

# **CURRICULUM VITAE**

**(April 9, 2010)**



**Peter L. Pedersen, Ph.D.**

**(Professor, Biological Chemistry and Center for Metabolism)**

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# CURRICULUM VITAE

(Peter L. Pedersen)

## **1. PRIOR TO UNIVERSITY**

Born: Muskogee, Oklahoma

Attended Catoosa (Indian) Schools, Catoosa, Cherokee Nation (Near Tulsa, Okla)

School Salutatorian; Letters in Baseball (First base), Basketball (Center), Football (End)

## **2. UNIVERSITY DEGREES AND APPOINTMENTS**

**1961** B.S. in Chemistry (Engineering School), University of Tulsa, Tulsa, Oklahoma

**1964** Ph.D. in Chemistry, (Biochemistry Major), University of Arkansas, Fayetteville, Arkansas, (Research Advisor, Jacob Sacks, M.D., Ph.D)

**1964** Postdoctoral Fellow, Department of Physiological Chemistry, The Johns Hopkins University School of Medicine, Baltimore, Maryland (Research Advisor: A. L. Lehninger, Ph.D.)

**1967** Instructor, Department of Physiological Chemistry, The Johns Hopkins University School of Medicine

**1968** Assistant Professor, Department of Physiological Chemistry, The Johns Hopkins University School of Medicine

**1972** Associate Professor, Department of Physiological Chemistry, The Johns Hopkins University School of Medicine

**1975** Professor, Department of Biological Chemistry\*, The Johns Hopkins University School of Medicine

**1992-1993** Fogarty Scholar in Residence, NIH (NCI), Bethesda, MD. (Sponsor, Claude Klee; interacted with laboratories of C. Klee, M. Gottesman and I. Pastan at the NCI)

(\*Department name changed in 1984)

**2009–Present** Professor, Department of Biological Chemistry & Center for Cell Metabolism and Obesity Research, The Johns Hopkins University, School of Medicine

## **3. AWARDS/HONORS/ACCOMPLISHMENTS**

### **A. Teaching/Research (General)**

**1.** Eight certified teaching awards (Believed to be most among JHUSOM faculty)

**2.** Forty three consecutive years (no absence) as a Teacher of Medical Students (JHUSOM)

**3.** Above the 95<sup>th</sup> percentile of the distribution of (extramural) NIH grants (Past 25 yrs.)

**4.** Consistent funding from the NIH (> 40 yrs.)

**5.** One of the longest NIH R01 grants (39 yrs, NCI.)

**6.** Longest term (> 25 years) as Director of a JHUSOM Biotechnology Facility, “The Synthesis and Sequencing Facility” [Founded the facility; Now a self-supporting Biotechnology facility managed by Jody Franklin (<http://biolchem.bs.jhmi.edu/tssf/personnel/index.asp>)]

### **B. Teaching**

**1974** Certificate of Excellence in Teaching Preclinical Sciences

**1976** Certificate of Excellence in Teaching Preclinical Sciences

**1977** Certificate of Excellence in Teaching Preclinical Sciences

**1981** W. Barry Wood Award for Excellence in Teaching Preclinical Sciences

**1982** Certificate of Excellence in Teaching Preclinical Sciences  
**1984** Certificate of Excellence in Teaching Preclinical Sciences  
**1984** Professors' Award for Distinction in Teaching in the Preclinical Divisions (Highest award given at JHU for teaching)  
**1994** Certificate of Excellence in Teaching Preclinical Sciences  
**1984-2010** Consistently ranked at or near the top by Medical Students for excellence in teaching Biochemistry/Metabolism and Relationship to Disease

### **C. Research / Grant Support)**

**1966-1968** NIH Postdoctoral Fellowship  
**1968-Present** NIH R01 Grant (CA 10951), "Control of Enzymatic Phosphate Transfer in Mitochondria" (**Active**)  
**1969-1974** NIH (NCI) Research Career Development Award  
**1982-1997** NIH R01 Grant (CA 32742), "Glucose Catabolism in Neoplastic Tissues"  
**1992-1993** NIH Fogarty Scholar in Residence at the NCI  
**1990-2005** NIH R01 Grant (DK 43692), "Molecular and Chemical Description of CFTR Function"  
**1998-Present** NIH R01 Grant (CA 80118) "Cancer Related Glycolytic Gene: Regulation and Targeting" (**Active**) ((R01 grant)  
**2005 – Present** NIH PPG grant 1P01 HL081427-01 "Mitochondrial Function in Ischemic Heart Disease" Project 4 "Regulation of the mitochondrial ATP synthase" (**Active**)

### **D. Invited Lectures (Seminars are not included)**

**Invited Lectures on Cancer (Metabolism, Gene Regulation, Therapy):** Hepatoma Conference in San Diego, California, 1972; M.D. Anderson Hospital and Tumor Institute, Houston, Texas, 1974; Gordon Research Conferences, 1979 and 1984; Catholic University & Pathological Institute, Rome, Italy, 1985; New York Academy Sciences meeting in Villa Olmo, Italy, 1986; AACR Meeting, Ontario Canada, 1995; the CARSO Conference on Oncology Research, Bari, Italy, 1996; Johns Hopkins University Continuing Education Course, Baltimore, MD, 1997; Univ. of Washington, Seattle, 1998; International Conference on Tumor Cell Metabolism, Mobile, Alabama, 2001; EBEC Meeting, Arcachon, France 2002; Meeting on Interventional Oncology, Tyson's Corner, Virginia, 2002; NIH , NCI Workshop on Mitochondrial Function and Cancer, Bethesda, MD, 2004; NCI, Bethesda, MD, 2006, 2009; SMU, Houston, TX, 2007; MD Anderson Hospital and Tumor Institute, Houston, TX, 2009; AICR (American Institute of Cancer research), Washington DC, 2009; Plenary Lecture, EBEC Meeting, Warsaw, Poland 2010. Major Lecturer, Ann. Meeting Brazilian Biochem./Mol. Biol. Society, Iguacu Falls, Brazil 2010

**Invited Lectures on Mitochondrial ATP Synthase:** in Bressanone, Italy, 1973; Mosbach, Germany, 1978; Bologna, Italy, 1980; Lyon, France, 1982; Hannover, Germany, 1984; Bari, Italy, 1985; Prague, Czechoslovakia, 1986; Bresica, Italy, 1987; Bari, Italy, 1989, and Gothenburg, Sweden, 1991, Helsinki, Finland, 1992; Schwangau, Germany, 1992, Bari, Italy 1993, Zurich, Switzerland, 1994; Bari, Italy, 1996; Osnabruck, Germany (1998); FEBS Congress, Warsaw, Poland (2004) Gordon Research Conferences (1971, 1979, 1981, 1983, 1995, 1997, 1999, 2001, 2003, 2005, 2006, 2009)

**Invited Speaker at Symposia on Transport ATPases:** at the FASEB meeting, New Orleans, 1979; ACS meeting in Las Vegas, Nevada, 1980; The Biophysical Society meeting in La Jolla, California, 1983; The Biophysical Society meeting in Baltimore, Maryland, 1985, The FASEB meeting in Washington, D. C., 1986, Biophysical Society meeting, Baltimore, Maryland, 1990, ASBMB meeting,

Houston, Texas, 1992, New York Academy of Sciences Meeting, Cleveland, Ohio, 1992, FASEB Summer Research Conference, Copper Mountain, Colorado, 1996; 29<sup>th</sup> FEBS Congress, Warsaw, 2004; FASEB Summer Research Conference, Snowmass, Colorado (1999, 2001, 2003) and Saxtons River, Vermont (2005, 2007), Snowmass, Colorado (2010)

**FASEB Awards to Present Symposia Papers:** on ATP Synthesis and ATP Hydrolysis at International Congresses in Lucerne, Switzerland, 1969; Stockholm, Sweden, 1973; Hamburg, Germany, 1976; and Jerusalem, Israel, 1991

**Invited Speaker at Cystic Fibrosis Meetings:** NIH, 1991; Williamsburg, Virginia, 1991, 1992, 1993, 1995, 1996; 1997; 1998; Dallas Texas, 1991, 1993; NIH (NIDDK), 1994, Woods Hole, 1994; Orlando, Florida, 1996; Univ. of Mich., 1996 (Keynote Speaker); NIH, 1997 (NIA); Bordeaux, France, 1999 (Keynote Speaker); NIH (NCI), 1999 (Helped bring the field to a molecular level; *Left the field to place more effort on cancer research and also to pursue a new research project on heart disease.*)

#### **E. Honorary / Distinguished Presentations**

Oklahoma State University (Stillwater), University of Arkansas (Fayetteville), Bordeaux, France, University of Central Florida (Orlando)

#### **4. HONORARY AND PROFESSIONAL SOCIETIES (PRESENT OR PAST)**

ASBMB (FASEB), Sigma Xi, Alpha Chi Sigma Chemical Fraternity, Biophysical Society, American Association for Cancer Research, Bioenergetics Subgroup, American Association for the Advancement of Science, Association of Biomolecular Resource Facilities (ABRF), The Mitochondrial Research Society

#### **5. EDITORIAL BOARDS AND OUTSIDE COMMITTEES**

**1973-1978** Journal of Biological Chemistry (Editorial Board)

**1982-present** Archives of Biochemistry and Biophysics (Editorial Board)

**1985-present** Journal of Bioenergetics and Biomembranes (Editorial Board)

**1990-present** **Journal of Bioenergetics and Biomembranes (Editor-in-Chief)**

**1986-1996** Cancer Research (Associate Editor)

**1985-1995** Current Topics in Bioenergetics (Advisory Board)

**1979** Gordon Research Conference on Energy Coupling Mechanisms (Advisory Committee)

**1980-1987** U. S. Bioenergetics Sub-group (Executive Secretary)

**1981** Gordon Research Conference on Energy Coupling Mechanisms (Co-Chairman - Elect)

**1983** Gordon Research Conference on Energy Coupling Mechanisms (Chairman - Elect)

**1985-1990** Member, U. S. National Committee for the International Union for Pure and Applied Biophysics (USNC/IUPAB)

**1986-1992** IUB/IUPAB Bioenergetics Group (Chairman - Elect)

**1986** Biophysical Society Council (elected)

**1987** Biophysical Society Executive Committee (elected)

**1990** Biophysical Society (Program Chairman, 1990 Meeting)

**1992** American Society for Biochemistry and Molecular Biology (Co-Program Chairman, 1992 meeting)

**1993-1996** FASEB Conference Committee (Chairman)

**1997** Review Committee, NIH Heart, Blood, and Lung Institute

**1998** Nominating Committee, Biophysical Society

**1999** FASEB Meeting on Transport ATPases (Co-Chairman-Elect)

2001 FASEB Meeting on Transport ATPases (Chairman –Elect)

2001-present Mitochondrion (Editorial Board)

## **6. STUDY SECTIONS**

1975-1977 National Institutes of Health (Biochemistry Study Section) (Ad Hoc Member)

1983-1987 National Institutes of Health (Physical Biochemistry Study Section)

1985-1987 Chairperson (Elect), Physical Biochemistry Study Section

1994-1998 National Institutes of Health (Physical Biochemistry Study Section)

2005 & 2007 National Institutes of Health (Special Emphasis Panels)

## **7. STUDENTS TRAINED OR HELPED TRAIN (54)**

### **A. Ph.D (17)\*/ MS\*\* (1), (BIOLOGICAL CHEMISTRY)**

#### **Year Awarded**

1972\* Dr. William A. Catterall, Professor and Chairman, Dept. of Molecular Pharmacology, University of Washington, Seattle, Washington (Member, National Academy of Sciences)

1974\* Dr. William A. Coty, Director, Array Platform Development, Motorola Life Sciences, Tempe, AZ

1977\* Dr. Ernesto Bustamante, Scientific Director, BioGenomica, Lima, Peru; Also Political Analyst, Lima, Peru

1978\* Dr. Nitza Cintron, Formerly Biochemistry Lab Chief, NASA Space Center, Houston, Texas; then Deputy Chief, Space Medicine and Health Care System, NASA Space Center, Houston, Texas. NASA Hall of Fame; **Present:** Associate Professor Internal Medicine, University of Texas Medical Branch, Galveston, Texas

1982\* Dr. Naomi Geller-Lipsky, Research Biochemist, now Decorative Artist

1984\* Dr. Maureen McEnery, Associate Professor, Department of Physiology and Biophysics, Case Western Reserve University

1989\* Dr. David Garboczi, Investigator, Structural Biology Section, NIH (NIAID)

1991\* Dr. John Barnard; Last Known Position: Research Associate, State University of New York at Buffalo

1992 (Visiting) Dr. A.R. LoPiero, Faculty, University of Catania, Sicily

1995\* Dr. Michael Lebowitz, Director of Research, Biotech Co., Rockville, MD

1998\* Dr. Weiyang Pan, Biosafety, Johns Hopkins University, School of Medicine

1998\* Dr. Tamara Golden, Research Scientist, Buck Institute for Research on Aging, Novato, CA

1998\*\* Dr. Curt Heese, Received MS degree, entered medical school, now a Physician

2000-2001 (Visiting) Marek Verbacky, Member, Institute of Physiology, Academy of Science of the Czech Republic, Prague

2004\* Dr. Min Gyu Lee, Assistant Professor, MD Anderson Hospital and Tumor Institute, Houston, Texas

2006\* Dr. Chen Chen, Research Associate, Center for Advanced Technology (CARB), Rockville, MD

2009\* David Blum, in training

2009\* Han Gil Lee, in training

### **B. Postdoctoral (32), Biological Chemistry**

Drs. T. L. Chan, John Soper, Klaus Schwerzmann, Joseph Houstek, Ronald Kaplan, Richard Nakashima, Janna Wehrle, David Parry, Noreen Williams, Goffredo Petrone, Marco Paggi, Raymond Pratt, Krishan

Arora, Gloria Ferreira, Philip Thomas, Maurizio Fancuilli, Michael Bauman, Young Hee Ko, Harry Price, Saroj Mathupala, Julie Reeves, Annette Rempel, Natalie Lu, Sangjin Hong, Jean-Phillippe Annereau, Ashish Goel, Chris Jeffers, Min-Gyu Lee, Jiang Tao, Mohammad Abusedera, Qining Qin, Gang Shi

### **C. Art as Applied to Medicine (4)**

**2000** David Blum  
**2005** Alison Burke  
**2005** Karen Bucher  
**2008** Ammon Posey

## **8. CURRENT EDUCATIONAL RESPONSIBILITIES**

Member, Educational Policy Committee at JHUSOM  
Co-Director, Metabolism Section Medical Student "Scientific Foundations of Medicine" Course  
Course; Lecturer, Metabolism Section, "Scientific Foundations of Medicine" Course  
Participant; Special Topics in Biological Chemistry

## **9. GRADUATE PROGRAMS (MEMBER)**

Biological Chemistry  
Molecular and Cellular Medicine  
Biochemistry, Cellular, and Molecular Biology (BCMB)  
Intercampus Program in Biophysics

## **10. NIH TRAINING PROGRAMS (Previous)**

Nephrology (member)  
Cancer Pathology (member)

## **11. UNIVERSITY COMMITTEE RESPONSIBILITIES**

### **A. Current**

**1978**-present Director or Co-Director, Metabolism Section, Molecules and Cells Course  
**1986**-present Director, Synthesis and Sequencing Core Facility  
**1986**-present Chairman, Albert L. Lehninger Lectureship Committee  
**1993**-present Educational Policy Committee  
**1998**-present Member, Admission's Committee, Graduate Program in Biological Chemistry  
**1999**-Present Member Chesapeake Biological Laboratories Lectureship Committee

### **B. Past**

**1972-1978** Chairman, Admissions Subcommittee, Graduate Program in Biochemistry, Cellular and Molecular Biology (BCMB)  
**1979-1996** Member, Admissions Subcommittee, BCMB Graduate Program  
**1975-1976** Member, Committee to Assess Indirect Cost  
**1976** Acting Director, Graduate Program in Biochemistry, Cellular and Molecular Biology (BCMB)  
**1976-1979** Member, Awards Committee  
**1977-1978** Member, Preclinical Teaching Building Committee  
**1978-1982** Member, Professorial Promotions Committee

1983-1989 Associate Professors' Review Committee  
1986-1989 Clinician Scientists Awards Committee  
1986-2009 Educational Policy Committee  
1987-1996 Searle/Pew Scholars Program Selection Committee  
1991 Chairman, LCME Committee for Review of Basic Sciences  
1994-1998 Molecular Medicine Curriculum Committee  
1998 Chairman, LCME Committee for Review of Basic Sciences  
2004 -2009 Oversight Committee for the Mass Spectrometry Core Facility

## **12. RESEARCH ACCOMPLISHMENTS (With Co-Workers and Collaborators)**

A. Participated with Drs. Carl Schnaitman, Jack W. Greenawalt, and T.L. Chan in the development of procedures routinely used today for the *separation of the 4 components of mitochondria (inner membrane, outer membrane, inter-membrane space, and matrix)* (**Publications 8, 10, and 12**). [*This procedure and modified versions thereof have been used to determine the submitochondrial location of almost every known mitochondrial enzyme.*]

B. Characterized *mitochondrial nucleoside diphosphokinase* with regard to enzymatic and hydrodynamic properties, submitochondrial location, and function (**Publications 5-10, and 22**). [*Mutations in this enzyme are now known to cause developmental problems in Drosophila. This enzyme is also believed to be involved in the development of certain childhood tumors, e.g., neuroblastomas, and to be involved also in cancer metastasis.*]

C. Helped guide work of a number of predoctoral students and postdoctoral fellows that led to the *purification from liver mitochondria of the complete ATP synthase complex and its associated F<sub>1</sub>-ATPase, F<sub>0</sub> proton channel, and inhibitory peptide regulator* (**Publications 15, 17, 21, 39, 45, 62, and 92**). [*The ATP synthase complex, present in all nucleated cells, provides ATP either directly to energize cellular processes or indirectly as NTPs through the action of the above nucleoside diphosphokinase.*]

D. Guided work of William Catterall that demonstrated concurrently with Drs. Alan Senior and Alex Tzagoloff (then at the U. of Wisconsin) that the catalytic *F<sub>1</sub> moiety of ATP synthases is comprised of 5 non-identical subunits* (**Publications 15 and 21**). We were the first to observe both  $\alpha$  and  $\beta$  subunits of F<sub>1</sub> in SDS-PAGE gels (**Publication 17**), and to demonstrate the unusual  *$\alpha_3\beta_3\gamma\delta\epsilon$  stoichiometry* (**Publications 15 and 21**). *These finding have now been reproduced for all ATP synthases from bacteria to people.* Finally, we were also able to demonstrate with an electron microscopist (Glenn Decker) that the F<sub>1</sub> moiety consists of a *hexagonal array of subunits* ( $\alpha$  and  $\beta$ ) with a central mass, predicted to be the small subunits ( $\gamma\delta\epsilon$ ). (**Publication 3 under "Review articles" etc.**). [*The F<sub>1</sub> moiety of the ATP synthase is now known from work of Yoshida and coworkers in Japan to be an ATP hydrolysis driven motor and the small central subunits ( $\gamma\delta\epsilon$ ) the rotor of this motor. In mitochondria the enzyme works in reverse being driven by an electrochemical gradient of protons to make ATP as proposed by Peter Mitchell's chemiosmotic hypothesis.*]

E. Obtained *crystals of the catalytic F<sub>1</sub> moiety of the ATP synthase* for the first time (1978) together with Mario Amzel, now Chair of Biophysics, JHUSOM, (**Publications 34 and 37**), and then collaborated with Mario Amzel, Michael McKinney, and P. Narayanan to elucidate the *3-dimensional structure of the enzyme complex at 9 Å resolution* (**Publication 58**). Finally, in a collaborative project with Mario Bianchet and Mario Amzel, the *structure of F<sub>1</sub> was obtained first at 3.6 Å resolution* (**Publication 105**) and finally *at atomic resolution (2.8 Å)* (**Publication 135**). The final structure represents the first of the active conformation. Most recently, a *transition state structure* (**Publication 157**) in the presence of

vanadate has been obtained with crystals prepared by Dr. Young Ko via a project led by her in collaboration with the NIH laboratory headed by David Garboczi. [*The importance of the latter work (157) is that it shows for the first time how ATP is made at the active site of the complex ATP synthase.*]

F. First to visualize with colleagues John Soper, Glenn Decker, Jack Greenawalt, Maureen McEnery, M., Buhle, Jr., and U. Aebi, the ***structure of a complete ATP synthase molecule*** under the electron microscope (**Publications 45, and 62**). This has now led to the discovery by Young Ko that the ATP synthase in mitochondria exists as a larger complex consisting also of the adenine nucleotide carrier and the phosphate carrier. [*The complete ATP synthase/phosphate carrier/adenine nucleotide carrier complex isolated in pure form by Young Ko has been named the “ATP synthasome”*] (**Publications 150,**). A 3-D structure of this large super complex has been obtained at 23 Å resolution by Young Ko and Chen Chen in collaboration with the laboratory of Wah Chiu at Baylor College of Medicine (**Publication 153**).

G. Prepared morphologically and functionally intact mitochondria from hepatoma tissue (**Publication 13**). [*This was the first clear demonstration that tumor mitochondria have a normal capacity to make ATP.*]

H. Helped guide work of Ernesto Bustamante (**Publications 31 and 49**) that showed that ***hexokinase bound to mitochondria of cancer cells is essential for the “Warburg Effect”***, i.e., a high glycolytic activity even in the presence of oxygen. [*Hexokinase binding to mitochondria now forms the clinical basis of PET analysis for detecting many cancers.*] Guided work of Richard Nakashima in collaboration with Marco Colombini that showed that the ***outer mitochondrial membrane receptor for hexokinase (Publications 77) is a protein called VDAC***. [*It is now known from the work of others that hexokinase bound to VDAC helps immortalize cancer cells by preventing cell death by apoptosis*]. Later, together with Richard Nakashima and Marco Paggi, the hexokinase bound to tumor mitochondria was purified and categorized as ***hexokinase 2 (HK-2) (Publication 86)***.

I. Help guide work of Krishan Arora that demonstrated that the bound hexokinase has preferred access to ATP generated by the mitochondria (**Publication 88**). A full length cDNA of the tumor enzyme was cloned, sequenced, and overexpressed in active form in *E. coli* (**Publication 99**), and the first site directed mutations marking the catalytic site were completed (**Publication 104**). Krishan Arora showed also that tumor hexokinase is a protein kinase (**Publication 114**).

Significantly, the predominant form of tumor hexokinase has been confirmed in work by Annette Rempel and Saroj Mathupala as HK-2. The ***HK-2 promoter region*** has now been isolated and sequenced (**Publication 121**). Finally, the HK-2 gene has been shown to be amplified (**Publication 126**) and to be activated by the mutated tumor suppressor p53 (**Publication 131**) as well as glucose, hypoxic conditions, and a variety of known transcription factors (**Publications 144, 151, 152**). In other work Ashish Goel presented evidence that the proximal promoter region of the HK-2 gene has several methylation sites that are demethylated in a highly malignant hepatoma cell line (**Publication 151**) and Min Gyu Lee has demonstrated that much of the strength of the the HK-2 promoter region lies near the transcription start site (**Publication 152**).

J. Helped guide experiments of Young Ko and collaborators where she independently discovered that the simple alkylating agent 3-bromopyruvate (3BP) is a powerful anticancer agent in cells in culture. This agent was shown also to be a powerful inhibitor of cancers in animal models (**Publications 142, 146, 155**). A single injection of 3BP into liver implanted tumors kills 70-90 percent of the tumor cells (**Publication 146**), and systemic injection suppresses metastatic lung cancers (**Publication 146**). ***Significantly, in a project led by Young Ko, advanced hepatocellular carcinomas growing in a rodent model were eradicated in all tested cases without apparent toxicity and without recurrence (Publication***



**155).** More recent work by Young Ko has demonstrated that 3-bromopyruvate is far superior in killing human cancer cells in culture (derived from a wide variety of tissues) than a number of different chemotherapeutic agents widely used to treat human cancers.

**K.** Helped guide experiments of William Coty to label the mitochondrial phosphate transport system, and estimate its molecular size (**Publication 25**); later via the involvement of several Postdoctoral Fellows (Ronald Kaplan, Gloria Ferreria, and Raymond Pratt) this transport system was purified, cloned and sequenced, and its import into mitochondria clearly demonstrated (**Publications 60, 78, 95, and 102**).

**L.** Helped guide work of Ronald Kaplan that resulted in the first method for obtaining a reconstitutively active dicarboxylate carrier from mitochondria (**Publication 74**).

**M.** Helped guide work of William Coty and Janna Wehrle that showed that calcium is transported from the mitochondrial matrix to the cytoplasm (**Publications 19 and 47**). Later exit mechanisms for  $\text{Ca}^{++}$  from mitochondria became widely identified in many tissues.

**N.** Helped guide work of Naomi Geller that showed that the inner and outer mitochondrial membranes are subject to different rates of degradation and synthesis *in vivo*. This work led us to propose the first *in vivo* model for mitochondrial biogenesis (**Publications 50, and 55**).

**O.** Helped design and have synthesized with David Garboczi a peptide predicted from homology arguments to be at the catalytic site of the mitochondrial ATP synthase, and then demonstrated that this peptide does, in fact, interact with ATP (**See Publication 84**) [First, chemical synthesis of an ATP binding site]. The NMR structure of this peptide in the presence of ATP was later elucidated in a collaborative study with Albert Mildvan and W-J Chuang (**Publication 122**).

**P.** Helped guide work of David Gaboczi that resulted in the overproduction of both  $\alpha$  and  $\beta$  subunits of rat liver ATP synthase in *E. coli*, purified them to homogeneity, and showed they bind nucleotide (**Publications 87, and 98**). Site directed, random, and deletion mutations were made to localize the nucleotide binding domain of the  $\beta$  "catalytic" subunits (**Publications 100 and 109**).

**Q.** Helped guide work of John Barnard that led to the characterization of the terminal steps of glycolysis in African trypanosomes that cause *African sleeping sickness* (**Publications 89, 111, 118**). Significantly, a single enzyme (pyruvate kinase) supplies all the ATP to energize trypanosomal division and replication in the infectious form of this parasite and is therefore a potential drug target.

**R.** Helped guide work of Philip Thomas to design and have P, Shenbagamurthi, synthesize a 67 amino acid peptide corresponding to the central region of the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR), and showed it binds ATP. Postulated with these collaborators and others a simple structural model to explain the *chemical basis of Cystic Fibrosis* (**Publication 103**). Helped guide additional work of Philip Thomas to have P. Shenbagamurthi synthesize the CFTR peptide lacking the phenylalanine (F508), the deletion responsible for 70% of CF cases, and demonstrated it is structurally different from the wild type peptide (**Publication 107**). *These studies were the first to obtain "in the test tube" a functional part of the CFTR protein and to implicate that most cases of the disease Cystic Fibrosis are the result of a protein folding problem* (**Publication 110**). Later, helped guide work of Young Ko that demonstrated that the first nucleotide binding domain functions as a weak but active ATPase (**Publication 123**). Help guide work initiated by Young Ko that led Drs. Michael Massiah and Albert Mildvan to obtain by NMR the solution structures of folded and unfolded peptides representative of both the normal region and the diseased causing  $\Delta\text{F508}$  region of the CFTR protein (**Publication 138**).

*This is the first work to show at a 3-dimensional level the structural change caused by the  $\Delta F508$  disease causing mutation that is responsible for most cases of Cystic Fibrosis.*

S. First to predict with Philip Thomas and Young Ko that many common genetic diseases may result because of problems in protein folding (**Publication 110, and Publication 56 under “Review Articles”**).

T. Helped design with Young Ko and have chemically synthesized a 51 amino acid segment of the second predicted nucleotide binding domain of CFTR and showed that it also binds ATP (**Publication 117**).

U. Helped guide the original work of Young Ko who confirmed her hypothesis that tracheal epithelial cells *in vitro* have the capacity to kill bacteria (*P. aeruginosa*) that infect the lungs of most people, but not those of CF patients whose lungs have a defective CFTR protein. This work resulted in the discovery that human tracheal epithelial cells express one or more antimicrobial peptides (**Publication 129**) that protect most people against lung infections but not  $\Delta F508$  CF patients.

V. Designated together with Dr. Ernesto Carafoli the simple classification for Transport ATPases as P, V, and F types and later extended this to include the ABC-type Transport ATPases. This classification is now used in almost all publications on the subject (**Publication 32** under “Review Articles etc.”). Also, see **Publications 47, 69, and 71 under “Review Articles” etc.**

Meeting supported by FASEB to discuss recent progress on these transport ATPases have been held every 2-3 years since 1997

### **13. PUBLICATIONS (Total = 366 with Abstracts; 241 without Abstracts)**

#### **A. Refereed Papers Summarizing Original Work (159)**

1. Pedersen, P.L., and Sacks, J. (1965) Formation of Fructose-Diphosphate in Muscular Contraction. **Arch. Biochem. Biophys.** 109, 197-199.
2. Pedersen, P.L., and Sacks, J. (1965) Hexosephosphate Formation and the Regulation of Glycolysis in Muscle. **Arch. Biochem. Biophys.** 112, 548-553.
3. Goffeau, A.G., Pedersen, P.L., and Lehninger, A.L. (1967) The Kinetics and Inhibition of the Adenosine Diphosphate-Adenosine Triphosphate Exchange Catalyzed by a Purified Mitochondrial Nucleoside Diphosphokinase. **J. Biol. Chem.** 242, 1845-1853.
4. Erwin, V.G., and Pedersen, P.L. (1968) A Sensitive Gel Filtration Method for Determination of Protein Sulfhydryl Groups with  $^{14}C$ -Chloromercuribenzoate. **Anal. Biochem.** 25, 477-485.
5. Goffeau, A.G., Pedersen, P.L., and Lehninger, A.L. (1968) Reactivity of Thiol Groups in Active and Inactive Forms of a Mitochondrial Nucleoside Diphosphokinase. **J. Biol. Chem.** 243, 1685-1691.
6. Goffeau, A.G., Pedersen, P.L., and Lehninger, A.L. (1968) Regulation de l'activite d'une nucleoside diphosphokinase mitochondriale. **Arch. Intern. de Physiol. et de Biochim.** 76, 179-181.
7. Pedersen, P.L. (1968) Molecular Weight, Sulfhydryl Content, and Phosphorylation of a Homogeneous Mitochondrial Nucleoside Diphosphokinase. **J. Biol. Chem.** 243, 4305-4311.

8. Schnaitman, C.A., and Pedersen, P.L. (1968) Localization of Oligomycin-sensitive ADP-ATP Exchange Activity in Rat Liver Mitochondria. **Biochem. Biophys. Res. Commun.** 30, 428-433.
9. Goffeau, A.G., and Pedersen, P.L. (1969) Inactivations et Protections d'une Nucleoside Diphosphokinase Mitochondriale Purifiee. **Arch. Intern. de Physiol. et de Biochim.** 77, 550-552.
10. Pedersen, P.L., and Schnaitman, C.A. (1969) The Oligomycin-sensitive Adenosine Diphosphate-Adenosine Triphosphate Exchange in an Inner Membrane Matrix Fraction of Rat Liver Mitochondria. **J. Biol. Chem.** 244, 5065-5073.
11. Catterall, W.A., and Pedersen, P.L. (1970) Effects of Phosphotungstic Acid and Silicotungstic Acid on Respiration and Integrity of Rat Liver Mitochondria. **Biochem. Biophys. Res. Commun.** 38, 400-405.
12. Chan, T.L., Greenawalt, J.W., and Pedersen, P.L. (1970) Biochemical and Ultrastructural Properties of a Mitochondrial Inner Membrane Fraction Deficient in Outer Membrane and Matrix Activities. **J. Cell Biol.** 45, 291-305.
13. Pedersen, P.L., Greenawalt, J.W., Chan, T.L., and Morris, H.P. (1970) A Comparison of Some Ultrastructural and Biochemical Properties of Mitochondria from Morris Hepatomas 9618A, 7800 and 3924A. **Cancer Res.** 30, 2620-2626.
14. Schreiber, J.R., Balcavage, W.X., Morris, H.P., and Pedersen, P.L. (1970) Enzymatic and Spectral Analysis of Cytochrome Oxidase in Adult and Fetal Rat Liver and Morris Hepatoma 3924A. **Cancer Res.** 30, 2497-2501.
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## **D. Inventions**

**1. Project Title:** Method for Identifying an Agent that Corrects Defective Protein Folding, September, 2000: Office of Technology Licensing, The Johns Hopkins University, School of Medicine U.S. Patent and Trademark Office (Application 09/668,415) [Now in Public Domain]

Inventors: Ko, Y.H. and **Pedersen, P.L.**

**2. Project Title:** Therapeutics for Cancer using 3-Bromopyruvate and Other Selective Inhibitors of ATP Production. US Patent and Trademark Office (Application No. 10/243,550, Patent No. 7,547,673)

Ko, Y.H., Geschwind, J.F., and **Pedersen, P.L.**)

**3.** Therapeutics for Cancer related to 3-Bromopyruvate (Ko, Y.H. has several pending technologies related to 3-bromopyruvate's highly potent anti-cancer properties and use as a therapy for cancer)

#### **14. HOBBIES**

Gardening (Specialty in Strawberries), Picking the Guitar, Walking

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