James B. Lewis, PhD
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Summary

I have a PhD in chemistry and more than 25 years experience in research, mostly in molecular biology, cancer research, virology, and immunology, working at top-ranked research institutes and at a major pharmaceutical company. During my years doing molecular biology as a bench scientist I developed extensive skills in problem solving and trouble shooting experiments, requiring exceptional attention to detail. I have held faculty-level positions in major research institutions and been the principal investigator on a number of federal and private research grants. I then spent the next 17 years writing about developments in nanotechnology and various medical topics. I have an exceptionally wide knowledge of science, with depth in biotechnology and nanotechnology. I am adept at learning quickly and excel at integrating knowledge from different areas.

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.
- 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://dslweb.nwnexus.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

Apr. 2010-present. Writing about nanotechnology as Research Analyst and Technical Editor for the Foresight Institute, the leading think tank and public interest institute on nanotechnology, plus at various times tutoring a wealthy client on molecular nanotechnology, consulting with two nanotechnology start-ups, and writing about other medical topics for two other clients. My most recent writing about nanotechnology can be found here: http://www.foresight.org/nanodot/. Some of the most recent papers I've written on medical topics can be found here: http://daghealth.com/category/research-papers/.

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Oct. 2009-Feb. 2010. Postdoctoral Research Associate in the Division of Gastroenterology, Hepatology, and Nutrition (Curt Hagedorn, MD, chief), Department of Medicine, University of Utah School of Medicine. I worked under the supervision of Dr. Li Wang to develop a method of using nanoparticles to deliver selected microRNAs to hepatocellular carcinoma cells to re-establish normal cellular gene expression in mouse models of liver cancer. After working for four months, obtaining some preliminary results, and preparing the Research Narrative section of an NIH R21 research grant application, I became sick, was hospitalized, and was unable to work or to complete the R21 application for the February 2010 deadline.

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. Links to various articles, report chapters, and blog posts that I wrote during this period can be found at http://dslweb.nwnexus.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://dslweb.nwnexus.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 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://dslweb.nwnexus.com/nanojbl/JBLBio.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://dslweb.nwnexus.com/nanojbl/JBLBio.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://dslweb.nwnexus.com/nanojbl/JBLBio.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://dslweb.nwnexus.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://dslweb.nwnexus.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

Publications and other writing

Writing about 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 published in the *Journal on Geoethical Nanotechnology*, Volume 4, Issue 1 May 2009.
http://www.terasemjournals.org/gn0401/jl1.html
“Productive Nanosystems as a Milestone Toward Geoethical Nanotechnology" James B. Lewis, Ph.D.

A 4,000-word article for Terasem Movement, Inc.'s 5th Annual Workshop on Geoethical Nanotechnology examining to what extent the 1975 Asilomar Conference, held to recommend safety procedures for recombinant DNA research, provides a model for regulating self-replicating molecular manufacturing, once this technology becomes imminent was published in the *Journal of Geoethical Nanotechnology*, Volume 4, Issue 2 4th Quarter 2009.
http://www.terasemjournals.org/GNJournal/GN0402/lewis1.html
"Recombinant DNA and Self-replicating Molecular Manufacturing: Parallels and Lessons" James B. Lewis, Ph.D.

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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://dslweb.nwnexus.com/nanojbl/JBL/index.html

I still write about nanotechnology here: http://www.foresight.org/nanodot/

Recent (2013) writing on sleep apnea can be found here:
http://daghealth.com/category/research-papers/

Research publications, 1970-1993

A complete list of my research publications covering the period 1970-1993 is available at http://dslweb.nwnexus.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.*.