

CHEMICAL HERITAGE FOUNDATION

**JAMES R. LUPSKI**

The Pew Scholars Program in the Biomedical Sciences

Transcript of an Interview  
Conducted by

Andrea R. Maestrejuan

at

Baylor College of Medicine  
Houston, Texas

on

14, 15, and 16 August 1995

From the Original Collection of the University of California, Los Angeles

## ACKNOWLEDGEMENT

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INTERVIEWEE

x James R. Lupski  
(Signature)

James R. Lupski  
(Typed Name)

Baylor College of Medicine

One Baylor Plaza  
(Address)

Houston, Texas 77030

x Date August 14, 1995

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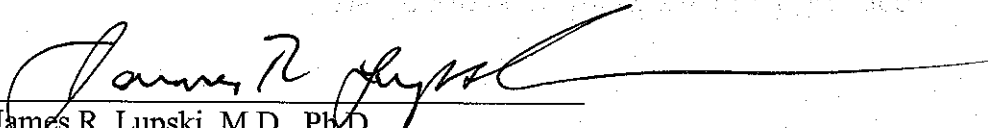
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## **JAMES R. LUPSKI**

1957 Born in Hicksville, New York on 22 February

### Education

1979 B.A., New York University  
1984 Ph.D., New York University  
1985 M.D., New York University

### Research Appointments

1985-1986 New York University Medical Center  
Research Assistant Professor

1986-1989 Baylor College of Medicine  
Research Assistant Professor and Resident

### Professional Experience

1989-1992 Baylor College of Medicine  
Assistant Professor

1992-1995 Associate Professor

1995-present Cullen Professor of Molecular and Human Genetics and  
Professor of Pediatrics

1991-present Various Houston-area Hospitals  
Consulting Geneticist, Attending Pediatrician, and  
Medical Geneticist

### Honors

1987 Inducted into the Hicksville Hall of Fame

1988 Young Investigator Award, American Society for Microbiology  
Interscience Conference on Antimicrobial Agents and Chemotherapy

1989 Young Investigator of the Year Award, Abbott Laboratories

1990-1994 Pew Scholar in the Biomedical Sciences

1991 Young Investigator Award, American Federation for Clinical  
Research Southern Section

1993 Distinguished Research Award for Outstanding Contributions to the



1994 Understanding of the Genetics of Charcot-Marie-Tooth Disorders,  
Charcot-Marie-Tooth Association  
Outstanding Alumni Award, Alpha Omega Alpha, New York  
University School of Medicine

#### Selected Publications

- Lupski, J.R. et al., 1982. Cloning and characterization of the *Escherichia coli* chromosomal region surrounding the dnaG gene, with a correlated physical and genetic map of dnaG generated via transposon Tn5 mutagenesis. *Molecular and General Genetics*, 185:120-28.
- Lupski, J.R. et al., 1983. Regulation of the rpsU-dnaG-rpoD macromolecular synthesis operon and the initiation of DNA replication in *Escherichia coli* K-12. *Molecular and General Genetics*, 189:48-57.
- Lupski, J.R. et al., 1983. Localization of a Plasmodium surface antigen epitope by Tn5 mutagenesis mapping of a recombinant cDNA clone. *Science*, 220:1285-88.
- Lupski, J.R. et al., 1984. Specificity of Tn5 insertions into a 36 nucleotide DNA sequence repeated in tandem seven times. *Gene*, 30:99-106.
- Lupski, J.R. et al., 1984. Promotion, termination, and anti-termination in the rpsU-dnaG-rpoD macromolecular synthesis operon of *E. coli* K-12. *Molecular and General Genetics*, 195:391-401.
- Lupski, J.R. et al., 1986. A temperature dependent pBR322 copy number mutant resulting from a Tn5 position effect. *Proceedings of the National Academy of Sciences USA*, 83:7381-85.
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- Grompe, M. et al., 1991. Mutations in the *Escherichia coli* dnaG gene suggest coupling between DNA replication and chromosome partitioning. *Journal of Bacteriology*, 173:1268-78.
- Lupski, J.R. et al., 1991. DNA duplication associated with Charcot-Marie-Tooth disease type 1A. *Cell*, 66:219-32.
- Greenberg, F. et al., 1991. Molecular analysis of the Smith-Magenis syndrome: A possible contiguous gene syndrome associated with del(17) (p11.2). *American Journal of Human Genetics*, 49:1207-18.
- Versalovic, J. et al., 1991. Distribution of repetitive DNA sequences in Eubacteria and application to fingerprinting of bacterial genomes. *Nucleic Acids Research*, 19:6823-31.
- Lupski, J.R. et al., 1991. Discordance of muscular dystrophy in monozygotic female twins: Evidence supporting asymmetric splitting of the inner cell mass in a manifesting carrier. *American Journal of Medical Genetics*, 40:354-64.
- Lupski, J.R. et al., 1992. Gene dosage is a mechanism for Charcot-Marie-Tooth disease type 1A. *Nature Genetics*, 1:29-33.
- Pentao, L. et al., 1992. Charcot-Marie-Tooth type 1A duplication appears to arise from recombination at repeat sequences flanking the 1.5Mb monomer unit. *Nature Genetics*, 2:292-300.

- Lupski, J.R. et al., 1993. Stable inheritance of the CMT1A DNA duplication in two patients with CMT1 and NF1. *American Journal of Medical Genetics*, 45:92-96.
- Versalovic, J. et al., 1993. Conservation and evolution of the rpsU-dnaG-rpoD macromolecular synthesis operon in eubacteria. *Molecular Microbiology*, 8:343-55.
- Roa, B.B. et al., 1993. Charcot-Marie-Tooth disease type 1A: Association with a spontaneous point mutation in the PMP22 gene. *New England Journal of Medicine*, 329:96-101.
- Wise, C.A. et al., 1993. Molecular analyses of unrelated Charcot-Marie-Tooth disease patients reveal a high frequency of the CMT1A duplication. *American Journal of Human Genetics*, 53:853-63.
- Roa, B.B. et al., 1993. Dejerine-Sottas syndrome associated with point mutation in the PMP22 gene. *Nature Genetics*, 5:269-73.
- Versalovic, J. and J.R. Lupski, 1993. The *Haemophilus influenzae* dnaG sequence and conserved bacterial primase motifs. *Gene*, 136:281-86.
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- Garcia, C.A. et al., 1995. Clinical variability in identical twins with the Charcot-Marie-Tooth disease type 1A duplication. *Neurology*, 45:2090-93.
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## ABSTRACT

**James R. Lupski** was born and raised on Long Island, New York, one of eight children. He attended a Roman Catholic elementary school but a public high school. Lupski and three of his siblings manifested, at different times and to different degrees, Charcot-Marie-Tooth disease (CMT); James's disease was serious enough to require several surgeries when he was in high school, surgeries that kept him at home for much of his high school years. He became interested in his disease and in genetics and decided he wanted to become a doctor. He also became a professional chess player. He won a full scholarship to New York University (NYU), where he majored in chemistry and biology and minored in mathematics and psychology. In David Schuster's laboratory he tried to isolate brain receptors; and during his summers he worked at Cold Spring Harbor Laboratory, learning to clone genes. Accepted early to NYU Medical School, Lupski then won acceptance to the MD/PhD program. He wrote his doctoral thesis on the macromolecular synthesis operon. The discovery of the gene associated with Huntington's disease inspired him to search for the CMT disease gene. He was courted by Baylor College of Medicine, where he was given a faculty appointment while he was still an intern. At Baylor he set up his own lab and began his research into the genetics of CMT, studying a large family in Louisiana. Lupski eventually patented a diagnostic test for CMT and continues his research on the disease. Lupski continues to teach, to manage his lab, to publish, to consult for private industry, to take out patents, and to balance work and family life with his wife and two daughters.

## UCLA INTERVIEW HISTORY

### INTERVIEWER:

Andrea R. Maestrejuan, Interviewer, UCLA Oral History Program; B.A., History, University of California, Irvine, 1988; B.S., Biological Sciences, University of California, Irvine, 1988; C.Phil., History, University of California, Riverside.

### TIME AND SETTING OF INTERVIEW:

**Place:** Lupski's office, Baylor College of Medicine.

**Dates,** length of sessions: August 14, 1995 (155 minutes); August 15, 1995 (190); August 16, 1995 (102).

**Total number of recorded hours:** 7.45

**Persons present during interview:** Lupski and Maestrejuan.

### CONDUCT OF INTERVIEW:

This interview is one in a series with Pew scholars in the biomedical sciences conducted by the UCLA Oral History Program in conjunction with the PewCharitable Trusts's Pew Scholars in the Biomedical Sciences Oral History and Archives Project. The Project has been designed to document the backgrounds, education, and research of biomedical scientists awarded four-year Pew scholarships, from 1988 through 1992. In preparing for this interview, Maestrejuan, in consultation with the director of the UCLA Oral History Program and three UCLA faculty project consultants, developed a topic outline to provide an overall interview framework. Maestrejuan then held a telephone preinterview conversation with Lupski to obtain extensive written background information (curriculum vitae, copies of published articles, etc.) and agree on a research and interviewing timetable. Maestrejuan further reviewed the documentation in Lupski's file at the Pew Scholars Program office in San Francisco, including his proposal application, letters of recommendation, and reviews by Pew Scholars Program national advisory committee members. For general background on the recent history of the biological sciences, Maestrejuan consulted such works as: J.D. Watson et al., *The Molecular Biology of the Gene*. 4th ed. 2 vols. Menlo Park, CA: Benjamin/Cummings, 1987; Lubert Stryer, *Biochemistry*. 3d ed. New York: W.H. Freeman, 1988; *The Journal of the History of Biology*; H.F. Judson, *The Eighth Day of Creation: Makers of the Revolution in Biology*. New York: Simon and Schuster, 1979; and recent issues of *Science*, *Nature*, and *Cell*. The interview is organized chronologically, beginning with Lupski's childhood illness with Charcot-Marie-Tooth (CMT) disease and his decision to become a scientist and continuing through his education at New York University and Cold Spring Harbor Laboratory and the establishment of his laboratory at Baylor College of Medicine. Major topics discussed include the genetic basis of disease, CMT, science funding, and the training of physician-scientists.

#### ORIGINAL EDITING:

Kristian London, editor, edited the interview. He checked the verbatim transcript of the interview against the original tape recordings, edited for punctuation, paragraphing, and spelling, and verified proper names. Words and phrases inserted by the editor have been bracketed.

Lupski reviewed the transcript. He verified proper names and made minor corrections.

Steven J. Novak, senior editor, prepared the table of contents and index. London assembled the biographical summary. Gregory M. Beyrer, editorial assistant, compiled the interview history.

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