* 17:511-519, 2001.
189. Feng, J., Drost, J.B., Scaringe, W.A., Liu, Q., and Sommer, S.S.: **Mutations in the factor IX gene (F9) during the past 150 years have relative rates similar to ancient mutations.** *Hum Mutat.* 19:(1):49-57, 2001.

**Somatic Mutation: the p53 Gene as a "Mutagen Test in Breast Cancer"**

34. Sommer, S.S.: **Mutagen test.** *Nature* 346:22-23, 1990.
120. Kovach, J.S., Hartmann, A., Blaszyk, H., Cunningham, J., Schaid, D., and Sommer, S.S.: **Mutation detection by highly sensitive methods indicates that p53 gene mutations in breast cancer can have important prognostic value.** *Proc. Natl. Acad. Sci. USA* 93:1093-1096, 1996.

127. Blaszyk, H., Hartmann, A., Liao, D-z., Kovach, J.S., and Sommer, S.S.: Evidence for diverse mutagens in breast cancer. Lancet 348: 68-684, 1996.

**The Big Blue transgenic mouse mutation detection system: A system for examining in detail the relationship between mutational stress and either cancer or neurodegenerative disease.**

99. Knoll, A., et al.: Spontaneous mutations in *lacI*-containing 8 lysogens derived from transgenic mice: the observed patterns differ in liver and spleen. Mutation Research 311: 57-67, 1994.
111. Nishino, H. et al.: p53 wild-type and p53 nullizygous Big Blue® transgenic mice have similar frequencies and patterns of observed mutation in liver, spleen and brain. Oncogene 11: 263-270, 1995.
119. Knöll, A., et al.: A selectable system for mutation detection in the Big Blue™ *lacI* transgenic mouse system: what happens to the mutational spectra over time Mutation Research 352: 9-22, 1996.
129. Nishino, H., et al.: Towards validation of the Big Blue™ transgenic mouse mutagenesis assay: the mutational spectrum of ex vivo pinpoint mutant plaques. Mutation Research 372: 97-105, 1996.
131. Nishino, H., et al.: Spontaneous mutation in Big Blue® Transgenic Mice: Analysis of age, gender, and tissue type. Env. And Mol. Mutagenesis 28: 299-312, 1996.
132. Nishino, H., et al.: Mutation frequencies but not mutant frequencies in Big Blue mice fit a poisson distribution. Env. And Mol. Mutagenesis 28: 414-417, 1996.
186. Kunishige, M., Hill, K.A., Riemer, M., Farwell, K., Halangoda, A., Heinmöller, E., Moore, S.R, Turner, D., and Sommer, S.S.: Mutation frequency is reduced in the cerebellum of Big Blue® mice overexpressing a human wild type *SOD1* gene. Mutation Research 473(2): 139-149, 2001.
188. Halangoda, A., Still, J. G., Hill, K.A., and Sommer, S.S.: Spontaneous Microdeletions and Microinsertions in a transgenic mouse mutation detection system: analysis of age, tissue, and sequence specificity. Environ Mol. Mutagen 37:311-323, 2001.
215. Hill, K.A., Wang, Jichen, Farwell, Kelly D., Scaringe, W.A., and Sommer, S.S.: Spontaneous multiple mutations show proximal spacing consistent with chronocoordinate events and alterations with p53-deficiency. *In press*
204. Hill, K.A., Wang, J., Farwell, K.D., Sommer, S.S.: Spontaneous tandem-base mutations (TBM) show dramatic tissue, age, pattern and spectrum specificity. Mutat Res. 534:173-86, 2003
214. Hill, K.A., Buettner, V.L., Halangoda, A., Kunishige, M., Moore, S.R., Longmate, J., Scaringe, W.A., and Sommer, S.S.: Spontaneous Mutation in Big Blue® Mice from Fetus to Old Age: Tissue-Specific Time Courses of Mutation Frequency But Similar Mutation Types. Environmental and Molecular Mutagenesis:43:110-120, 2004.

**Selected Reviews/Hypotheses Highlighting Work from the Laboratory**

90. Sommer, S.S.: Does cancer kill the individual and save the species? Human Mutation 3:166-169, 1994.
- R24 Sommer, S.S.; Ketterling, R.P.: How precisely can data from transgenic mouse mutation-detection systems be extrapolated to humans?: lessons from the study of spontaneous germline mutations in the human factor IX gene. Mutation Research 307:517-531, 1994.
- R26 Sommer, S.S.: Recent human germ-line mutation: Inferences from patients with hemophilia B. Trends in Genetics 11:141-147, 1995.
- R33 Sommer, S.S.; and Ketterling, R.P.: The factor IX gene as a model for analysis of human germline mutations: an update. Hum. Mol. Genet.5:1505-1514, 1996.
- R36 Hartmann, A., Blaszyk, H., Kovach, J.S., and Sommer, S.S.: The molecular epidemiology of p53 gene mutations in human breast cancer. Trends in Genetics 13:27-33, 1997.
- R41 Hill, K.A., Buettner, V.L., Glickman, B.W., Sommer, S.S.: Spontaneous mutations in the Big Blue transgenic system are primarily mouse derived. Mutation Research Mini Review 436:11-19, 1999.

**BIOGRAPHICAL SKETCH C: Molecular Epidemiology**

Name Steve S. Sommer, M.D., Ph.D.	Position Title Professor of Molecular Biology
--------------------------------------	--

**EDUCATION/TRAINING**

INSTITUTION AND LOCATION	DEGREES	YEAR(s)	FIELD OF STUDY
Rockefeller University, New York, NY	B.A.	1972-1978	Molecular Biology
Cornell University Med. College, New York, NY	Ph.D.	1972-1979	Medicine
NIH, Multicenter Indiv. Fellowship, Bethesda, Maryland	M.D.	1982-1984	Genetics
NIADDK, NIH, Medical Staff Fellow, Bethesda, Maryland		1980-1985	Genetics

**Medical Specialties:** ABMG Diplomate in Clinical Genetics (1984) and Clinical Molecular Genetics (1993)

**Experience:**

- 1979-1980: Resident, Surgical Pathology and Postmortem Section; with Dr. Alan S. Rabson, National Cancer Institute, NIH
- 1980-1985: Medical Staff Fellow, Killer System of Yeast; with Dr. Reed Wickner, NIADDOX, NIH
- 1982-1984: Multicenter Individual Fellowship in Clinical Genetics
- 7/85-8/96: Assistant Associate and Full Professor of Molecular Biology, Department of Biochemistry and Molecular Biology, Mayo Foundation School of Medicine, Rochester, MN
- 8/96-Present: Director, Departments of Molecular Genetics and Molecular Diagnosis, City of Hope, Duarte, CA
- 8/96-Present: Medical Director, City of Hope Clinical Molecular Diagnostic Laboratory

**Selected papers emphasizing molecular epidemiology: 39 of 251 publications (206 published or in press original papers and 45 reviews, letters...)**

**P53 Gene as a Mutagen Test**

34. Sommer, S.S.: Mutagen test. *Nature* 346:22-23, 1990.
55. Kovach, J.S., McGovern, R.M., Cassady, J.D., Swanson, S.K., Wold, L.E., Vogelstein, B., and Sommer, S.S.: Direct sequencing from touch preparations of human carcinomas: analysis of p53 mutations in breast carcinomas. *J. Natl. Cancer Inst.* 83:1004-1009, 1991.
58. Sommer, S.S.; Cunningham, J., McGovern, R.M., Saitoh, S., Schroeder, J.J., Wold, L.E., Kovach, J.S.: Pattern of p53 gene mutations in breast cancers of women of the Midwestern United States. *J. Natl. Cancer Inst.* 84:246-252, 1992.
90. Sommer, S.S.: Does cancer kill the individual and save the species? *Human Mutation* 3:166-169, 1994.
96. Blaszyk, H., Vaughn, C.B., Hartmann, A., McGovern, R.M., Schroeder, J.J., Cunningham, J., Schaid, D., Sommer, S.S.: and Kovach, J.S.: Novel pattern of p53 gene mutations in an American black cohort with high mortality from breast cancer. *Lancet* 343:1195-1197, 1994.
98. Saitoh, S., Cunningham, J., DeVries, E.M.G., McGovern, R.M., Schroeder, J.J., Hartmann, A., Blaszyk, H., Schaid, D., Sommer, S.S.: and Kovach, J.S.: p53 gene mutations in breast cancers in Midwestern U.S. women: null as well as missense-type mutations are associated with poor prognosis. *Oncogene* 9:2869-2875, 1994.
107. Hartmann, A., Rosanelli, G., Blaszyk, H., Cunningham, J.M., McGovern, R.M., Schroeder, J.J., Schaid, D., Kovach, J.S., and Sommer, S.S.: Novel pattern of p53 mutation in breast cancers from Austrian women. *J. Clin. Invest.* 95:686-689, 1995.
120. Kovach, J.S., Hartmann, A., Blaszyk, H., Cunningham, J., Schaid, D., and Sommer, S.S.: Mutation detection by highly sensitive methods indicates that p53 gene mutations in breast cancer can have important prognostic value. *Proc. Natl. Acad. Sci. USA* 93:1093-1096, 1996.
127. Blaszyk, H., Hartmann, A., Liao, D-z., Kovach, J.S., and Sommer, S.S.: Evidence for diverse mutagens in breast. *Lancet* 348: 683-684, 1996.

130. Blaszyk, H., Hartmann, A., Tamura, Y., Saitoh, S., Cunningham, J.M., McGovern, R.M., Schroeder, J.J., Schaid, D.J., Ii, K., Monden, Y., Morimoto, T., Komaki, K., Sasa, M., Hirata, K., Okazaki, M., Kovach, J.S., and Sommer, S.S.: **Molecular epidemiology of breast cancers in northern and southern Japan: the frequency, clustering, and pattern of p53 gene mutations differ among these two low-risk populations.** *Oncogene* 13:2159-2166, 1996.
195. Heinmoller, E., Liu, Q., Sun, Y., Schlake, G., Hill, K.A., Weiss, L.M., Sommer, S.S.: **Toward efficient analysis of mutations in single cells from ethanol-fixed paraffin - embedded and immunohistochemically-stained tissue.** *In press Laboratory Investigation*, 2002

#### Molecular Epidemiology of Human Germline Mutations

20. Koeberl, D.D., Bottema, C.D.K., Buerstedde, J-M., and Sommer, S.S.: **Functionally important regions of the factor IX gene have a low rate of polymorphism and a high rate of mutation in the dinucleotide CpG.** *Am. J. Hum. Genet.* 45:448-457, 1989.
32. Koeberl, D.D., Bottema, C.D.K., Ketterling, R.P., Bridges, P.J., Lillicrap, D.P., and Sommer, S.S.: **Mutations causing hemophilia B: direct estimate of the underlying rates of spontaneous germline transitions, transversions, and deletions in a human gene.** *Am. J. Hum. Genet.* 47:202-217, 1990.
33. Bottema, C.D.K., Ketterling, R.P., Yoon, H-S., and Sommer, S.S.: **The pattern of factor IX germline mutations in Asians is similar to that of Caucasians.** *Am. J. Hum. Genet.* 47:835-841, 1990.
48. Ketterling, R.P., Bottema, C.D.K., Phillips, J.P., III, and Sommer, S.S.: **Evidence that descendants of three founders comprise about 25% of hemophilia B in the United States.** *Genomics* 10:1093-1096, 1991.
69. Ketterling, R.P., Vielhaber, E., Bottema, C.D.K., Schaid, D.J., Cohen, M.P., Sexauer, C.L., and Sommer, S.S.: **Germline origins of mutation in families with hemophilia B: the sex ratio varies with the type of mutation.** *Am. J. Hum. Genet.* 52:152-166, 1993.
71. Gostout, B., Vielhaber, E., Ketterling, R.P., Yoon, H-S., Bottema, C.D.K., Kasper, C.K., Koerper, M., and Sommer, S.S.: **Germline mutations in the factor IX gene: a comparison of the pattern in Caucasians and non-Caucasians.** *Hum. Molec. Genet.* 2:293-298, 1993.
93. Sommer, S.S., Tillotson, V., Vielhaber, E.L., Ketterling, R.P., and Dutton, C.M.: **"Cryptic" dinucleotide polymorphism in the 3' region of the factor IX gene shows substantial variation among different populations.** *Hum. Genet.* 93:357-358, 1994.
95. Rossiter, J.P., Young, M., Kimberland, M.L., Hutter, P., Ketterling, R.P., Gitschier, J., Horst, J., Morris, M.A., Schaid, D.J., de Moerloose, P., Sommer, S.S.: Kazazian, H.H., Jr., and Antonarakis, S.E.: **Factor VIII gene inversions causing severe hemophilia A originate almost exclusively in male germ cells.** *Hum. Mol. Genet.* 3:1035-1039, 1994.
121. Thorland, E.C., Weinschenker, B.G., Liu, J-z., Ketterling, R.P., Vielhaber, E.L., Kasper, C.K., Ambriz, R., Paredes, R., and Sommer, S.S.: **Molecular epidemiology of factor IX germline mutations in Mexican Hispanics: pattern of mutation and potential founder effects.** *Thrombosis and Haemostasis* 74:1416-1422, 1995.
167. Ketterling, R.P., Vielhaber, E., Li, X., Drost, J.B., Schaid, D.J., Kasper, C.K., Phillips, J.A., Koerper, M.A., Kim, H., C., Grupp, R., Ambriz, R., Paredes, R., and Sommer, S.S.: **Germlines origins in the human F9 gene: frequent somatic mosaicism with G:C>A:T and increased mutations with advanced maternal, but not paternal age.** *Human Genetics* 105(6):629-40, 1999.
176. Drost, J.B., Scaringe, W.A., Jaloma-Cruz, A.R., Li, X., Ossa, D.F., Kasper, C.K., and Sommer, S.S.: **Novel hotspot detector software reveals a non-CpG hotspot of germline mutation in the factor IX gene (F9) in Latin Americans.** *Human Mutation* 16(3):203-10, 2000.
179. Li, X., Drost, J.B., Roberts, S., Kasper, C., and Sommer, S.S.: **Factor IX mutations in South Africans and African Americans are compatible with primarily endogenous influences upon recent germline mutations.** *Human Mutation* 16(4): 371, 2000.

#### VAPSE-Based Analysis Candidate Gene Approach: Statistical Issues & Exposition of the Approach

66. Sobell, J.L., Heston, L., and Sommer, S.S.: **Delineation of genetic predisposition to multifactorial disease: A general approach on the threshold of feasibility.** *Genomics* 12:1-6, 1992.
81. Schaid, D.J., and Sommer, S.S.: **Genotype relative risks: methods for design and analysis of candidate gene association studies.** *Am. J. Hum. Genet.* 53:1114-1126, 1993.
83. Sobell, J.L., Heston, L.L., and Sommer, S.S.: **Novel association approach for determining the genetic predisposition to schizophrenia: case-control resource and testing of the first candidate gene.** *Am. J. Med. Genet. (Neuropsychiatric Genetics)* 48:28-35, 1993.
101. Schaid, D.J., and Sommer, S.S.: **Need to confirm promising case-control association studies.** *Am. J. Med. Genet. (Neuropsychiatric Genetics)* 54:156-157, 1994.



102. Schaid, D.J., and Sommer, S.S.: Comparison of statistics for candidate-gene association studies with case and parents. Am. J. Hum. Genet. 55:402-409, 1994

#### VAPSE-Based Analysis Genetics of Psychiatric Disease

57. Sarkar, G., Kapelner, S., Grandy, D.K., Civelli, O., Sobell, J., Heston, L., and Sommer, S.S.: Direct sequencing of the dopamine D<sub>2</sub> receptor (DRD2) in schizophrenics reveals three polymorphisms but no structural change in the receptor. Genomics 11:8-14, 1991.
118. Sobell, J.L., Lind, T.J., Sigurdson, D.C., Zald, D.H., Snitz, B.E., Grove, W.W., Heston, L.L., and Sommer, S.S.: The D5 dopamine receptor gene in schizophrenia: identification of a nonsense change and multiple missense changes but lack of association with disease. Hum. Mol. Genet. 4:507-514, 1995.
137. Sobell, J.L., Sigurdson, D.C., Heston, L.L., Byerley, W.F., and Sommer, S.S.: Genotype-to-phenotype analysis: search for clinical characteristics of a missense change in the GABA<sub>A</sub>-β1 receptor gene. Am. J. Med. Genet. 67:81-84, 1996.
138. Sommer, S.S., and Rocca, W.A.: Prion analogues and twin studies in Parkinson's disease. Neurology 46:273-275, 1996.
162. Feng, J., Sobell, J.L., Heston, L.L., Cook, E.H., Jr., Goldman, D., and Sommer, S.S.: Analysis of the Dopamine D1 and D5 Receptors by Restriction Endonuclease Fingerprinting (REF) in Patients with Neuropsychiatric Disease Reveals Missense Change In A Highly conserved Amino Acid. Am. J. Med. Genet. (Neuropsych. Genet) 81:172-178, 1998.
185. Feng, J., Zheng, J., Bennett, W.P., Heston, L.L., Jones, I.R., Craddock, N., and Sommer, S.S.: Five Missense Variants in the Amino-Terminal Domain of the Glucocorticoid Receptor: No Association with Puerperal Psychosis or Schizophrenia. Am. J. Med. Genet. (Neuropsychiatric Genetics) 96(3):412-7, 2000.
192. Feng, J., Zheng, J., Gelernter J, Kranzler H, Cook E, Goldman D, Jones IR, Craddock N, Heston LL, Delisi L, Peltonen L, Bennett WP, Sommer, S.S.: An in-frame deletion in the alpha (2C)adrenergic receptor is common in African-Americans. Mol Psychiatry (6):168-172, 2001.
194. Feng, J., Yan, J., Michaud, S., Craddock, N., Jones, I., Cook, E.H., Jr., Goldman, D., Heston, L.L., Peltonen, L.E., Delis, L.E., and Sommer, S.S.: Scanning of estrogen receptor a (ERα) and thyroid hormone receptor a (TRα) genes in patients with psychiatric diseases: Four missense mutations identified in ERα gene. Am. J. Med. Genet. 105:369-374, 2001.
191. Weinshenker, B.G., and Sommer, S.S.: Vapsee-Based Analysis: a two-phased candidate gene approach for elucidating genetic predisposition to complex disorders. Mutation Research Genomics, 458: 7-17, 2001.

#### Selected Reviews

- R33 Sommer, S.S.: and Ketterling, R.P.: The factor IX gene as a model for analysis of human germline mutations: an update. Hum. Mol. Genet. 5:1505-1514, 1996.
- R36 Hartmann, A., Blaszyk, H., Kovach, J.S., and Sommer, S.S.: The Molecular Epidemiology of P53 Gene Mutations in Human Breast Cancer. Trends in Genetics 13:27-33, 1997.
191. Weinshenker, B.G., and Sommer, S.S.: Vapsee-Based Analysis: a two-phased candidate gene approach for elucidating genetic predisposition to complex disorders. Mutation Research Genomics 458:7-17, 2001.

**BIOGRAPHICAL SKETCH D: Clinical Testing**

Name Steve S. Sommer, M.D., Ph.D.	Position Title Professor of Molecular Biology
--------------------------------------	--

**EDUCATION/TRAINING**

INSTITUTION AND LOCATION	DEGREES	YEAR(s)	FIELD OF STUDY
Rockefeller University, New York, NY	B.A.	1972-1978	Molecular Biology
Cornell University Med. College, New York, NY	Ph.D.	1972-1979	Medicine
NIH, Multicenter Indiv. Fellowship, Bethesda, Maryland	M.D.	1982-1984	Genetics
NIADDK, NIH, Medical Staff Fellow, Bethesda, Maryland		1980-1985	Genetics

**Medical Specialties:** ABMG Diplomate in Clinical Genetics (1984) and Clinical Molecular Genetics (1993)

**Experience:**

- 1980-1985: Medical Staff Fellow, Killer System of Yeast; with Dr. Reed Wickner, NIADOX, NIH  
 1982-1984: Multicenter Individual Fellowship in Clinical Genetics  
 7/85-8/96: Assistant Associate and Full Professor of Molecular Biology, Department of Biochemistry and Molecular Biology, Mayo Foundation School of Medicine, Rochester, MN  
 8/96-Present: Director, Departments of Molecular Genetics and Molecular Diagnosis, City of Hope, Duarte, CA

**Selected papers emphasizing the development, validation, and extension of novel methods: 31 of 251 publications (206 published or in press original papers and 45 reviews, letters...)**

**Clinical Molecular Testing**

19. Sarkar, G., Evans, M.I., Kogan, S., Lusher, J., and Sommer, S.S.: **Accurate prenatal diagnosis with novel polymerase chain reaction primers in a family with sporadic hemophilia A.** *Obstet. Gynecol.* 74:414-417, 1989.
24. Bottema, C.D.K., Koeberl, D.D., and Sommer, S.S.: **Direct carrier testing in 14 families with hemophilia B.** *The Lancet* ii:526-529, 1989.
39. Koeberl, D.D., Bottema, C.D.K., and Sommer, S.S.: **Comparison of direct and indirect methods of carrier detection in an X linked disease.** *Am. J. Med. Genet.* 35:600-608, 1990.
40. Bottema, C.D.K., Fisch, R.O., Michels, V.V., and Sommer, S.S.: **Direct carrier testing for phenylketonuria by PCR amplification of specific alleles.** *Amplifications* 4:27-29, 1990.
53. Ii, S., Minnerath, S., Ii, K., Dyck, P.J., and Sommer, S.S.: **Two tiered DNA-based diagnosis of transthyretin amyloidosis reveals two novel point mutations.** *Neurology* 41:893-898, 1991.
89. Vielhaber, E., Freedenberg, D., and Sommer, S.S.: **Mutation detection, prenatal testing, and delineation of the germline origin in a family with sporadic hemophilia B and no living hemophiliacs.** *Am. J. Med. Genet.* 49:257-258, 1994.
157. Liu, Q., Nozari, G., and Sommer, S.S.: **Single-tube polymerase chain reaction for rapid diagnosis of the inversion of mutation in hemophilia A.** *Blood* 92: 1458-1459, 1998.

**Studies of Direct Clinical Relevance**

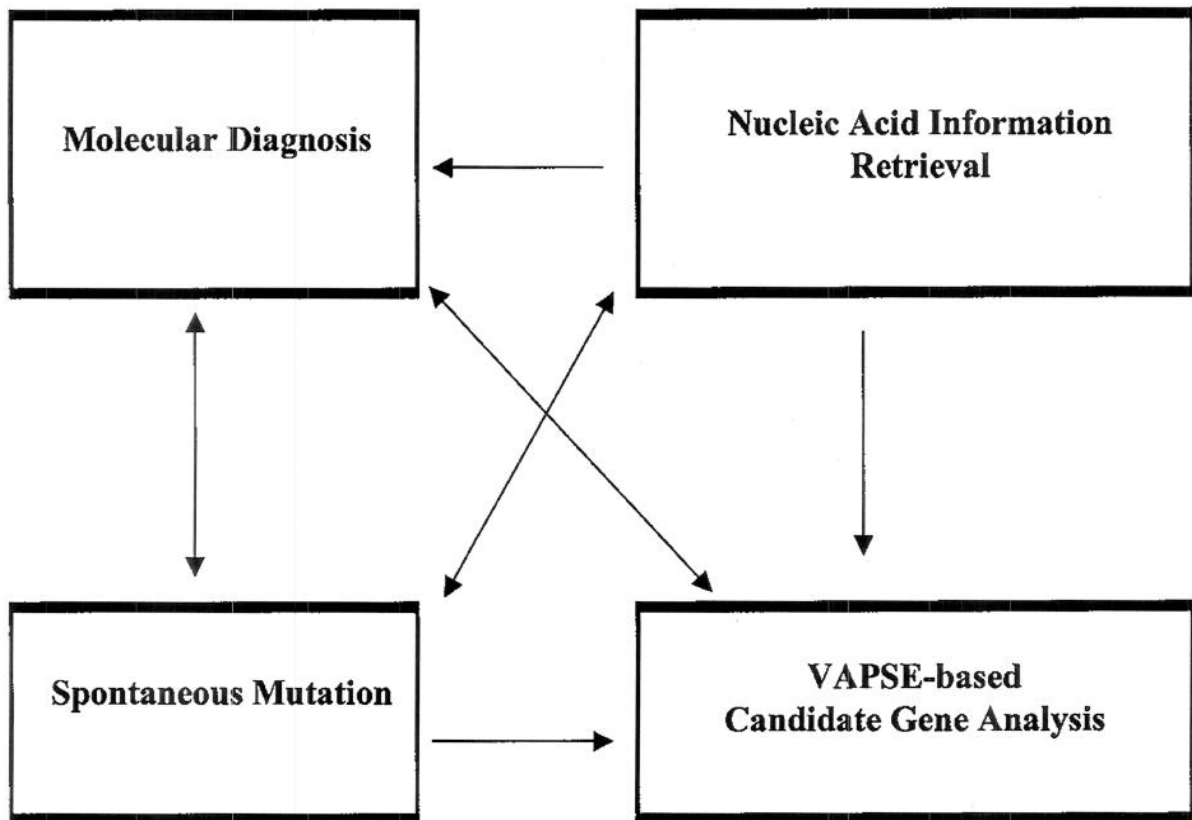
31. Bottema, C.D.K., Koeberl, D.D., Ketterling, R.P., Bowie, E.J.W., Taylor, S.A.M., Lillicrap, D., Shapiro, A., Gilchrist, G., and Sommer, S.S.: **A past mutation at isoleucine<sup>397</sup> is now a common cause of moderate/mild hemophilia B.** *Br. J. Haemat.* 75:212-216, 1990.
45. Ketterling, R.P., Bottema, C.D.K., Koeberl, D.D., Ii, S., and Sommer, S.S.: **T<sup>296</sup>->M, a common mutation causing mild hemophilia B in the Amish and others: Founder effect, variability in factor IX activity assays and rapid carrier detection.** *Hum. Genet.* 87:333-337, 1991.
67. Ii, S., Sobell, J., and Sommer, S.S.: **From molecular variant to disease: initial steps in evaluating the association of transthyretin M<sup>119</sup> with disease.** *Am. J. Hum. Genet.* 50:29-41, 1992.
110. Sommer, S.S.: Knöll, A., Greenberg, C.R., and Ketterling, R.P.: **Germline mosaicism in a female who seemed to be a carrier by sequence analysis.** *Hum. Mol. Genet.* 4:2181-2182, 1995.

115. Felmlee, T.A., Liu, Q., Whelen, A.C., Sommer, S.S., and Persing, D.H.: **Genotypic detection of *Mycobacterium tuberculosis* rifampin resistance: comparison of single-strand conformation polymorphism and dideoxy fingerprinting.** *J. Clin. Microbiol.* 33:1617-1623, 1995.
143. Warrier I., Ewenstein B.M., Koerper, M.A., Shapiro, A., Key, N., DiMichele, D., Miller, R.T., Pasi, J., Rivard, G.E., Sommer, S.S.: Katz, J., Bergmann, F., Ljung, R., Petrini, P., Lusher, J.M.: **Factor IX Inhibitors and Anaphylaxis in Hemophilia B.** *Journal of Pediatric Hematology-Oncology* 19: 23-27, 1997.
155. Heit, J.A., Kettering, R.P., Zapata, R.E., Ordonez, S.M., Kasper, C.K., Sommer, S.S.: **Haemophilia B Brandenburg-type promoter mutation.** *Haemophilia* 4: 1-3, 1998.
163. Ketterling, R.P., Drost, J.B., Scaringe, W.A., Liao, D-z., Liu, J-z., Kasper, C.K., and Sommer, S. S.: **Reported in vivo splice site mutations in the factor IX gene - severity of splicing defects and a hypothesis for predicting deleterious splice donor mutations.** *Human Mutation* 13:221-231, 1999.
164. Thorland, E.C., Drost, J.B., Lusher, J.M., Warrier, I., Shapiro, A., Koerper, M.A., DiMichele, D., Westman, J., Key, N.S., and Sommer, S.S.: **Anaphylactic response to factor IX replacement therapy in hemophilia B patients: complete gene deletions confer the highest risk.** *Haemophilia* 5:101-105, 1999
165. Feng, J.F., Liu, Q.L., Drost, J.B., and Sommer, S.S.: **Deep intronic mutations are rarely a cause of Hemophilia B.** *Mutation* 14:267-268, 1999.
190. Mendell, J.R., Buzin, C.H., Feng, J., Yan, J., Serrano, C., Sengani, D., Prior, T.W. and Sommer, S.S.: **Diagnosis of Duchenne dystrophy by enhanced detection of small mutations.** *Neurology* 57: (4): 645-50, 2001.
209. Buzin, C.H., Gatti, R.A., Nguyen, V.Q., Wen, C.Y., Mitui, M., Sanal, O., Chen, J.S., Nozari, G., Mengos, A., Li, X., Fujimura, F., and Sommer, S.S.: **Comprehensive Scanning of the ATM Gene with DOVAM-S.** Submitted.

#### Selective Novel Methods Applied to Clinical testing

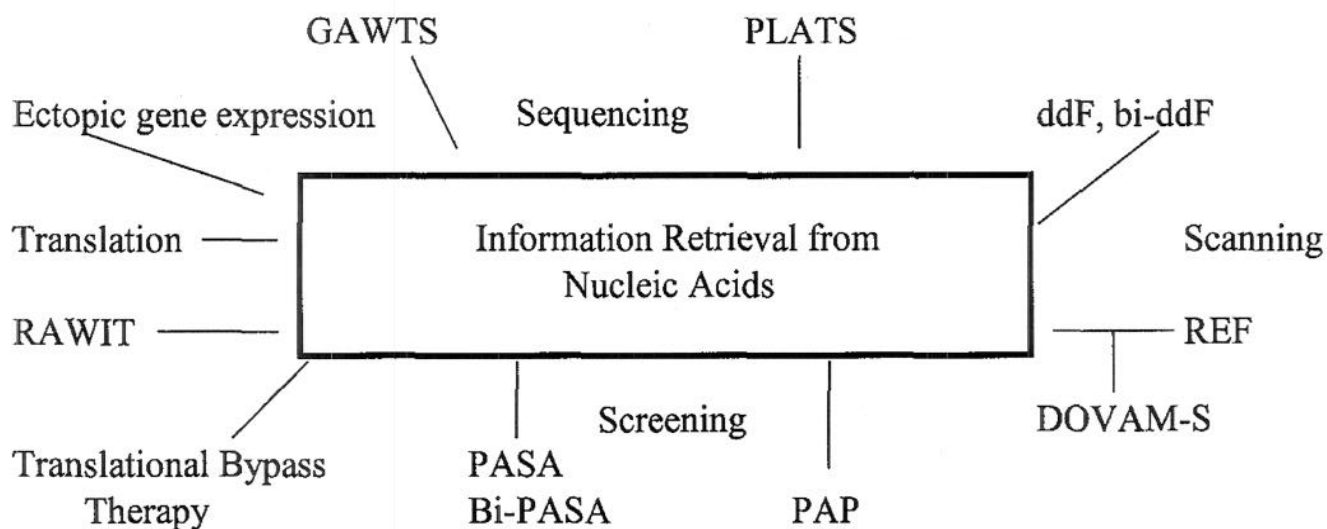
13. Gustafson, S., Proper, J.A., Bowie, E.J.W., and Sommer, S.S.: **Parameters affecting the yield of DNA from human blood.** *Anal. Biochem.* 165:294-299, 1987.
17. Haqqi, T.M., Sarkar, G., David, C.S., and Sommer, S.S.: **Specific amplification with PCR of a refractory segment of genomic DNA.** *Nucleic Acids Res.* 16:11844, 1988.
23. Sarkar, G., and Sommer, S.S.: **Access to a messenger RNA sequence or its protein product is not limited by tissue or species specificity.** *Science* 244:331-334, 1989.
25. Sommer, S.S.: Cassady, J., Sobell, J.L., and Bottema, C.D.K.: **A novel method of detecting point mutations or polymorphisms and its application to population screening for carriers of phenylketonuria.** *Mayo Clinic Proceedings* 64:1361-1372, 1989.
36. Sarkar, G., and Sommer, S.S.: **Shedding light on PCR contamination.** *Nature* 343:27, 1990.
52. Sarkar, G., and Sommer, S.S.: **Haplotyping by double PCR amplification of specific alleles.** *BioTechniques* 10:436-440, 1991.
62. Sommer, S.S.: Groszbach, A., and Bottema, C.D.K.: **PCR Amplification of Specific Alleles (PASA) is a general method for rapidly detecting known single-base changes.** *Biotechniques* 12:82-87, 1992.
80. Dutton, C.M., Paynton, C., and Sommer, S.S.: **General method for amplifying regions of very high G + C content.** *Nucleic Acids Res.* 21:2953-2954, 1993.
158. O'Donovan, M.C., Oefner, P.J., Roberts, S.C., Austin, J., Hoogendoorn, B., Guy, C., Speight, G., Upadhyaya, M., and Sommer, S.S.: McGuffin, P.: **Blind Analysis of denaturing high-performance liquid chromatography as a tool for mutation detection.** *Genomics* 52:44-49, 1998.
170. Liu, Q., Feng, J., Buzin, C., Wen, C., Nozari, G., Mengos, A., Nguyen, V., Liu, J-Z., Crawford, L., Fujimura, F.K., and Sommer, S.S.: **[Detection Of Virtually All Mutations] - SSCP (DOVAM-S): A rapid method for mutation scanning with virtually 100% sensitivity.** *BioTechniques* 26:932-942, 1999.
174. Scaringe, W.A., Liao, D., Liu, Q., and Sommer S.S.: **REF Select: Expert system software for selecting restriction endonucleases for restriction endonucleas fingerprinting (REF).** *BioTechniques* 27(6):1188-90, 1192-7, 1999.
182. Buzin, C., Wen, C., Nguyen, V., Nozari, G., Mengos, A., Li X., Chen, J., Liu, Q., Gatti, R.A., Fujimura, F.K. and Sommer, S.S.: **Scanning by DOVAM-S detects all unique sequence changes in blinded analyses: Evidence that the scanning conditions are generic.** *BioTechniques* 28:746-753, 2000.

# FOUR COMPONENTS OF THE LABORATORY



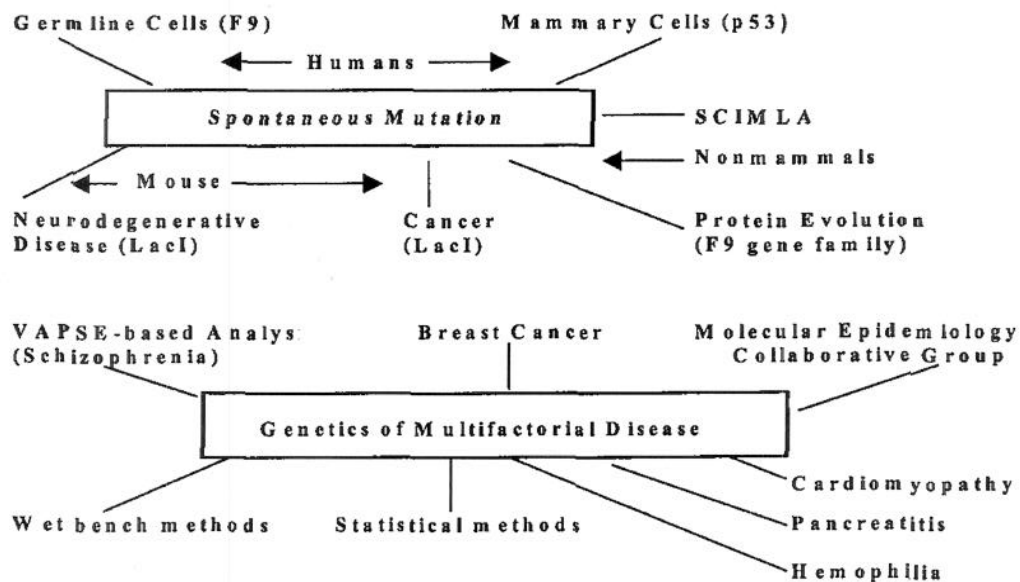


# SCHEMATIC OF LABORATORY PROJECTS MADE POSSIBLE THROUGH INTERACTIONS WITH MANY EXCELLENT COLLABORATORS



**Selected Additional Methods**

PCR of high G+C templates; Restriction endonuclease fingerprinting; DNA stability in blood; UV inactivation of PCR contamination; Megapriming--duplex DNA of 200 bp can amplify human genomic DNA; PCR across great evolutionary distances; Protein truncation assays; Statistical methods for candidate gene association studies; pK-matched electrophoresis buffers



## I. Original Publications, Peer Reviewed

### 1976 - 1980: mRNA Metabolism

1. Sommer, S.S., Salditt-Georgieff, M., Bachenheimer, S., Darnell, J.E., Furuichi, Y., Morgan, M., and Shatkin, A.J.: The methylation of adenovirus-specific nuclear and cytoplasmic RNA. Nucleic Acid Res. 3:749-765, 1976.
2. Sommer, S.S., Lavi, U., and Darnell, J.E.: The absolute frequency of labeled m<sup>6</sup>A in HeLa cell mRNA decreases with label time. J. Mol. Biol. 124:487-499, 1978.
3. Sommer, S.S., and Rin, N.A.: The lognormal distribution fits the decay profile of eukaryotic mRNA. Biochem. Biophys. Res. Commun. 90:135-141, 1979.
4. Sommer, S.S.: Prediction of the electrophoretic mobilities of nucleotides on neutral paper. Anal. Biochem. 98:8-12, 1979.
5. Sommer, S.S., and Cohen, J.E.: The size distributions of proteins, mRNA, and Nuclear RNA. J. Mol. Evol. 15:37-57, 1980.

### 1982 - 1987: Yeast Molecular Genetics

6. Sommer, S.S., and Wickner, R.B.: Co-curing of plasmids affecting killer double-stranded RNAs of Saccharomyces cerevisiae: [HOK], [NEX], and the abundance of L are related and further evidence that M<sub>1</sub> requires L. J. Bacteriol. 150:545-551, 1982.
7. Sommer, S.S., and Wickner, R.B.: Yeast L dsRNA consists of at least three distinct RNAs; evidence that the non-Mendelian genes [HOK], [NEX] and [EXL] are on one of these dsRNAs. Cell 31:429-441, 1982.
8. Ridley, S.P., Sommer, S.S., and Wickner, R.B.: Superkiller mutations in Saccharomyces cerevisiae suppress exclusion of M<sub>2</sub> Double-Stranded RNA by L-A-HN and confer cold sensitivity in the presence of M and L-A-HN. Mol. Cell. Biol. 4:761-770, 1984.
9. Sommer, S.S., and Wickner, R.B.: Double-Stranded RNAs that Encode Killer Toxins in Saccharomyces cerevisiae: Unstable size of M Double-Stranded RNA and Inhibition of M<sub>2</sub> Replication by M<sub>10</sub>. Mol. Cell. Biol. 4:1747-1753, 1984.
10. Icho, T., Lee, H.S., Sommer, S.S., and Wickner, R.B.: Molecular characterization of chromosomal genes affecting double-stranded RNA replication in Saccharomyces cerevisiae. Basic Life Sci. 40:165-171, 1986.
11. Sommer, S.S., and Wickner, R.B.: Gene disruption indicates that the only essential function of the SK18 chromosomal gene is to protect Saccharomyces cerevisiae from viral cytopathology. Virology 157:252-256, 1987.

### 1986: Human Molecular Genetics

12. Sommer, S.S.: Need for guidelines for reporting of recombination between a gene and a closely linked polymorphism. Lancet i:1101, 1986.

### 1987: Information Retrieval from Nucleic Acids

13. Gustafson, S., Proper, J.A., Bowie, E.J.W., and Sommer, S.S.: Parameters affecting the yield of DNA from human blood. Anal. Biochem. 165:294-299, 1987.
14. Al-Hakeem, M., and Sommer, S.S.: Terbium identifies double-stranded RNA on gels by quenching the fluorescence of intercalated ethidium bromide. Anal. Biochem. 163:433-439, 1987.

### 1988: Information Retrieval from Nucleic Acids

15. Stofflet, E.S., Koeberl, D.D., Sarkar, G. and Sommer, S.S.: Genomic amplification with transcript sequencing. Science 239:491-494, 1988.
16. Sarkar, G., and Sommer, S.S.: RNA amplification with transcript sequencing (RAWTS). Nucleic Acids Res. 16:5197, 1988.
17. Haqqi, T.M., Sarkar, G., David, C.S., and Sommer, S.S.: Specific amplification with PCR of a refractory segment of genomic DNA. Nucleic Acids Res. 16:11844, 1988.

#### 1989: Pattern of Spontaneous Mutation

18. Patterson, M., Gitschier, J., Bloomfield, J., Bell, M., Dorkins, H., Froster-Iskenius, U., Sommer, S., Sobell, J., Schaid, D., Thibodeau, S., and Davies, K.E.: **An intronic region within the human factor VIII gene is duplicated within Xq28 and is homologous to the polymorphic locus DXS115 (767).** Am. J. Hum. Gen. 44:679-685, 1989.
19. Sarkar, G., Evans, M.I., Kogan, S., Lusher, J., and Sommer, S.S.: **Accurate prenatal diagnosis with novel polymerase chain reaction primers in a family with sporadic hemophilia A.** Obstet. Gynecol. 74:414-417, 1989.
20. Koeberl, D.D., Bottema, C.D.K., Buerstedde, J-M., and Sommer, S.S.: **Functionally important regions of the factor IX gene have a low rate of polymorphism and a high rate of mutation in the dinucleotide CpG.** Am. J. Hum. Genet. 45:448-457, 1989.
21. Bottema, C.D.K., Ketterling, R.P., Cho, H.I, and Sommer, S.S.: **Hemophilia B in a male with a four-base insertion that arose in the germline of his mother.** Nucleic Acid Res. 17:10139, 1989.

#### 1989: Information Retrieval from Nucleic Acids

22. Schowalter, D.B., and Sommer, S.S.: **The generation of radiolabeled DNA and RNA probes with polymerase chain reaction.** Anal. Biochem. 177:90-94, 1989
23. Sarkar, G., and Sommer, S.S.: **Access to a messenger RNA sequence or its protein product is not limited by tissue or species specificity.** Science 244:331-334, 1989.
24. Bottema, C.D.K., Koeberl, D.D., and Sommer, S.S.: **Direct carrier testing in 14 families with hemophilia B.** The Lancet ii:526-529, 1989.
25. Sommer, S.S., Cassady, J., Sobell, J.L., and Bottema, C.D.K.: **A novel method of detecting point mutations or polymorphisms and its application to population screening for carriers of phenylketonuria.** Mayo Clinic Proceedings 64:1361-1372, 1989.

#### 1990: Yeast Molecular Genetics

26. Boone, C., Sommer, S.S., Hensel, A., and Bussey, H.: **Yeast KRE genes provide evidence for a pathway of cell wall  $\beta$ -glucan assembly.** J. Cell Biol. 110:1833-1843, 1990.
27. Meaden, P., Hill, K., Wagner, J., Slipetz, D., Sommer, S.S., and Bussey, H.: **The yeast KRE5 gene encodes a probable endoplasmic reticulum protein required for (1 $\rightarrow$ 6)- $\beta$ -D-glucan synthesis and normal cell growth.** Mol. Cell. Biol. 10:3013-3019, 1990.

#### 1990: Pattern of Spontaneous Mutation

28. Sarkar, G., Koeberl, D.D., and Sommer, S.S.: **Direct sequencing of the activation peptide and the catalytic domain of the factor IX gene of six species.** Genomics 6:133-143, 1990.
29. Koeberl, D.D., Bottema, C.D.K., Sarkar, G., Ketterling, R.P., Chen, S.-H., and Sommer, S.S.: **Recurrent nonsense mutations at arginine residues cause severe hemophilia B in unrelated hemophiliacs.** Hum. Genet. 84:387-390, 1990.
30. Bottema, C.D.K., Ketterling, R.P., Koeberl, D.D., Taylor, S.A., and Sommer, S.S.: **Mutations at arginine residues in two Asian hemophilia B patients.** Nucleic Acids Res. 18:1924, 1990.
31. Bottema, C.D.K., Koeberl, D.D., Ketterling, R.P., Bowie, E.J.W., Taylor, S.A.M., Lillicrap, D., Shapiro, A., Gilchrist, G., and Sommer, S.S.: **A past mutation at isoleucine<sup>397</sup> is now a common cause of moderate/mild hemophilia B.** Br. J. Haemat. 75:212-216, 1990.
32. Koeberl, D.D., Bottema, C.D.K., Ketterling, R.P., Bridges, P.J., Lillicrap, D.P., and Sommer, S.S.: **Mutations causing hemophilia B: direct estimate of the underlying rates of spontaneous germline transitions, transversions, and deletions in a human gene.** Am. J. Hum. Genet. 47:202-217, 1990.
33. Bottema, C.D.K., Ketterling, R.P., Yoon, H-S., and Sommer, S.S.: **The pattern of factor IX germline mutations in Asians is similar to that of Caucasians.** Am. J. Hum. Genet. 47:835-841, 1990.
34. Sommer, S.S.: **Mutagen test.** Nature 346:22-23, 1990.

### 1990: Information Retrieval from Nucleic Acids

35. Schowalter, D.B., Toft, D.O., and Sommer, S.S.: A method of sequencing without subcloning and its application to the identification of a novel ORF with a sequence suggestive of a transcriptional regulator in the water mold, *Achlya ambisexualis*. *Genomics* 6:23-32, 1990.
36. Sarkar, G., and Sommer, S.S.: Shedding light on PCR contamination. *Nature* 343:27, 1990.
37. Sarkar, G., and Sommer, S.S.: The "megaprimer" method of site-directed mutagenesis. *BioTechniques* 8:404-407, 1990.
38. Sarkar, G., Cassady, J., Bottema, C.D.K., and Sommer, S.S.: Characterization of polymerase chain reaction amplification of specific alleles. *Anal. Biochem.* 186:64-68, 1990.
39. Koeberl, D.D., Bottema, C.D.K., and Sommer, S.S.: Comparison of direct and indirect methods of carrier detection in an X-linked disease. *Am. J. Med. Genet.* 35:600-608, 1990.
40. Bottema, C.D.K., Fisch, R.O., Michels, V.V., and Sommer, S.S.: Direct carrier testing for phenylketonuria by PCR amplification of specific alleles. *Amplifications* 4:27-29, 1990.
41. Sarkar, G., and Sommer, S.S.: More light on PCR contamination. *Nature* 347:340-341, 1990.
42. Sarkar, G., Kapelner, S., and Sommer, S.S.: Formamide can dramatically improve the specificity of PCR. *Nucleic Acids Res.* 18:7465, 1990.

### 1991: Pattern of Spontaneous Mutation

43. Sarkar, G., Paynton, C., and Sommer, S.S.: Segments containing alternating purine and pyrimidine dinucleotides: patterns of polymorphism in humans and prevalence throughout phylogeny. *Nucleic Acids Res.* 19(3):631-636, 1991.
44. Paynton, C., Sarkar, G., and Sommer, S.S.: Identification of mutations in two families with sporadic hemophilia A. *Hum. Genet.* 87:397-400, 1991.
45. Ketterling, R.P., Bottema, C.D.K., Koeberl, D.D., Ii, S., and Sommer, S.S.: T<sup>296</sup>→M, a common mutation causing mild hemophilia B in the Amish and others: Founder effect, variability in factor IX activity assays and rapid carrier detection. *Hum. Genet.* 87:333-337, 1991.
46. Wang, T., Okano, Y., Eisensmith, R.C., Harvey, M.L., Lo, W.H.Y., Yuan, L-F., Huang, S-Z., Zeng, Y-T., Furuyama, J-I., Oura, T., Sommer, S.S., and Woo, S.L.C.: Founder effect of a prevalent PKU mutation in the Oriental population. *Proc. Natl. Acad. Sci. USA* 88:2146-2150, 1991.
47. Sarkar, G., Cassady, J.D., Pyeritz, R.E., Gilchrist, G.S., and Sommer, S.S.: Isoleucine<sup>397</sup> is changed to threonine in two females with hemophilia B. *Nucleic Acids Res.* 19:1165, 1991.
48. Ketterling, R.P., Bottema, C.D.K., Phillips, J.P., III, and Sommer, S.S.: Evidence that descendants of three founders comprise about 25% of hemophilia B in the United States. *Genomics* 10:1093-1096, 1991.
49. Bottema, C.D.K., Ketterling, R.P., Ii, S., Yoon, H-S., Phillips, J.A., III, and Sommer, S.S.: Missense mutations and evolutionary conservation of amino acids: evidence that many of the amino acids in factor IX function as "spacer" elements. *Am. J. Hum. Genet.* 49:820-838, 1991.
50. Bottema, C.D.K., Bottema, M.J., Ketterling, R.P., Yoon, H-S, Janco, R.L., Phillips, J.A., III, and Sommer, S.S.: Why does the human factor IX gene have a G + C content of 40%? *Am. J. Hum. Genet.* 49:839-850, 1991.

### 1991: Information Retrieval and Analysis from Nucleic Acids

51. Sarkar, G., and Sommer, S.S.: Parameters affecting susceptibility of PCR contamination to UV inactivation. *Biotechniques* 10:590-594, 1991.
52. Sarkar, G., and Sommer, S.S.: Haplotyping by double PCR amplification of specific alleles. *BioTechniques* 10(4): 436-440, 1991.
53. Ii, S., Minnerath, S., Ii, K., Dyck, P.J., and Sommer, S.S.: Two tiered DNA-based diagnosis of transthyretin amyloidosis reveals two novel point mutations. *Neurology* 41:893-898, 1991.
54. Dutton, C., and Sommer, S.S.: Simultaneous detection of multiple single-base alleles at a polymorphic site. *Biotechniques* 11:700-702, 1991.
55. Kovach, J.S., McGovern, R.M., Cassady, J.D., Swanson, S.K., Wold, L.E., Vogelstein, B., and Sommer, S.S.: Direct sequencing from touch preparations of human carcinomas: analysis of p53 mutations in breast carcinomas. *J. Natl. Cancer Inst.* 83:1004-1009, 1991.

### Methodology Described Within Other Papers

56. Computer software for estimating steady state dinucleotide compositions of genomic DNA given 96 possible dinucleotide mutation rates and, conversely, estimating a minimal set of 96 dinucleotide mutation rates given a set of genomic dinucleotide frequencies (Bottema et al., 1991: reference 50).

### 1991: Genetic Predisposition to Schizophrenia

57. Sarkar, G., Kapelner, S., Grandy, D.K., Civelli, O., Sobell, J., Heston, L., and Sommer, S.S.: Direct sequencing of the dopamine D<sub>2</sub> receptor (DRD2) in schizophrenics reveals three polymorphisms but no structural change in the receptor. *Genomics* 11:8-14, 1991.

### 1992: Pattern of Spontaneous Mutation

58. Sommer, S.S., Cunningham, J., McGovern, R.M., Saitoh, S., Schroeder, J.J., Wold, L.E., Kovach, J.S.: Pattern of p53 gene mutations in breast cancers of women of the Midwestern United States. *J. Natl. Cancer Inst.* 84:246-252, 1992.
59. Sommer, S.S., Bowie, E.J.W., Ketterling, R.P., and Bottema, C.D.K.: Missense mutations and the magnitude of functional deficit: the example of factor IX. *Hum. Genet.* 89:295-297, 1992.
60. Ricke, D.O., Ketterling, R.P., and Sommer, S.S.: PRE: a novel element with the hallmarks of a retrotransposon derived from an unknown structural RNA. *Nucleic Acids Res.* 20:5233, 1992.
61. Schotland, H.M., Eldridge, R., Sommer, S.S., and Malawar, M.: Neurofibromatosis 1 and osseous fibrous dysplasia in a family. *Am. J. Med. Genet.* 43:815-822, 1992.

### 1992: Information Retrieval and Analysis from Nucleic Acids

62. Sommer, S.S., Groszbach, A., and Bottema, C.D.K.: PCR Amplification of Specific Alleles (PASA) is a general method for rapidly detecting known single-base changes. *Biotechniques* 12:82-87, 1992.
63. Sarkar, S., Yoon, H-S., and Sommer, S.S.: Screening for mutations by RNA single-strand conformation polymorphism (rSSCP): Comparison with DNA-SSCP. *Nucleic Acids Res.* 20:871-878, 1992.
64. Sarkar, G., Yoon, H-S., and Sommer, S.S.: Dideoxy fingerprinting (ddF): a rapid and efficient screen for the presence of mutations. *Genomics* 13:441-443, 1992.
65. Sarkar, G., and Sommer, S.S.: Double-stranded DNA segments can efficiently prime the amplification of human genomic DNA. *Nucleic Acids Res.* 20:4937-4938, 1992.
66. Sobell, J.L., Heston, L., and Sommer, S.S.: Delineation of genetic predisposition to multifactorial disease: A general approach on the threshold of feasibility. *Genomics* 12:1-6, 1992.

### 1992: Genetic Predisposition to Schizophrenia

67. Li, S., Sobell, J., and Sommer, S.S.: From molecular variant to disease: initial steps in evaluating the association of transthyretin M<sup>119</sup> with disease. *Am. J. Hum. Genet.* 50:29-41, 1992. See also Sobell et al., Reference 65.

### 1993: Yeast Molecular Genetics

68. Matsumoto, Y., Sarkar, G., Sommer, S.S., and Wickner, R.B.: A yeast antiviral protein, SKI8, shares a repeated amino acid sequence pattern with  $\beta$ -subunits of G proteins and several other proteins. *Yeast* 9:43-51, 1993.

### 1993: Spontaneous Mutation

69. Ketterling, R.P., Vielhaber, E., Bottema, C.D.K., Schaid, D.J., Cohen, M.P., Sexauer, C.L., and Sommer, S.S.: Germline origins of mutation in families with hemophilia B: the sex ratio varies with the type of mutation. *Am. J. Hum. Genet.* 52:152-166, 1993.



70. Ketterling, R.P., Ricke, D.O., Wurster, M.W., and Sommer, S.S.: Deletions with inversions: report of a mutation and review of the literature. Hum. Mutation 2:53-57, 1993.
71. Gostout, B., Vielhaber, E., Ketterling, R.P., Yoon, H-S, Bottema, C.D.K., Kasper, C.K., Koerper, M., and Sommer, S.S.: Germline mutations in the factor IX gene: a comparison of the pattern in Caucasians and non-Caucasians. Hum. Molec. Genet. 2(3):293-298, 1993.
72. Sommer, S.S. and Ketterling, R.P.: A postulated mechanism for deletions with inversions. Am. J. Hum. Genet. 52:1016-1018, 1993.
73. Li, S. and Sommer, S.S.: The high frequency of TTR M<sup>30</sup> in familial amyloidotic polyneuropathy is not due to a founder effect. Hum. Molec. Genet. 2:1303-1305, 1993.
74. Bottema, C.D.K., Ketterling, R.P., Vielhaber, E., Yoon, H-S., Gostout, B., Jacobson, D.P., Shapiro, A., and Sommer, S.S.: The pattern of spontaneous germ-line mutation: relative rates of mutation at or near CpG dinucleotides in the factor IX gene. Hum. Genet. 91:496-503, 1993.
75. Gostout, B., Liu, Q., and Sommer, S.S.: "Cryptic" repeating triplets of purines and pyrimidines [cRRY(i)] are frequent and polymorphic: Analysis of coding cRRY(i) in the POMC and TATA-binding Protein (TBP) genes. Am. J. Hum. Genet. 52:1182-1190, 1993.
76. Jacobson, D.P., Schmelting, P., and Sommer, S.S.: Characterization of the patterns of polymorphism in a "cryptic repeat" reveals a novel type of hypervariable sequence. Am. J. Hum. Genet. 53:443-450, 1993.
77. Lindor, N.M., Sommer, S.S., Sobell, J., Heston, L., Thibodeau, S.N.: Eight novel polymorphisms in the dystrophin gene of African-Americans: the rate of polymorphism is high. Human Mutation 2:485-488, 1993.
78. Dutton, C.M., Bottema, C.D.K., and Sommer, S.S.: Alu repeats in the human factor IX gene: the rate of polymorphism is not substantially elevated. Human Mutation 2:468-472, 1993.
79. Vielhaber, E., Jacobson, D., Ketterling, R.P., Liu, J-Z., and Sommer, S.S.: A mutation in the 3' untranslated region of the factor IX gene in four families with hemophilia B. Hum. Mol. Genet. 2:1309-1310, 1993.

#### 1993: Information Retrieval and Analysis from Nucleic Acids

- Dutton, C.M., Paynton, C., and Sommer, S.S.: General method for amplifying regions of very high G + C content. Nucleic Acids Res. 21(12):2953-2954, 1993.
81. Schaid, D.J., and Sommer, S.S.: Genotype relative risks: methods for design and analysis of candidate-gene association studies. Am. J. Hum. Genet. 53:1114-1126, 1993.

#### *Methodology Described In Other Papers*

Statistical methodology and computer software for obtaining unbiased sex ratios of mutation from molecular data given the pedigree structure of the ascertained families (see Ketterling et al., Reference 68).  
 Statistical approach for addressing the problem of multiple comparisons in candidate gene analyses of multifactorial disease (see Sobell et al., reference 81).

#### 1993: Genetic Predisposition to Schizophrenia

- Sobell, J.L., Heston, L.L., and Sommer, S.S.: Novel association approach for determining the genetic predisposition to schizophrenia: case-control resource and testing of the first candidate gene. Am. J. Med. Genet. (Neuropsychiatric Genetics) 48:28-35, 1993.
84. Sommer, S.S., Lind, T.J., Heston, L.L., and Sobell, J.L.: Dopamine D<sub>4</sub> receptor variants in unrelated schizophrenic cases and controls. Am. J. Med. Genet. (Neuropsychiatric Genetics) 48:90-93, 1993.
85. Sommer, S.S., Sobell, J.L., and Heston, L.L.: A common exonic polymorphism in the human D<sub>5</sub> dopamine receptor. Hum. Genet. 92:633-634, 1993.
86. Arnholt, J.C., Sobell, J.L., Heston, L.L., and Sommer, S.S.: APP mutations and schizophrenia. Biol. Psychiatry 34:739-740, 1993.
87. Lindor, N.M., Sobell, J., Heston, L., Thibodeau, S.N., and Sommer, S.S.: Screening the dystrophin gene suggests a high rate of polymorphism in general but no exonic deletions in schizophrenics. Am. J. Med. Genet. (Neuropsychiatric Genetics) 54:1-4, 1994.

#### 1994: Spontaneous Mutation

88. Ketterling, R.P., Vielhaber, E.L., Lind, T.J., Thorland, E.C., and Sommer, S.S.: The rates and patterns of deletions in the human factor IX gene. Am. J. Hum. Genet. 54:201-213, 1994.
89. Vielhaber, E., Freedenberg, D., and Sommer, S.S.: Mutation detection, prenatal testing, and delineation of the germline origin in a family with sporadic hemophilia B and no living hemophiliacs. Am. J. Med. Genet. 49:257-258, 1994.
90. Sommer, S.S.: Does cancer kill the individual and save the species? Human Mutation 3:166-169, 1994.
91. Ketterling, R.P., and Sommer, S.S.: Microdeletions in the factor IX gene: three recurrences associated with a quasipalindromic sequence. Hum. Mol. Genet. 3:191-192, 1994.
92. Ketterling, R.P., Vielhaber, E., and Sommer, S.S.: The rates of G:C→T:A and G:C→C:G transversions at CpG dinucleotides in the human factor IX gene. Am. J. Hum. Genet. 54:831-835, 1994.
93. Sommer, S.S., Tillotson, V., Vielhaber, E.L., Ketterling, R.P., and Dutton, C.M.: "Cryptic" dinucleotide polymorphism in the 3' region of the factor IX gene shows substantial variation among different populations. Hum. Genet. 93:357-358, 1994.
94. Caglayan, S.H., Vielhaber, E., Gürsel, T., Aktuglu, G., Güler, E., and Sommer, S.S.: Identification of mutations in hemophilia B patients of Turkish origin. Human Mutation 4:163-165, 1994.
95. Rossiter, J.P., Young, M., Kimberland, M.L., Hutter, P., Ketterling, R.P., Gitschier, J., Horst, J., Morris, M.A., Schaid, D.J., de Moerloose, P., Sommer, S.S., Kazazian, H.H., Jr., and Antonarakis, S.E.: Factor VIII gene inversions causing severe hemophilia A originate almost exclusively in male germ cells. Hum. Mol. Genet. 3:1035-1039, 1994.
96. Blaszyk, H., Vaughn, C.B., Hartmann, A., McGovern, R.M., Schroeder, J.J., Cunningham, J., Schaid, D., Sommer, S.S., and Kovach, J.S.: Novel pattern of p53 gene mutations in an American black cohort with high mortality from breast cancer. Lancet 343:1195-1197, 1994.
97. Blaszyk, H., Hartmann, A., Wold, L.E., Schroeder, J.J., McGovern, R.M., Sommer, S.S., and Kovach, J.S.: A tandem CC→TT transition in the p53 gene of a breast cancer. Human Mutation 4:158-160, 1994.
98. Saitoh, S., Cunningham, J., DeVries, E.M.G., McGovern, R.M., Schroeder, J.J., Hartmann, A., Blaszyk, H., Schaid, D., Sommer, S.S., and Kovach, J.S.: p53 gene mutations in breast cancers in Midwestern U.S. women: null as well as missense-type mutations are associated with poor prognosis. Oncogene 9:2869-2875, 1994.
99. Knöll, A., Jacobson, D.P., Kretz, P.L., Lundberg, K.S., Short, J.M., and Sommer, S.S.: Spontaneous mutations in *lacI*-containing  $\lambda$  lysogens derived from transgenic mice: the observed patterns differ in liver and spleen. Mutation Research 311:57-67, 1994.

#### 1994: Information Retrieval and Analysis from Nucleic Acids

100. Liu, Q., and Sommer, S.S.: Parameters affecting the sensitivities of dideoxy fingerprinting and SSCP. PCR Methods and Applications 4:97-108, 1994.
101. Schaid, D.J., and Sommer, S.S.: Need to confirm promising case-control association studies. Am. J. Med. Genet. (Neuropsychiatric Genetics) 54:156-157, 1994.
102. Schaid, D.J., and Sommer, S.S.: Comparison of statistics for candidate-gene association studies with case and parents. Am. J. Hum. Genet. 55:402-409, 1994

#### 1994: Genetic Predisposition to Schizophrenia

103. Sobell, J.L., Sigurdson, D.C., Heston, L.L., and Sommer, S.S.: S311C *D2DR* variant: no association with schizophrenia. Lancet 344:621-622, 1994.
104. Coon, H., Sobell, J., Heston, L., Sommer, S., Hoff, M., Holik, J., Robertson, M., Reimherr, F., Wender, P., Vest, K., Myles-Worsley, M., Gershon E.S., DeLisi, L.E., Shields, G., Dale, P.W., Polloi, A., Waldo, M., Leonard, S., Sikela, J., Freedman, R., and Byerley, W.: A search for mutations in the  $\beta_1$  GABA<sub>A</sub> receptor subunit gene in patients with schizophrenia. Am. J. Med. Genet. (Neuropsychiatric Genetics) 54:12-20, 1994.

#### 1995: Spontaneous Mutation

105. Ketterling, R.P., Liao, D., and Sommer, S.S.: Are some apparently simple deletions actually two concerted deletions that result from interacting RY(i) hairpin loops? Am. J. Hum. Genet. 56:343-346, 1995.

106. Hartmann, A., Blaszyk, H., McGovern, R.M., Schroeder, J.J., Cunningham, J., De Vries, E.M.G., Kovach, J.S., and Sommer, S.S.: **p53 gene mutations inside and outside of exons 5-8: the patterns differ in breast and other cancers.** *Oncogene* 10:681-688, 1995.
107. Hartmann, A., Rosanelli, G., Blaszyk, H., Cunningham, J.M., McGovern, R.M., Schroeder, J.J., Schaid, D., Kovach, J.S., and Sommer, S.S.: **Novel pattern of p53 mutation in breast cancers from Austrian women.** *J. Clin. Invest.* 95:686-689, 1995.
108. Ricke, D.O., Liu, Q., Gostout, B. and Sommer, S.S.: **Nonrandom patterns of simple and cryptic triplet repeats in coding and noncoding sequences.** *Genomics* 26:510-520, 1995.
109. Ketterling, R.P., Liu, J-z., Liao, D., Kasper, C.K., Ambriz, R., Paredes, R., and Sommer, S.S.: **Two novel factor IX promoter mutations: incremental progress towards "saturation in vivo mutagenesis" of a human promoter region.** *Hum. Mol. Genet.* 4: 769-770, 1995.
110. Sommer, S.S., Knöll, A., Greenberg, C.R., and Ketterling, R.P.: **Germline mosaicism in a female who seemed to be a carrier by sequence analysis.** *Hum. Mol. Genet.* 4: 2181-2182, 1995.
111. Nishino, H., Knöll, A., Buettner, V.L., Frisk, C.S., Maruta, Y., Haavik, J., and Sommer, S.S.: **p53 wild-type and p53 nullizygous Big Blue<sup>®</sup> transgenic mice have similar frequencies and patterns of observed mutation in liver, spleen and brain.** *Oncogene* 11:263-270, 1995.
112. Antonarakis, S.E., Rossiter, J.P., Young, M., Horst, J., deMoerloose, P., Sommer, S.S., Ketterling, R.P., Kazazian, H.H., Jr., Négrier, C., Vinciguerra, C., Gitschier, J., Goossens, M., Girodon, E., Ghanem, N., Plassa, F., Lavergne, J.M., Vidaud, M., Costa, J.M., Laurian, Y., Lin, S.-W., Lin, S.-R., Shen, M.-C., Lillcrap, D., Taylor, S.A.M., Windsor, S., Valleix, S.V., Nafa, K., Sultan, Y., Delpech, M., Vnencak-Jones, C.L., Phillips, J.A., III, Ljung, R.C.R., Koumbarelis, E., Gialeraki, A., Mandalaki, T., Jenkins, P.V., Collins, P.W., Pasi, K.J., Goodeve, A., Peake, I., Preston, F.E., Schwartz, M., Scheibel, E., Ingerslev, J., Cooper, D.N., Millar, D.S., Kakkar, V.V., Giannelli, F., Naylor, J.A., Tizzano, E.F., Baiget, M., Domenech, M., Altisent, C., Tusell, J., Beneyto, M., Lorenzo, J.I., Gaucher, C., Mazurier, C., Peerlinck, K., Matthijs, G., Cassiman, J.J., Vermynen, J., Mori, P.G., Aquila, M., Caprino, D., and Inaba, H.: **Factor VIII gene inversions in severe hemophilia A: results of an International Consortium Study.** *Blood* 86: 2206-2212, 1995.

#### 1995: Information Retrieval and Analysis from Nucleic Acids

113. Liu, Q., and Sommer, S.S.: **Restriction endonuclease fingerprinting (REF): A sensitive method for screening mutations in long, contiguous segments of DNA.** *BioTechniques* 18:470-477, 1995.
114. Blaszyk, H., Hartmann, A., Schroeder, J.J., McGovern, R.M., Sommer, S.S., and Kovach, J.S.: **Rapid and efficient screening for p53 gene mutations by dideoxy fingerprinting.** *BioTechniques* 18:256-260, 1995.
115. Felmler, T.A., Liu, Q., Whelen, A.C., Sommer, S.S., and Persing, D.H.: **Genotypic detection of *Mycobacterium tuberculosis* rifampin resistance: comparison of single-strand conformation polymorphism and dideoxy fingerprinting.** *J. Clin. Microbiol.* 33:1617-1623, 1995.
116. Nishino, H., Herath, J.F., Jenkins, R.B., and Sommer, S.S.: **Fluorescence in situ hybridization for rapid differentiation of zygosity in transgenic mice.** *BioTechniques* 19:587-592, 1995.

#### 1995: Genetic Predisposition to Schizophrenia

117. Liu, Q., Sobell, J.L., Heston, L.L., and Sommer, S.S.: **Screening the dopamine D<sub>1</sub> receptor gene in 131 schizophrenics and eight alcoholics: identification of polymorphisms but lack of functionally significant sequence changes.** *Am. J. Med. Genet. (Neuropsych. Genet.)* 60:165-171, 1995.
118. Sobell, J.L., Lind, T.J., Sigurdson, D.C., Zald, D.H., Snitz, B.E., Grove, W.W., Heston, L.L., and Sommer, S.S.: **The D<sub>5</sub> dopamine receptor gene in schizophrenia: identification of a nonsense change and multiple missense changes but lack of association with disease.** *Hum. Mol. Genet.* 4(4):507-514, 1995.

#### 1996: Spontaneous Mutation

119. Knöll, A., Jacobson, D.P., Nishino, H., Kretz, P.L., Short, J.M., and Sommer, S.S.: **A selectable system for mutation detection in the Big Blue<sup>®</sup> lacI transgenic mouse system: what happens to the mutational spectra over time** *Mutation Research* 352:9-22, 1996.
120. Kovach, J.S., Hartmann, A., Blaszyk, H., Cunningham, J., Schaid, D., and Sommer, S.S.: **Mutation detection by highly sensitive methods indicates that p53 gene mutations in breast cancer can have important prognostic value.** *Proc. Natl. Acad. Sci. USA* 93:1093-1096, 1996.



121. Thorland, E.C., Weinschenker, B.G., Liu, J-z., Ketterling, R.P., Vielhaber, E.L., Kasper, C.K., Ambriz, R., Paredes, R., and Sommer, S.S.: **Molecular epidemiology of factor IX germline mutations in Mexican Hispanics: pattern of mutation and potential founder effects.** *Thrombosis and Haemostasis* 74:1416-1422,1995.
122. Hartmann, A., Blaszyk, H., Saitoh, S., Tsushima, K., Tamura, Y., Cunningham, J.M., McGovern, R.M., Schroeder, J.J., Sommer, S.S., and Kovach, J.S.: **High frequency of p53 gene mutations in primary breast cancers in Japanese women, a low incidence population.** *Br. J. Cancer* 73:896-901, 1996.
123. Haavik, J., Nishino, H., Liu, Q., and Sommer, S.S.: **Bidirectional dideoxy fingerprinting (Bi-ddF): rapid and efficient screening for mutations in the Big Blue<sup>®</sup> transgenic mouse mutation detection system.** *BioTechniques* 20:988-994, 1996.
124. Blaszyk, H., Hartmann, A., Sommer, S.S., and Kovach, J.S.: **A polymorphism but no mutations in the GADD45 gene in breast cancers.** *Hum. Genet.* 97:543-547, 1996.
125. Knöll, A., Ketterling, R.P., Sommer, S.S.: **Absence of somatic mosaicism in 17 families with hemophilia B: An analysis with a sensitivity 10- to 1000-fold greater than that of sequencing gels.** *Hum. Genet.* 98(5): 539-545.
126. Hartmann, A., Blaszyk, H., Cunningham, J.S., McGovern, R.M., Schroeder, J.S., Helander, J.A., Pittelkow, M.R., Sommer, S.S., and Kovach, J.S.: **Overexpression and mutations of p53 in metastatic malignant melanomas.** *Int. J. Cancer* 67:313-317, 1996.
127. Blaszyk, H., Hartmann, A., Liao, D-z., Kovach, J.S., and Sommer, S.S.: **Evidence for diverse mutagens in breast cancer-** *Lancet* 348: 683-684, 1996.
128. Buettner, V.L., Nishino, H., and Sommer, S.S.: **Large deletions detected with Big Blue<sup>®</sup> transgenic mouse mutagenesis assay.** *Mutation Research* 361: 187-189, 1996.
129. Nishino, H., Buettner, V.L., and Sommer, S.S.: **Towards validation of the Big Blue<sup>®</sup> transgenic mouse mutagenesis assay: the mutational spectrum of *ex vivo* pinpoint mutant plaques.** *Mutation Research* 372:97- 105, 1996.
130. Blaszyk, H., Hartmann, A., Tamura, Y., Saitoh, S., Cunningham, J.M., McGovern, R.M., Schroeder, J.J., Schaid, D.J., Ii, K., Monden, Y., Morimoto, T., Komaki, K., Sasa, M., Hirata, K., Okazaki, M., Kovach, J.S., and Sommer, S.S.: **Molecular epidemiology of breast cancers in northern and southern Japan: the frequency, clustering, and pattern of p53 gene mutations differ among these two low-risk populations.** *Oncogene* 13:2159-2166, 1996.
131. Nishino, H., Buettner, V.L., Haavik, J., Schaid, D.J., and Sommer, S.S.: **Spontaneous Mutation in Big Blue<sup>®</sup> Transgenic Mice: Analysis of Age, Gender, and Tissue Type.** *Env. and Mol. Mutagenesis* 28:299-312, 1996.
132. Nishino, H., Schaid, D.J., Buettner V.L., Haavick, J., Sommer, S.S.: **Mutation Frequencies But Not Mutant Frequencies in Big Blue<sup>®</sup> Mice Fit a Poisson Distribution.** *Env. and Mol. Mutagenesis* 28:414-417, 1996.
133. Buettner, V.L., Hill, K.A., Nishino, H., Schaid, D.J., Frisk, C.S., and Sommer, S.S.: **Increased mutation frequency and altered spectrum in one of four thymic lymphomas derived from tumor prone p53/Big Blue<sup>®</sup> transgenic mice.** *Oncogene* 13: 2407-2413, 1996.

#### 1996: Information Retrieval and Analysis from Nucleic Acids

134. Liu, Q., Feng, J., and Sommer, S.S.: **Bi-directional dideoxy fingerprinting (Bi-ddF): a rapid method for quantitative detection of mutations in genomic regions of 300-600 bp.** *Hum. Mol. Genet.* 5:107-114, 1996.
135. Haavik, J., Nishino, H., Liu, Q., and Sommer, S.S.: **Bi-directional dideoxy fingerprinting (Bi-ddF): rapid and efficient screening for mutations in the Big Blue<sup>®</sup> transgenic mouse mutation detection system.** *BioTechniques* 20(6):988-994, 1996.
136. Goldrick, M.M., Kimball, G.R., Tseng, J.Y.-H., Sommer, S.S., and Liu, Q.: **NIRCA<sup>™</sup>: A rapid and robust method for screening for unknown point mutations.** *BioTechniques* 21:106-112, 1996.

#### 1996: VAPSE-based Analysis: Genetic Predisposition to Mental Illness and other Complex Diseases

137. Sobell, J.L., Sigurdson, D.C., Heston, L.L., Byerley, W.F., and Sommer, S.S.: **Genotype-to-phenotype analysis: search for clinical characteristics of a missense change in the GABA<sub>A</sub>-β1 receptor gene.** *Am. J. Med. Genet.* 67:81-84, 1996.
138. Sommer, S.S., and Rocca, W.A.: **Prion analogues and twin studies in Parkinson's disease.** *Neurology* 46:273-275, 1996.
139. Mikesell, M.J., Sobell, J.L., Sommer, S.S., and McMurray, C.T.: **Identification of a missense mutation and several polymorphisms in the proenkephalin A gene of schizophrenic patients.** *Am. J. Med. Genet.* 67: 459-467, 1996.
140. Sobell, J.L., Lind, T.J., Hebrink, D.D., Heston, L.L., and Sommer, S.S.: **Screening the monoamine oxidase B gene in 100 male schizophrenics: a cluster of polymorphisms in African-Americans but lack of functionally significant sequence changes.** *Neuropsychiatric Genetics* 74: 44-49, 1997.

141. Mikesell, M.J., Barron, Y.D., Nimgaonkar, V.L., Sobell, J.L., Sommer, S.S., and McMurray, C.T.: No evidence for association of the Gly(247)->Asp Proenkephalin A mutation with schizophrenia. Am. J. Med. Genet. (Neuropsych. Genet.)74:213-215, 1997.

#### 1997: Spontaneous Mutation

142. Caglayan, S.H., Gökmen, Y., Aktuglu, G., Gürgey, A., and Sommer, S.S.: Mutations associated with hemophilia B Turkish patients: progress towards determining the pattern of germline mutation in this population. Human Mutation 10: 76-79, 1997.
143. Warrier I., Ewenstein B.M., Koerper, M.A., Shapiro, A., Key, N., DiMichele, D, Miller, R.T., Pasi, J., Rivard, G.E., Sommer, S.S., Katz, J., Bergmann, F., Ljung, R., Petrini, P., Lusher, J.M.: Factor IX Inhibitors and Anaphylaxis in Hemophilia B. Journal of Pediatric Hematology-Oncology 19: 23-27, 1997.
144. Buettner, V.L., Nishino, H., Haavik, J., Knoll, A., Hill, K., Sommer, S.S.: The spontaneous mutation frequency and spectrum in p53 (+/+) and p53 (-/-) mice. Mutation Research 379: 13-20, 1997.

#### 1997: Information Retrieval and Analysis from Nucleic Acids

145. Liu Q., Thorland E.C., Sommer S.S.: Inhibition of PCR Amplification by a Point Mutation Downstream of a Primer. BioTechniques 22:292-300, 1997.
146. Kukita Y., Tahira T., Sommer S.S., Hayashi K: SSCP Analysis of Long DNA Fragments in Low pH Gel. Human Mutation 10:400-407, 1997.
147. Liu, Q., Thorland E.C., Heit J.A., Sommer S.S.: Overlapping PCR for Bidirectional PCR Amplification of Specific Alleles: A Rapid One-Tube Method for Simultaneously Differentiating Homozygotes and Heterozygotes. Genome Research 7: 389-398, 1997.
148. Liu, Q., Feng, J., Sommer, S.S.: In a blinded analysis, restriction endonuclease fingerprinting (REF) detects all the mutations in a 1.9 kb segment. BioTechniques 23: 836-839, 1997.
149. Liu, J., Feng, J., Wang, L., Liu, Q., Sommer, S.S.: Gene Mutation Screening by Using Coupled in Vitro Transcription and Translation System. High Technology Letters 7: 5-9, 1997.

#### 1997: VAPSE-based Analysis: Genetic Predisposition to Mental Illness and other Complex Diseases

150. Mikesell, M.J., Barron, Y.D., Nimgaonkar, V.L., Sobell, J.L., Sommer, S.S., and McMurray, C.T.: Gly(247)> Asp Proenkephalin A mutation is rare in schizophrenia populations. Neuropsychiatric Genetics 74: 213-215, 1997.
151. Weinschenker B.G., Wingerchuk D.M., Liu Q., Bissonnett A.S., Schaid D.J., Sommer S.S.: Genetic Variation in the Tumor Necrosis Factor  $\alpha$  Gene and The Outcome of Multiple Sclerosis. Neurology 49: 378-385, 1997.
152. Wingerchuk D., Liu Q., Sobell J., Sommer S.S., Weinschenker B.G.: A Population-Based Case-Control Study of the Tumor Necrosis Factor Alpha-308 Polymorphism in Multiple Sclerosis. Neurology 49: 626-628, 1997.

#### 1998: Spontaneous Mutation

153. Heit, J.A., Thorland, E.C., Ketterling, R.P., Lind, T.J., Daniels, T.M., Zapata, R.E., Ordonez, S.M., Kasper, C.K., and Sommer, S.S.: Germline mutations in Peruvian patients with hemophilia B: pattern of mutation in AmerIndians is similar to the putative endogenous germline pattern. Human Mutation 11: 372-376, 1998.
154. You, H.Y., Halangoda, A., Buettner, V., Hill, K., Sommer, S.S., Pfeifer, G.: Methylation of CpG dinucleotides in the *lacI* gene of the Big Blue<sup>®</sup> transgenic mouse. Mutation Research 420:55-65, 1998.
155. Heit, J.A., Kettering, R.P., Zapata, R.E., Ordonez, S.M., Kasper, C.K., Sommer, S.S.: Haemophilia B Brandenburg-type promoter mutation. Haemophilia 4: 1-3, 1998.

#### 1998: Information Retrieval and Analysis From Nucleic Acids

156. Gejman P.V., Cao Q., Guedj F., and Sommer S.S.: The Sensitivity of Denaturing Gradient Gel Electrophoresis: A Blinded Analysis. Mutation Research Genomics 382: 109-114, 1998.
157. Liu, Q., Nozari, G., and Sommer, S.S.: Single-tube polymerase chain reaction for rapid diagnosis of the inversion of mutation in hemophilia A. Blood 92: 1458-1459, 1998.
158. O'Donovan, M.C., Oefner, P.J., Roberts, S.C., Austin, J., Hoogendoorn, B., Guy, C., Speight, G., Upadhyaya, M., and Sommer, S.S., McGuffin, P.: Blind Analysis of denaturing high-performance liquid chromatography as a tool for mutation detection. Genomics 52:44-49, 1998.

159. Liu, Q., Weinschenker, B.G., Wingerchuk, D.M., and Sommer, S.S.: Denaturation fingerprinting: two related mutation detection methods especially advantageous for high G+C regions. *BioTechniques* 24:140-147, 1998.
160. Liu, Q., and Sommer, S.S.: Subcycling-PCR for multiplex long distance amplification of regions with high and low GC content: application to the inversion hotspot in the factor VIII gene. *BioTechniques* 25:1022-1028, 1998.

**1998: VAPSE-based Analysis: Genetic Predisposition to Mental Illness and other Complex Diseases**

161. Feng, J., Sobell, J.L., Heston, L.H., Goldman, D., Cook Jr., E., Kranzler, H.R., Gelernter, J., and Sommer, S.S.: Variants in the  $\alpha_{2A}$  AR adrenergic receptor gene in psychiatric patients. *Am. J. Med. Genet. (Neuropsych. Genet.)* 81: 405-410, 1998.
162. Feng, J., Sobell, J.L., Heston, L.L., Cook, E.H., Jr., Goldman, D., and Sommer, S.S.: Analysis of the Dopamine D1 and D5 Receptors by Restriction Endonuclease Fingerprinting (REF) in Patients with Neuropsychiatric Disease Reveals Missense Change In A Highly conserved Amino Acid. *Am. J. Med. Genet. (Neuropsych. Genet.)* 81:172-178, 1998.

**1999: Spontaneous Mutation**

163. Ketterling, R.P., Drost, J.B., Scaringe, W.A., Liao, D-z., Liu, J-z., Kasper, C.K., and Sommer, S. S.: Reported in vivo splice site mutations in the factor IX gene - severity of splicing defects and a hypothesis for predicting deleterious splice donor mutations. *Human Mutation* 13:221-231, 1999.
164. Thorland, E.C., Drost, J.B., Lusher, J.M., Warriar, I., Shapiro, A., Koerper, M.A., DiMichele, D., Westman, J., Key, N.S., and Sommer, S.S.: Anaphylactic response to factor IX replacement therapy in hemophilia B patients: complete gene deletions confer the highest risk. *Haemophilia* 5:101-105, 1999.
165. Feng, J.F., Liu, Q.L., Drost, J.B., and Sommer, S.S.: Deep intronic mutations are rarely a cause of Hemophilia B. *Human Mutation* 14:267-268, 1999.
166. Hill, K.A., Nishino, H., Buettner, V.L., Halangoda, A., Li, W., and Sommer, S.S.: The Big Blue<sup>®</sup> transgenic mouse mutation detection assay: the mutation pattern of sectored mutant plaques. *Mutation Research* 10:425(1):47-54, 1999.
167. Ketterling, R.P., Vielhaber, E., Li, X., Drost, J.B., Schaid, D.J., Kasper, C.K., Phillips, J.A., Koerper, M.A., Kim, H., C., Gruppo, R., Ambriz, R., Paredes, R., and Sommer, S.S.: Germ lines origins in the human F9 gene: frequent G:C→A:T mosaicism and increased mutations with advanced maternal age. *Human Genetics* 105(6):629-40, 1999.
168. Moore, S.R., Hill, K.A., Heinmoller, P.W., Halangoda, A., Kunishige, M., Buettner, V.L., Graham, K.S., and Sommer, S.S.: (1999) Spontaneous mutation frequency and pattern in Big Blue<sup>®</sup> mice fed a vitamin E supplemented diet. *Env. & Mol. Mutagen* 34:195-200, 1999
169. Buettner, V.L., Hill, K.A., Halangoda, A., and Sommer, S.S.: Tandem-base mutations occur in mouse liver and adipose tissue preferentially as G:C to T:A transversions and accumulate with age. *Env. & Mol. Mutagen* 33: 320-324, 1999.

**1999: Information Retrieval and Analysis From Nucleic Acids**

170. Liu, Q., Feng, J., Buzin, C., Wen, C., Nozari, G., Mengos, A., Nguyen, V., Liu, J-Z., Crawford, L., Fujimura, F.K., and Sommer, S.S.: [Detection Of Virtually All Mutations] - SSCP (DOVAM-S): A rapid method for mutation scanning with virtually 100% sensitivity. *BioTechniques* 26:932-942, 1999.
171. Feng, J.F., Buzin, C.H., Tang, S-H.E., Scaringe, W.A., and Sommer, S.S.: Highly sensitive mutation screening by REF with low concentrations of urea: a blinded analysis of a 2 kb region of the p53 gene reveals two common haplotypes. *Human Mutation* 14:175-180, 1999
172. Liu, Q., Li, X., and Sommer, S.S.: pK-matched running buffers for gel electrophoresis. *Analytical Biochemistry* 270:112-122, 1999.
173. Liu, J-z., Liu, Q., Liang, Y., Wang, L., Nozari, G., Xiao, B., Zhu, Z., Liu, L., Guan, Y., Zhang, J., and Sommer, S.S.: PCR assay for the inversion causing severe Hemophilia A and its application. *Chinese Medical Journal* 112(5): 419-423, 1999.
174. Scaringe, W.A., Liao, D., Liu, Q., and Sommer, S.S.: REF Select: Expert system software for selecting restriction endonucleases for restriction endonucleas fingerprinting (REF). *BioTechniques* 27(6):1188-90, 1192-7, 1999.

**2000: Spontaneous Mutation**

175. Jaloma-Cruz, A.R., Scaringe, W.A., Drost, J.B., Roberts, S., Li, W., Nunez-Barros, P., Figuera, L.E., Rivas, F., Cantu, J.M., and Sommer, S.S.: **Nine independent factor IX mutations in the Mexican hemophilia B population: Nonrandom recurrences of point mutation events in the human germline.** *Human Mutation* 15(1):116-7, 2000.
176. Drost, J.B., Scaringe, W.A., Jaloma-Cruz, A.R., Li, X., Ossa, D.F., Kaspar, C.K., and Sommer, S.S.: **Novel hotspot detector software reveals a non-CpG hotspot of germline mutation in the factor IX gene (F9) in Latin Americans.** *Human Mutation* 16(3): 203-10, 2000.
177. Liu, J-z, Li, X., Drost, J.B., Thorland, E.C., Liu, Q., Lind, T., Roberts, S., Wang, H.Y., and Sommer S.S.: **The human factor IX gene as a germline mutation test: Samples from Mainland China have the putatively endogenous pattern of mutation.** *Human Mutation* 16(1): 31-36, 2000.
178. Buettner, V.L., Hill, K.A., Scaringe, W.A., and Sommer, S.S.: **Evidence that proximal multiple mutations in Big Blue transgenic mice are dependent events.** *Mutat Res.* 2000 Sep 18;452(2):219-229, 2000.
179. Li, X., Drost, J.B., Roberts, S., Kasper, C., and Sommer, S.S.: **Factor IX mutations in South Africans and African Americans are compatible with primarily endogenous influences upon recent germline mutations.** *Human Mutation* 16(4): 371, 2000.
180. Blaszyk, H., Hartmann, A., Cunningham, J.M., Schaid, D., Wold, L.E., Kovach, J.S., Sommer, S.S.: **A prospective trial of midwest breast cancer patients: a p53 gene mutation is the most important predictor of adverse outcome.** *Int J Cancer* 89 (Pred. Oncol.) 89:32-8, 2000.

#### 2000: Information Retrieval and Analysis From Nucleic Acids

181. Liu, Q., Scaringe, W.A., and Sommer, S.S.: **Discrete mobility of single-stranded DNA in non-denaturing gel electrophoresis.** *Nucleic Acids Res.*28(4):940-943, 2000.
182. Buzin, C., Wen, C., Nguyen, V., Nozari, G., Mengos, A., Li X., Chen, J., Liu, Q., Gatti, R.A., Fujimura, F.K. and Sommer, S.S.: **Scanning by DOVAM-S detects all unique sequence changes in blinded analyses: Evidence that the scanning conditions are generic.** *BioTechniques* 28(4):746-753, 2000.
183. Heinmöller, P.W., Hill, K.A. and Sommer, S.S.: **High plating density improves Big Blue® system efficiency without loss of sensitivity.** *Mutation Research* 453: 97-103, 2000.
184. Liu, Q., and Sommer, S.S.: **Pyrophosphorolysis-activated polymerization (PAP): application to allele specific amplification.** *Biotechniques* 29: 1072-1083, 2000.

#### 2000: VAPSE-based Analysis: Genetic Predisposition to Mental Illness and other Complex Diseases

185. Feng, J, Zheng, J., Bennett, W.P., Heston, L.L., Jones, I.R., Craddock, N., and Sommer, S.S.: **Five Missense Variants in the Amino-Terminal Domain of the Glucocorticoid Receptor: No Association with Puerperal Psychosis or Schizophrenia.** *Am. J. Med. Genet. (Neuropsychiatric Genetics)* 96:412-417, 2000.

#### 2001: Spontaneous Mutation

186. Kunishige, M., Hill, K.A., Riemer, M., Farwell, K., Halangoda, A., Heinmöller, E., Moore, S.R, Turner, D., and Sommer, S.S.: **Mutation frequency is reduced in the cerebellum of Big Blue® mice overexpressing a human wild type SOD1 gene.** *Mutation Research* 473(2): 139-149, 2001.
187. Li, X., Scaringe, W.A., Hill, K.A., Roberts, S., Careri, D., Pinto, M., Kasper, C.K., and Sommer, S.S.: **Frequency of recent retrotransposition events in the human factor IX gene.** *Human Mutation* 17 :511-519, 2001.
188. Halangoda, A., Still, J. G., Hill, K.A., and Sommer, S.S.: **Spontaneous Microdeletions and Microinsertions in a transgenic mouse mutation detection system: analysis of age, tissue, and sequence specificity.** *Environ Mol. Mutagen* 37:311-323, 2001.
189. Feng, J., Drost, J.B., Scaringe, W.A., Liu, Q., and Sommer, S.S.: **Mutations in the factor IX gene (F9) during the past 150 years have relative rates similar to ancient mutations.** *Hum Mutat.* 19:(1):49-57, 2001.
190. Mendell, J.R., Buzin, C.H., Feng, J., Yan, J., Serrano, C., Sengani, D., Prior, T.W., Sommer, S.S.: **Diagnosis of Duchenne dystrophy by enhanced detection of small mutations.** *Neurology* 57: (4): 645-50,2001.

#### 2001: VAPSE-based Analysis: Genetic Predisposition to Mental Illness and other Complex Diseases

191. Weinshenker, B.G., and Sommer, S.S.: **Vapase-Based Analysis: a two-phased candidate gene approach for elucidating genetic predisposition to complex disorders.** *Mutation Research Genomics*, 458: 7-17, 2001.



192. Feng, J., Zheng, J., Gelernter J, Kranzler H, Cook E, Goldman D, Jones IR, Craddock N, Heston LL, Delisi L, Peltonen L, Bennett WP, Sommer, S.S.: An in-frame deletion in the alpha (2C)adrenergic receptor is common in African-Americans. Mol Psychiatry (6): 168-172, 2001.
193. Feng, J., Craddock, N., Jones, I.R., Cook Jr., E.H., Goldman, D., Heston, L.L., Peltonen, L., Delisi, L.E., and Sommer, S.S.: Systematic screening for mutations in glycine receptor alpha2 subunit gene (GLRA2) in patients with schizophrenia and Other psychiatric diseases. Psychiatr Genet 11:45-48, 2001.
194. Feng, J., Yan, J., Michaud, S., Craddock, N., Jones, I., Cook, E.H., Jr., Goldman, D., Heston, L.L., Peltonen, L.E., Delis, L.E., and Sommer, S.S.: Scanning of estrogen receptor alpha (ERalpha) and thyroid hormone receptor alpha (TRalpha) genes in patients with psychiatric diseases: four missense mutations identified in ERalpha gene. Am J Med Genet 105:369-374, 2001.

#### 2002: Spontaneous Mutation

195. Heinmoller, E., Liu, Q., Sun, Y., Schlake, G., Hill, K.A., Weiss, L.M., Sommer, S.S.: Toward efficient analysis of mutations in single cells from ethanol-fixed paraffin- embedded and immunohistochemically-stained tissue. Laboratory Investigation 82(4): 443-53, 2002.
196. Sommer, S.S., Scaringe, W., Hill, K.A.: Is Alu-mediated recombination an important cause of hemophilia? Thromb Haemost 88: 3-4, 2002.
197. Heinmoller, E., Schlake, G., Renke, B., Liu, Q., Hill, K.A., Sommer, S.S., Ruschoff, J.: Microdissection and molecular analysis of single cells or small cell clusters in pathology and diagnosis – significance and challenges. Anal. Cell. Pathol. 24:125-134, 2002.

#### 2002: Information Retrieval and Analysis From Nucleic Acids

198. Liu, Q., and Sommer, S.S.: Pyrophosphorolysis-activatable oligonucleotides may facilitate detection of rare alleles, mutation scanning and analysis of chromatin structures. Nucleic Acids Res. 30(2):598-604, 2002.
199. Liu, J., Li, Wenyan and Sommer, S.S.: Improvement of auto sequencing for increasing readable bases by using ABI-377 sequencer. Chinese Journal of Laboratory Medicine.25(1) 41-42, 2002.
200. Liu, Q., Swiderski, P., and Sommer, S.S.: Truncated Amplification: A method for High Fidelity Template-Drive Nucleic Acid Amplification. Biotechniques 33: 129-138, 2002.

#### 2002: VAPSE-based Analysis: Genetic Predisposition to Mental Illness and other Complex Diseases

201. Sommer, S.S., Buzin, C.H., Jung, M., Zheng, J., Liu, Q., Jeong, S.J., Moulds, J., Nguyen, V.Q., Feng, J., Bennett, W.P., Dritschilo, A.: Elevated frequency of ATM Gene Mutations in Breast Cancer Relative to Ethnically Matched Controls. Cancer Genetics and Cytogenetics 134(1): 25-32, 2002.
202. Feng, J., Yan, J., Buzin, C.H., Towbin, J.A. and Sommer, S.S.: Comprehensive Mutation Scanning of the Dystrophin Gene in Patients with Non-syndromic X-linked Dilated Cardiomyopathy. Journal of the American College of Cardiology 40: 1120-1124, 2002
203. Feng, J., Yan, J., Buzin, C.H., Towbin, J.A. and Sommer, S.S.: Mutations in the dystrophin gene are associated with sporadic dilated cardiomyopathy. Molecular Genetics and Metabolism 77: 119-126, 2002.

#### 2003: Spontaneous Mutation

204. Hill, K.A., Wang, J., Farwell, K.D., Sommer, S.S.: Spontaneous tandem-base mutations (TBM) show dramatic tissue, age, pattern and spectrum specificity. Mutat Res. 534:173-86, 2003

#### 2003: Information Retrieval and Analysis From Nucleic Acids

205. Liu, Q., Li, X., Chen, J.S., Sommer, S.S.: Robust Dosage-PCR (RD-PCR) for Detection of Heterozygous Chromosomal Deletions. BioTechniques 34:558-570; 2003.
206. Maciel, P., Yan, J., Feng, J., Accurso, F., and Sommer, S.: Improved single-tube method for determination of F508del genotype in the CFTR gene using Bidirectional PCR Amplification of Specific Alleles (Bi-PASA), BioTechniques 34:460-462.
207. Liu, Q and Sommer, S.S.: Pyrophosphorolysis by Type II DNA polymerases: implications for pyrophosphorolysis-activated polymerization. Analytical Biochemistry 324:22-28; 2003.

208. Schlake, G., Liu, Q., Heinmoller, E., Hill, K.A., Weiss, L., and Sommer, S.S.: **Single-Cell Immunohistochemical Mutation Load Assay (SCIMLA) Using Human Paraffin-Embedded Tissues.** *Environmental and Molecular Mutagenesis* 42:206-215; 2003.

**2003: VAPSE-based Analysis: Genetic Predisposition to Mental Illness and other Complex Diseases**

209. Buzin, C.H., Gatti, R.A., Nguyen, V.Q., Wen, C.Y., Mitui, M., Sanal, O., Chen, J.S., Nozari, G., Mengos, A., Li, X., Fujimura, F., and Sommer, S.S.: **Comprehensive Scanning of the ATM Gene with DOVAM-S.** *Hum Mutat* 21:123-31; 2003
210. Furnes, B., Feng, J., Sommer, S., Schlenk, D.: **Identification of novel variants of the flavin-containing monooxygenase gene family in African-Americans.** *Drug Metab Dispos* 31:187-193; 2003
211. Feng, J., Yan, J., Chen, J.S., Schlake, G., Jiang, Z., Buzin, C.H., Sommer, S.S., and Dritschilo, A.: **Absence of somatic ATM missense mutations in 58 mammary carcinomas.** *Cancer Genetics and Cytogenetics* 145:179-182, 2003
212. Sommer, S.S., Jiang, Z., Feng, J., Buzin, C.B., Zheng, J., Longmate, J., Jung, M., Moulds, J., and Dritschilo, A.: **ATM Missense Mutations Are More Frequent in Patients with Breast Cancer.** *Cancer Genetics and Cytogenetics* 145:115-120; 2003

**2004: Spontaneous Mutation**

213. Yan, J., Feng, J., Buzin, C.H., Scaringe, W., Liu, Q., Mendell, J.R., den Dunnen, J., Sommer, S.S.: **Three-Tiered Noninvasive Diagnosis in 96% of Patients With Duchenne Muscular Dystrophy (DMD).** *Human Mutation* 23:203-204; 2004.
214. Hill, K.A., Buettner, V.L., Halangoda, A., Kunishige, M., Moore, S.R., Longmate, J., Scaringe, W.A., and Sommer, S.S.: **Spontaneous Mutation in Big Blue<sup>®</sup> Mice from Fetus to Old Age: Tissue-Specific Time Courses of Mutation Frequency But Similar Mutation Types.** *Environmental and Molecular Mutagenesis* 43:110-120; 2004.
215. Hill, K.A., Wang, Jichen, Farwell, Kelly D., Scaringe, W.A., and Sommer, S.S.: **Spontaneous multiple mutations show both proximal spacing consistent with chronocoordinate events and alterations with p53-deficiency.** *Mutation Research* 554: 223-240; 2004.

**2004: Information Retrieval and Analysis From Nucleic Acids**

216. Liu, Q. and Sommer, S.S.: **Detection of extremely rare alleles by bidirectional pyrophosphorolysis-activated polymerization allele-specific amplification (Bi-PAP-A): measurement of mutation load in mammalian tissue.** *BioTechniques* 36:156-166; 2004.
217. Yan, J., Feng, J., and Sommer, S.S.: **Assessment of Multiple Displacement Amplification (MDA) in Molecular Epidemiology** *BioTechniques* 37:136-143; 2004.
218. Nguyen, V.Q., Shi, J., Liu, Q., and Sommer, S.S.: **Robust dosage (RD)-PCR for the detection of heterozygous deletions.** *BioTechniques* 37:3 360-364; 2004.
219. Shi, J., Liu, Q., Nguyen, V., Sommer, S.S.: **Elimination of locu-specific inter-individual variations in quantitative PCR.** *BioTechniques* 37:934-938; 2004.

**2004: VAPSE-based Analysis: Genetic Predisposition to Mental Illness and other Complex Diseases**

220. Yan, J., Feng, J., Goldman, D., Cook, E.H., Craddock, N., Jones, I.R., Heston, L.L., and Sommer, S.S.: **Mutation scanning of the androgen receptor gene in patients with psychiatric disorders reveals highly conserved variants in alcoholic and phobia patients.** *Psychiatric Genetics* 14:57-60; 2004.
221. Shibayama, A., Cook, Jr., E.H., Feng, J., Glanzmann, C., Yan, J., Craddock, N., Jones, I.R., Goldman, D., Heston, L.L., and Sommer, S.S.: **MECP2 structural and 3'-UTR variants in schizophrenia, autism and other psychiatric diseases.** *Am. J. of Medical Genetics (Neuropsychiatric Genetics)* 128B:50-53; 2004.

**2005: Spontaneous Mutation**

222. Buzin, C.H., Feng, J., Yan, J., Scaringe, W., Liu, Q., den Dunnen, J., Mendell, J.R., and Sommer, S.S.: **Mutation Rates in the Dystrophin Gene: A Hotspot of Mutation at a CpG Dinucleotide.** *Human Mutation*, 25: 177-88; 2005

223. Casey, G., Lindor, N.M., Papadopoulos, N., Moskow, J., Buzin, C.H., Sommer, S.S., Aaronson, M., Gallinger, S., Thibodeau, S.N., Barker, M.A., Young, J.P., Jass, J.R., Diep, A., Bapat, B., Seminara, D., and Haile, R.: **Conversion analysis significantly improves mutation detection in HNPCC families.** JAMA. Feb 16;(293(7)):799-809; 2005

#### 2005: Information Retrieval and Analysis From Nucleic Acids

224. Shi, J., Shibayama, A., Liu, Q., Nguyen, V.Q., Feng, J., Santos, M., Temudo, T., Maciel, P., Sommer, S.S.: **Detections and duplications in the MECP2 gene in Rett syndrome by robust dosage (PCR) (RD-PCR).** Human Mutation DOI: 10.1002/humu.9338; 2005.
225. Zhang, J., Li, K., Pardini, J.R., Sommer, S.S., Yao, K.: **Proofreading genotyping assays mediated by high fidelity exo+ DNA polymerases.** Trends in Biotechnology, (2): 92-96; 2005.
226. Hill, K.A., Halangoda, A., Heinmoeller, P.W., Gonzalez, K., Chitaphan, C., Longmate, J., Scaringe, W.A., Wang, J., and Sommer, S.S.: **Tissue-specific time courses of spontaneous mutation frequency and deviations in mutation pattern are observed in middle to late adulthood in Big Blue mice.** Environ Mol Mutagen. Jun;45(5):442-54.
227. Zhang, J., Li, K., Pardini, J.R., Sommer, S.S., Yao, K.: **Proofreading genotyping assays mediated by high fidelity exo+ DNA polymerases.** Trends in Biotechnology, (2): 92-96; 2005.
228. Hill, K.A., Halangoda, A., Heinmoeller, P.W., Gonzalez, K., Chitaphan, C., Longmate, J., Scaringe, W.A., Wang, J., and Sommer, S.S.: **Tissue-specific time courses of spontaneous mutation frequency and deviations in mutation pattern are observed in middle to late adulthood in Big Blue mice.** Environ Mol Mutagen. Jun;45(5):442-54.
229. Li, K., Zhang, J., Chen, L., Sommer, S.S.: **Superb Nucleotide Discrimination by a Novel On/Off Switch for DNA Polymerization and Its Applications.** Molecular Biotechnology 1073-6085/2005/29:2/93-100.
230. Chen, L.L., Zhang, J., Sommer, S.S., Li, K.: **Single-base Discrimination Mediated by Proofreading Inert Allele Specific Primers.** Journal of Biochemistry and Molecular Biology, Vol. 38, No. 1, January 2005, pp. 24-27.

#### 2005: VAPSE-based Analysis: Genetic Predisposition to Mental Illness and other Complex Diseases

231. Feng, J., Chen, J., Yan, J., Craddock, N., Jones, I.R., Cook, E.H., Goldman, D., Heston, L.L., and Sommer, S.S.: **Structural variants in retinoid receptor genes in patients with schizophrenia and other psychiatric diseases.** Am. J. of Medical Genetics (Neuropsychiatric Genetics) 133B: 50-53; 2005.
232. Yan, J., Oliveira, G., Coutinho, A., Yang, C., Feng, J., Katz, C., Sram, J., Bockholt, A., Jones, I.A., Craddock, N., Cook, E., Vicente, A., Sommer, S.S.: **Analysis of the neuroligin 3 and 4 genes in autism and other neuropsychiatric patients.** Molecular Psychiatry 10; 329-332; 2005.
233. Yan, J., Feng, J., Craddock, N., Jones, I.R., Cook, Jr., E.H., Goldman, D., Heston, L.L., Chen, J., Burkhart, P., Shibayama, A., and Sommer, S.S.: **Vitamin D receptor variants in 192 patients with schizophrenia and other psychiatric diseases.** Neurosci Lett. May 20-27; 380(1-2): 37-41; 2005
234. Cohn, J., Neoptolemos, J.P., Feng, J., Yan, J., Jiang, Z., Greenhalf, W., McFaul, C., Mountford, R., Sommer, S.S.: **Increased risk of idiopathic chronic pancreatitis in cystic fibrosis carriers.** Human Mutation. Oct;26(4):303-7; 2005.

#### 2006: published, in press, and submitted papers

235. Hill, K.A., Gonzalez, K.D., Scaringe W.A., Wang, J.C., Sommer, S.S.: **Preferential occurrence of 1-2 microindels.** Human Mutation. Jan;27(1):55-61; 2006
236. Hill, K.A., Buettner, V.L., Sundburg, A., Halangoda, A., Li, W., Gonzalez, K.D., Wang, J., Scaringe, W., Sommer, S.S.: **Most Spontaneous Tumors in a Mouse Model of Li-Fraumeni Syndrome do not have a Mutator Phenotype.** Carcinogenesis. *In press*
237. Gonzalez, K., Hill, K.A., Li, K., Li, X., Scaringe, W., Wang, J., Gu, D., Sommer, S.S.: **Somatic Microindels: Analysis in Mouse Soma and Comparison with the Human Germline.** Human Mutation. *In press*
238. Liu, Q., Nguyen, V., Li, X., Sommer, S.S.: **Multiplex PAP: Application to the detection for heterozygous deletions.** Biochemical. Biotechniques. *In press*
239. Feng J, Yan J, Li W, Chen J, Sommer SS (2006): **Candidate gene analyses by scanning or brute force fluorescent sequencing: a comparison of DOVAM-S with gel-based and capillary-based sequencing** Genetic Testing, *In press*
240. Feng J, Schroer R, Yan J, Song W, Yang C, Cook EH Jr., Skinner C, Schwartz C, and Sommer S (2006): **High Frequency of Neurexin 1b Signal Peptide Structural Variants in Patients with Autism.** Neuroscience Letters. *In press*
241. Feng J, Schroer R, Yan J, Song W, Yang C, Cook EH Jr., Skinner C, Schwartz C, and Sommer S (2006): **High Frequency of Neurexin 1b Signal Peptide Structural Variants in Patients with Autism.** Neuroscience Letters. *In press*
242. Li, X., Wen-Fong, C., Estaki, B., Fujimura, F., Hill, K., Sommer, S.S.: **Multiple mosaicism leads to daughters with different mutations.** Submitted

243. Escobar, M., Li, X., Yan, J., Hashimi, H., Saleh, A., Feng, J., Sommer, S.S.: **Absence of predisposing Factor VIII structural changes in patients with acquired hemophilia A.** Submitted
244. Chen Z, Feng J, Weiss L, and Sommer S (2006): **MOM-PAP-A detects ultra rare deletions and reveals that normal lung contains the EGFR microdeletions commonly found in lung cancers.** Submitted
245. Longmate, J.A., Larson, G., Buzin, C., Feng, J., Sommer, S., Krontiris, T.: **Selective discovery of uncommon alleles associated with common diseases.** Submitted
246. Pruthi, R.K., Thorland, E., Dongzhou Liao, Hill, K.A., and Sommer, S.S.: **Carboxyl-Termini of the Factor IX Gene Family: A Story Emphasizing Positive Values.** Submitted
247. Drost, J., Li, X., Halangoda, A., Scaringe, W.A., Hill, K., Ketterling, R., Kasper, C., Ettinger, L., Greenberg, C.R., Desposito, F., Granick, D., Bodurtha, J., Massey, G., Pinto, M.T., Gill, J.C., Sommer, S.S.: **Factor IX germline mutations in early embryo: Preferential occurrence of G:C>A:T non-CpG transitions.** Submitted
248. Saleh, E., Feng, J., Shi, J., Sommer, S.S.: **No correlation between retinoid receptors mutations and breast cancer.** Submitted
249. Singh, A.M., Jung, M., Feng, J., Buzin, C., Moulds, J., Zhang, Y., Gehan, E., Dritschilo, A., and Sommer, S.S.: **Clinical prognosis of breast cancer patients with ATM missense mutations.** Submitted

#### Reviews and Book Chapters

- R1 Wickner, R.B., and Sommer, S.S.: **L dsRNA of yeast comprises multiple compatible nonhomologous species: cytoplasmic genes [EXL], [HOK], and [NEX] are on one form of L.** In: Double-Stranded RNA Viruses, Bishop, D.H.L., and Compans, R.W., eds., Elsevier Science Publishing Co., New York, pp. 469-475, 1983.
- R2 Sommer, S.S., and Sobell, J.L.: **Application of DNA-based diagnosis to patient care: the example of hemophilia A.** Mayo Clin. Proc. 62:387-404, 1987.
- R3 Fradin, D. with Sommer, S.S.: **A New True Book: Heredity.** Children's Press, Chicago, 1987, ISBN 0-526--1233-9 (a book for elementary school children).
- R4 Sommer, S.S., and Sarkar, G.: **Are tissues a patch quilt of ectopic gene expression?** Science 246:261, 1989.
- R5 Koeberl, D.D., Buerstedde, J-M., Stoflet, E.S., Bottema, C.D.K., Sarkar, G., and Sommer, S.S.: **Genomic amplification with transcript sequencing (GAWTS) and its application to the rapid detection of mutations and polymorphisms in the factor IX gene.** In: Gene Transfer and Gene Therapy (UCLA Symposia on Molecular and Cellular Biology), Beaudet, A.L., Mulligan, R., and Verma, I.M., eds., Alan R. Liss, Inc., New York, Vol. 87, pp. 307-314. 1989.
- R6 Giannelli, F., Green, P.M., High, K.A., Lozier, J.N., Lillicrap, D.P., Ludwig, M., Olek, K., Reitsma, P.H., Goossens, M., Yoshioka, A., Sommer, S.S., and Brownlee, G.G.: **Haemophilia B: - database of point mutations and short additions and deletions.** Nucleic Acids Res. 18:4053-4059, 1990.
- R7 Sommer, S.S., Sarkar, G., Koeberl, D.D., Bottema, C.D.K., Buerstedde, J-M, and Cassady, J.: **Direct sequencing with the aid of phage promoters.** In: PCR-Protocols and Applications - A Laboratory Manual, Innis, M., Gelfand, D., and Sninsky, J., eds., Academic Press, pp. 197-205, 1990.
- R8 Sommer, S.S.: **Laboratory practices.** Nature 347:583, 1990.
- R9 Giannelli, F., Green, P.M., High, K.A., Sommer, S.S., Lillicrap, D.P., Ludwig, M., Olek, K., Reitsma, P.H., Goossens, M., Yoshioka, A., and Brownlee, G.G.: **Haemophilia: database of point mutations and short additions and deletion--second edition.** Nucleic Acids Res. 19:2193-2219, 1991.
- R10 Buerstedde, J-M., and Sommer, S.S.: **Sequencing of PCR products--analysis of factor IX genes and of recombination events in immunoglobulin genes.** In: PCR Topics, Usage of Polymerase Chain Reaction in Genetic and Infectious Diseases, Rolfs, M., Schumacher, H.C., and Marx, P., eds., Springer-Verlag, Berlin, Germany, pp. 9-14, 1991.
- R11 Sommer, S.S.: **TG or not TG?** Nature 353:468, 1991.
- R12 Sommer, S.S.: **PCR amplification of specific alleles.** Science 255:514, 1992.
- R13 Giannelli, F., Green, P.M., High, K.A., Sommer, S.S., Lillicrap, D.P., Ludwig, M., Olek, K., Reitsma, P.H., Goossens, M., Yoshioka, A., and Brownlee, G.G.: **Haemophilia B: database of point mutations and short additions and deletions--third edition.** Nucleic Acids Res. 20:2027-2063, 1992.
- R14 Sommer, S.S.: **Assessing the underlying pattern of human germline mutation: lessons from the factor IX gene.** FASEB J. 6:2767-2774, 1992.
- R15 Sarkar, G. and Sommer, S.S.: **Removal of DNA contamination in polymerase chain reaction reagents by ultraviolet irradiation.** Methods in Enzymology 218:381-388, 1993.
- R16 Bottema, C.D.K., Sarkar, G., Cassady, J.D., Li, S., Dutton, C.M., and Sommer, S.S.: **PCR amplification of specific alleles: a general method of rapidly detecting mutations, polymorphisms, and haplotypes.** Methods in Enzymology 218:388-402, 1993.



- R17 Giannelli, F., Green, P.M., Sommer, S.S., Poon, M.-C., Ludwig, M., Schwaab, R., Reitsman, P.H., Goossens, M., Yoshioka, A., and Brownlee, G.G.: **Haemophilia B: database of point mutations and short additions and deletions - fourth edition.** *Nucleic Acids Res.* 21:3075-3087, 1993.
- R18 Bottema, C.D.K., and Sommer, S.S.: **PCR amplification of specific alleles: rapid detection of known mutations and polymorphisms.** *Mutation Research* 288:93-102, 1993.
- R19 Sommer, S.S.: **Human genetic mutation. Book Review.** *Am. J. Hum. Genet.* 54:388, 1994.
- R20 Sommer, S.S., and Vielhaber, E.L.: **Phage promoter-based methods for sequencing and screening for mutations. In: The Polymerase Chain Reaction, Mullis, K., Ferre, F., and Gibbs, R.A., eds., Birkhäuser, 1994, pp. 214-221.**
- R21 Sobell, J.L., Heston, L.L., and Sommer, S.S.: **An approach to identifying genes that predispose to schizophrenia. In: New Genetic Approaches to Mental Disorders, Elliott S. Gershon and C. Robert Cloninger, eds., American Psychiatric Press, 1994, Chapter 9, pp. 123-139.**
- R22 Sommer, S.S.: **Carrier testing for hemophilia.** *Hemophilia Newsnotes* 12:pp. 3 and 10, 1993.
- R23 Sommer, S.S.: **Cryptic simplicity versus cryptic RY(i): Reply to Schwaiger and Epplen.** *Am. J. Hum. Genet.* 54:919-920, 1994.
- R24 Sommer, S.S., and Ketterling, R.P.: **How precisely can data from transgenic mouse mutation-detection systems be extrapolated to humans?: lessons from the study of spontaneous germline mutations in the human factor IX gene.** *Mutation Research* 307:517-531, 1994.
- R25 Giannelli, F., Green, P.M., Sommer, S.S., Lillicrap, D.P., Ludwig, M., Schwaab, R., Reitsma, P.H., Goossens, M., and Brownlee, G.G.: **Haemophilia B: database of point mutations and short additions and deletions - fifth edition, 1994.** *Nucleic Acids Res.* 22:3534-3546, 1994.
- R26 Sommer, S.S.: **Recent human germ-line mutation: Inferences from patients with hemophilia B.** *Trends in Genetics* 11:141-147, 1995.
- R27 DeVries, E.M.G., Ricke, D.O., DeVries, T.N., Hartmann, A., Blaszyk, H., Liao, D., Soussi, T., Kovach, J.S., and Sommer, S.S.: **Database of mutations in the p53 and APC tumor suppressor genes designed to facilitate molecular epidemiological analyses.** *Human Mutation* 7:202-213, 1996.
- R28 Bottema, C.D.K., Sarkar, G., Cassady, J.D., Ii, S., Dutton, C.M., and Sommer, S.S.: **Polymerase chain reaction amplification of specific alleles: a general method of detection of mutations, polymorphisms, and haplotypes. In: Recombinant DNA Methodology II: Selected Methods in Enzymology, Wu, R. ed., Academic Press, Inc., San Diego, pp. 693-706, 1995, (reprint of R16).**
- R29 Sommer, S.S.: **REF and ddF restriction endonuclease and dideoxy fingerprinting. In: Laboratory Protocols for Mutation Detection, U. Landegren (ed.), Oxford Press, Chapter 6, pp. 27-32, 1996.**
- R30 Sommer, S.S.: **PASA PCR amplification of specific alleles. In: Laboratory Protocols for Mutation Detection, U. Landegren (ed.), Oxford Press, Chapter 16, pp. 82-86, 1996.**
- R31 Giannelli, F., Green, P.M., Sommer, S.S., Poon, M.-C., Ludwig, M., Schwaab, R., Reitsma, P.H., Goossens, M., Yoshioka, A., and Brownlee, G.G.: **Haemophilia B (sixth edition): a database of point mutations and short additions and deletions.** *Nucleic Acids Res.* 24:103-118, 1996.
- R32 Lind, T., Thorland, E., and Sommer, S.S.: **Genomic Amplification with Transcript Sequencing (GAWTS).** *Methods Molecular Biology* 65: 193-200, 1996.
- R33 Sommer, S.S. and Ketterling, R.P.: **The factor IX gene as a model for analysis of human germline mutations: an update.** *Hum. Mol. Genet.* 5:1505-1514, 1996.
- R34 Sobell, J.L. and Sommer, S.S.: **Genetics. Psychiatry, A. Tasman, J. Kay, J.A. Lieberman et al (eds) Volume (1), Chapter 13, pp. 182-209, 1997.**
- R35 Sobell, J.L. and Sommer, S.S.: **Genetics. Psychiatry, Self Assessment and Review, D.H. Taylor, A. Tasman, J. Kay, J.A. Lieberman et al (eds) Chapter 13, pp. 34-35, 1997.**
- R36 Hartmann, A., Blaszyk, H., Kovach, J.S., and Sommer, S.S.: **The Molecular Epidemiology of P53 Gene Mutations in Human Breast Cancer.** *Trends in Genetics* 13:27-33, 1997.
- R37 Bottema, C.D.K. and Sommer, S.S.: **Selective amplification of specific alleles. In: Mutation Detection: A Practical Approach, S.M. Forrest and R.G.H. Cotton (eds), Oxford University Press, pp.161-187, 1998.**
- R38 Giannelli, F., Green, P.M., Sommer, S.S., Poon, M.-C., Ludwig, M., Schwaab, R., Reitsma, P.H., Goossens, M., Yoshioka, A., Figueiredo, M.S., Brownlee, G.G.: **Haemophilia B: database of point mutations and short additions and deletions, 7<sup>th</sup> edition.** *Nucleic Acids Research* 25:133-135, 1997.
- R39 Warren, W., Hovig, E., Smith-Sørensen, B., Børresen, A.-L., Fujimura, F.K., Liu, Q., Feng, J., and Sommer, S.S.: **Detection of mutation by single-strand conformation polymorphism (SSCP) analysis and hybrid SSCP methods.** *Current Protocols in Human Genetics, Supplement* 15:7.4.1-7.4.23, 1997.
- R40 Giannelli, F., Green, P.M., Sommer, S.S., Poon, M.-C., Ludwig, M., Schwaab, R., Reitsma, P.H., Goossens, M., Yoshioka, A., Figueiredo, M.S., Brownlee, G.G., Internet: <http://www.umds.ac.uk/molgen/intro/htm>: **Haemophilia B:**

**database of point mutations and short additions and deletions, 8<sup>th</sup> edition.** Nucleic Acids Research 26:(1) 265-8, 1998.

- ) R41 Hill, K.A., Buettner, V.L., Glickman, B.W., and Sommer, S.S.: **Spontaneous mutations in the Big Blue<sup>®</sup> transgenic system are primarily mouse derived.** Mutation Research Minireview 436: 11-19, 1999.
- R42 Sobell, J.L., Sommer, S.S., Kay, J.: **Genetics.** Psychiatry: Behavioral Science and Clinical Essentials, 2000.
- R43 Sommer, S.S., Scaringe W.A., Hill, K.A.: **Human Germline mutation in the factor IX gene.** Mutation Res. 2001. Nov 1, 487 (1-2): 1-17, 2001.
- R44 Hill, K.A., and Sommer, S.S., **P53 as a mutagen test in breast cancer.** Environmental and Molecular Mutagenesis 39: 216-227, 2002.
- R45 Sommer, S., **Científico estudia mutaciones genéticas para corregir defecto causante de Hemofilia.** Avances, Edición Invierno, 28-29, 2002.
- R46 Liu, Q., Sommer, S.S.: **PAP: Detection of ultra rare mutations depends on P\* oligonucleotides, “sleeping beauties” awakened by the kiss of pyrophosphorolysis.** Human Mutations 23:426-436 (2004)