

**James B. Lewis, PhD**

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## **Objective**

To combine my wide knowledge of molecular biology, biotechnology and nanotechnology and problem solving skills to help a research team focus on applying the latest technology to solve important, complex problems in biotechnology and biomedical science.

## **Summary**

I have a PhD in chemistry, spent 25 years doing research in molecular biology with emphasis on analyzing gene expression and on cancer research and immunology, and then spent the past 13 years writing about developments in nanotechnology. My principal accomplishment as a researcher (during the 1970s at Cold Spring Harbor Laboratory) involved adapting newly developed methods of cell-free translation of purified viral messenger RNA molecules to mapping the adenovirus genome by identifying the DNA sequences encoding various viral proteins, many of which had not been previously known. I continued this work as a faculty member at the Fred Hutchinson Cancer Research Center during the 1980s. The last segment of my research career involved working as part of a department developing vaccines for HIV and cancer. I was a principal investigator on several grants and authored or co-authored several dozen research articles. My recent career writing about nanotechnology broadened my scientific knowledge beyond molecular biology and I began to think about how results from different areas of science could be integrated to pursue complex and ambitious goals. I have followed some of what has been happening recently in molecular and cellular biology and am especially impressed by advancements in genomic and proteomic techniques, the application of computational methods to help understand emergent properties of networks of gene expression, and novel methods to manipulate those networks. At numerous points during my career I have learned and mastered new technologies and methods as needed to solve the problem at hand. I am confident that I can learn and apply whatever is needed for any project in which I am involved. I am eager to join a team where I can integrate advanced technology platforms with rapidly expanding knowledge in related fields to solve complex problems that impact major medical challenges.

## **Skills and Accomplishments**

- A broad knowledge of science and technology.
- Extensive knowledge of biotechnology and nanotechnology.
- Attention to detail and a facility for problem solving, as exemplified while developing early methods for mapping genes using cell-free translation of purified mRNAs.
- A facility for learning complex subjects, finding and organizing relevant information as needed. For example, I was led into nanotechnology from my knowledge of biochemistry and molecular biology, but then acquired background knowledge of physics and material science as necessary.

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- An ability to discern interrelationships in complex material. For example, after becoming interested in nanotechnology, I quickly recognized the importance of structural DNA nanotechnology, and as a result, in 1988 I invited Nadrian Seeman and his collaborator Bruce Robinson to speak at our 1989 NanoCon event, long before Seeman's work was widely recognized.  
<http://www.halcyon.com/nanojbl/NanoConProc/nanocon3.html#anchor772348>
- Facility for pursuing collaborations to provide needed skills and expertise to solve hard problems.
- An ability to describe research to a range of audiences, from general to professional.

## **Professional Experience**

**1996-2009.** Working as an independent contractor writing about nanotechnology, mostly as Research Analyst and Technical Editor for the Foresight Institute, the leading think tank and public interest institute on nanotechnology. My writing has ranged from current and near term applications of nanoscience and nanotechnology to technologies that could lead eventually to large-scale atomically precise manufacturing. Most recently, independently of my work for the Foresight Institute, I wrote a long overview article on the development of advanced nanotechnology that was published in the *Journal of Geoethical Nanotechnology*. <http://www.halcyon.com/nanojbl/JBL/index.html>

**1988-1996.** Senior Research Investigator, Immunodeficiency and Immunosuppression Dept., Bristol-Myers Squibb Pharmaceutical Research Institute - Seattle, WA. I supervised a small group of two to five scientists working on HIV and cancer vaccines within a department of 25-30 scientists headed by Shiu-Lok Hu. The work primarily involved recombinant vaccinia viruses and DNA vaccines. We first did some work on HIV proteins, and then spent 6 years working on active immunotherapy for cancer (cancer vaccines). During my last six months at BMS, I returned to molecular virology to begin a project to identify viral protein - cellular protein interactions that are important for the pathogenicity of HIV in the hope that these interactions would prove useful targets for drug screening. We were in the process of setting up yeast two-hybrid screens when my time at BMS came to an end. To see publications (numbers 44-46):  
<http://www.halcyon.com/nanojbl/JBLBio.html#pub44>

**1980-1988.** Associate Member, Basic Sciences Division, Fred Hutchinson Cancer Research Center, Seattle, WA. *Adenovirus gene expression and oncogenesis*. I led a small research group (2-6) studying various aspects of the molecular biology of adenoviruses, with special emphasis on gene expression and oncogenic properties. I continued a collaboration with Carl W. Anderson of Brookhaven National Laboratory using amino terminal sequencing of proteins and peptides synthesized *in vitro* to identify where proteins were encoded on the adenovirus genome. Circa 1982, working together with Robert Eisenman, I set up in my lab the first peptide synthesis machine to be used at the Fred Hutchinson. To complete the identification of region E1B proteins, I used RP-HPLC to separate two adenovirus E1B proteins that comigrated on SDS-PAGE. Within my research group, AW Senear demonstrated morphological transformation of rodent cell

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lines by high-level expression of the adenovirus E1A gene, RC Schmitt demonstrated differences in the nuclear localization of different E1A proteins, and ML Fahnestock mutagenized the E1A genes to define functions. My research was supported by several research grants, of which I was the principal investigator, from the National Institutes of Health, the National Science Foundation, and the American Cancer Society. To see publications (numbers 33-43): <http://www.halcyon.com/nanojbl/JLBLBio.html#pub33>.

**1974-1980.** Staff Investigator and Senior Staff Investigator, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY. *Molecular biology of adenoviruses*. Working with CW Anderson, JF Atkins, and RF Gesteland, I used cell-free translation to identify proteins encoded by adenovirus and to identify the genes for each protein. We initially used a translation system based on that of Schrier and Staehelin made more efficient by the addition of polyamines. To purify adenoviral mRNA and to fractionate it into populations complementary to specific restriction fragments of Ad DNA, we initially used liquid phase hybridization with fragmented DNA followed by urea-hydroxyapatite chromatography and recovery of the RNA by binding to oligo(dT)-cellulose. In this way various adenovirus proteins produced at early and at late times after infections were identified as coded by specific fragments of the viral DNA. Among the adenovirus early proteins identified by this work were the E1A proteins and one of the small E1B proteins. Investigation of why late protein mRNAs bound weakly to a second segment of DNA contributed in a small way to the discovery by others of RNA splicing in 1976. Later experiments done in collaboration with MB Mathews switched to using hybridization to DNA immobilized on nitrocellulose filters to purify mRNA species and to using nuclease-treated reticulocyte lysates for translation.

My work during this period benefited greatly from numerous collaborations with other scientists having expertise and skills that complemented my own. Of special note, in the research group that I shared with MB Mathews, I worked with postdoctoral fellows ML Harter on adenovirus early proteins, H Esche on adenovirus transforming region mRNAs, and BW Stillman on the adenovirus terminal protein. Outside of our research group, I contributed purified adenoviral mRNAs to LT Chow and TR Broker for their use in electron microscopy of heteroduplexes between viral DNA and RNA molecules to precisely map the structure of most of the adenovirus transcriptome. I was able to synthesize adenovirus proteins *in vitro* labeled with various amino acids and without N-terminal acetylation so that CW Anderson and JE Smart could determine specific protein sequences for alignment with the viral genome sequence. The last segment of my work at CSH contributed to the discovery of adenovirus region E-2B. To see publications (numbers 9-32): <http://www.halcyon.com/nanojbl/JLBLBio.html#pub09>.

**1973-1974.** Postdoctoral Researcher, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, under the supervision of Raymond Gesteland. *Molecular biology of adenoviruses*. As part of a large cancer center project, I set up a modified version of the cell free translation system that I had learned in Switzerland, and used it to translate RNA purified from cells infected with human adenovirus type 2. To see publications (numbers 7-8): <http://www.halcyon.com/nanojbl/JLBLBio.html#pub07>.

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**1971-1973.** Postdoctoral Researcher, Swiss Institute for Experimental Cancer Research (ISREC), Lausanne, Switzerland, under the supervision of Bernhard Hirt. *Molecular biology of small DNA tumor viruses SV40 and polyoma*. My goal was the cell-free synthesis of viral tumor antigen by translation of RNA transcribed from viral DNA using *E. coli* RNA polymerase. One reason for the failure of this approach became obvious several years later with the discovery of RNA splicing. While in Switzerland I learned from M. Schrier and T. Staehelin of the Basel Institute of Immunology (BII) how to set up a highly efficient system for mammalian cell-free translation. To see publications (numbers 5-6): <http://www.halcyon.com/nanojbl/JBLBio.html#pub05>.

**1968-1971.** Graduate research in the Chemistry Department of Harvard University, Cambridge, MA, under the supervision of Paul Doty. *RNA biochemistry and structure*. I developed a method to probe the secondary structure of *E. coli* 5S ribosomal RNA by equilibrium dialysis against tri- and tetra-ribonucleotides complementary to the 5S rRNA sequence to determine the accessibility of the oligomer antisequence in the 5S rRNA structure. To see publications (numbers 1-4): <http://www.halcyon.com/nanojbl/JBLBio.html#pub01>.

## **Education**

Ph.D., 1972, Harvard University, Cambridge, MA., Chemistry

M.A., 1968, Harvard University, Cambridge, MA., Chemistry

B.A., 1967, University of Pennsylvania, Philadelphia, PA., Chemistry

## **Professional Affiliations**

AAAS (American Association for the Advancement of Science). Professional member since 1981.

ASM (American Society for Microbiology). Professional member since 1985.

ACS (American Chemical Society). Professional member since 1986.

ACM (Association for Computing Machinery). Member since 1997.

IEEE (originally the Institute of Electrical and Electronics Engineers). Member since 1997.

AVS (originally the American Vacuum Society). Member since 1997.

IOP (Institute of Physics). Member since 2005.

## **Publications and other writing**

### **Summarizing progress toward advanced nanotechnology**

A 10,000-word article to provide an overview of the road from current to advanced nanotechnology, with emphasis on the most significant advances since the Productive Nanosystems Roadmap was completed in mid-2007 was published in the *Journal on Geoethical Nanotechnology*, Volume 4, Issue 1 May 2009.

<http://www.terasemjournals.org/gn0401/jl1.html>

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"Productive Nanosystems as a Milestone Toward Geoethical Nanotechnology" James B. Lewis, Ph.D.

### **Writing on nanotechnology published on the Foresight Institute web site, 1997-2009**

During 2007 I participated in a first attempt to map the developments needed to move from current capabilities in nanotechnology to advanced systems. [Productive Nanosystems: A Technology Roadmap](#) was developed by Foresight Institute and Battelle, with initial funding from the Waitt Family Foundation. I wrote two papers for the [Working Group Proceedings](#) (210 pages, 14.6 MB PDF) part of the roadmap: "Nucleic Acid Engineering" J. Lewis, pages 07-1 to 07-7 and "DNA as an Aid to Self-Assembly" J. Lewis, pages 08-1 to 08-9.

Links to about five dozen of the hundreds of pieces that I wrote on Nanotechnology for the Foresight Institute are available at:

<http://www.halcyon.com/nanojbl/JBL/index.html>

### **Other writing related to nanotechnology, 1988-1992**

With a partner (J Quel), I helped to organize a conference that was held in Seattle in 1989 and focused on nanotechnology and "the effects that these advanced technologies might have on society over the next 30 - 50 years". We transcribed and edited the conference proceedings and made it available, first for purchase, and then for free on the Internet.

*The NanoCon Proceedings* are available at

<http://www.halcyon.com/nanojbl/NanoConProc/nanocon1.html>.

I co-edited two books that resulted from nanotechnology conferences sponsored by the Foresight Institute:

- *Nanotechnology: Research and Perspectives*. Edited by BC Crandall and James Lewis. The MIT Press. 1992. This book contains papers from the [First Foresight Conference on Nanotechnology](#), held in October of 1989.
- *Prospects in Nanotechnology: Toward Molecular Manufacturing*. Edited by Markus Krummenacker and James Lewis. John Wiley & Sons, Inc. 1995. This book contains papers from the [First General Conference on Nanotechnology: Development, Applications, and Opportunities](#), held in November of 1992.

### **Research publications, 1970-1993**

A complete list of my research publications covering the period 1970-1993 is available at <http://www.halcyon.com/nanojbl/JBLBio.html>. These publications included papers published in *Nature*, *Biochemistry*, *Proc. Nat. Acad. Sci. USA*, *J. Biol. Chem.*, *Cell*, *J. Virol.*, and *J. Mol. Biol.*.