Curriculum Vitae

Peter Fritz Kador, Ph.D.
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Citizenship: United States

Education:

1968-1972	B.A. (Chemistry) Capital University, Columbus, OH
1972-1976	Ph.D. (Medicinal Chemistry) Ohio State University, Columbus, OH (Thesis: "Selected tetrahydroisoquinoline analogs and their fragmented derivatives as beta-adrenergic agonists" Advisor Prof. Duane D. Miller)

Brief Chronology of Employment:

Summers 1967-69	Laboratory technician, Ohio State University Bee Laboratory
Summer 1970	Laboratory technician, Ohio State University, Department of Physiological Chemistry
Summers 1971-72	Chemical Abstract Service, Selection and Assignment Section, American Chemical Society, Columbus, OH
1971-1972	Laboratory Instructor, Freshman Chemistry, Capital University, Columbus, OH
1972-1973	Recitation Teaching Assistant, Medicinal Chemistry, Ohio State University College of Pharmacy
1973-1976	Tutor, Ohio State University College of Pharmacy
1976-1979	Staff Fellow, Laboratory of Vision Research, National Eye Institute, National Institutes of Health, Bethesda, MD, Advisor Jin H. Kinoshita, Ph.D.
1979-1983	Research Chemist, GS 13, Laboratory of Vision Research, National Eye Institute, National Institutes of Health, Bethesda, MD
1983-1985	Research Chemist, GS 14, Laboratory of Vision Research, National Eye Institute, National Institutes of Health, Bethesda, MD.
1985-1989	Head, Section of Molecular Pharmacology, Laboratory of Mechanisms of Ocular Disease, National Eye Institute, National Institutes of Health, Bethesda, MD
1989-1991	Research Chemist, GS 15, Molecular Pharmacology Section, Laboratory of Mechanisms of Ocular Disease, National Eye Institute, National Institutes of Health, Bethesda, MD.
1991-2002	Chief, Laboratory of Ocular Therapeutics, National Eye Institute, National Institutes of Health
2002-2003	Professor and Chair, Department of Pharmaceutical Sciences, College of Pharmacy, University of Nebraska Medical Center, Omaha, NE
2003-present	Professor, Department of Pharmaceutical Sciences, College of Pharmacy, University of Nebraska Medical Center, Omaha, NE

Other Appointments

1999 – 2002	Courtesy Professor, Department of Veterinary and Biomedical Sciences, University of Nebraska, Lincoln, NE
2003 – Present	Adjunct Professor, School of Veterinary Medicine and Biomedical Sciences, University of Nebraska, Lincoln, NE
2003 – Present	Adjunct Professor, Department Ophthalmology, College of Medicine, University of Nebraska

2003 – 2006	Adjunct Professor, Department of Pharmacology and Neurosciences, College of Medicine, University of Nebraska Medical Center, Omaha, NE
2004- Present	President and C.E.O. Therapeutic Vision, Inc., Omaha, NE.
2010-2015	Guest Professor, Department of Ophthalmology, Xijing Hospital, Fourth Military Medical University, Xi'an, People's Republic of China.

Research Interests

- Diabetic complications, retinopathies, cataract development, neurodegeneration, macular degeneration
- Design and synthesis of multifunctional antioxidants and enzyme inhibitors
- Mechanism of action of neuroprotective drugs and for the treatment of age related degenerative diseases in the eye and neural tissues
- Development of animal models for ophthalmic complications
- Translational studies for applying drugs to the veterinary companion pet market.
- Development of ophthalmic nutraceuticals.

Major Accomplishments

Drug Development

- Synthesized new class of multifunctional antioxidants that possess a novel 2-amino-4-hydroxylpyrimidine ring system. These are orally active compounds that demonstrate selective chelation of transition metals associated with Fenton's reaction and possess free radical scavenger activity. Preliminary studies indicate that they are good candidates for the treatment of cataract, macular degeneration, and Alzheimer's and Parkinson's disease.
- Developed the topical formulation Kinostat™ and demonstrated clinical efficacy of this drug for the prevention of cataracts in diabetic dogs. Obtained SBIR Phase 1 and 2 funding and FDA MUMS designation for commercial development.
- Invented topical nutraceutical Optixcare EH for the reduction of ocular oxidative stress and treatment of dry eye.

Lens Studies

- Expert on conducting *in vitro* lens culture studies using rat, rabbit, dog and human lenses to elucidate the cataractogenic mechanism of select drugs.
- Discovered a choline transport system in the lens that is a sensitive measure of lens biochemical viability.
- Demonstrated sugar cataracts in dogs are osmotic in nature, and that these cataracts can be inhibited by aldose reductase inhibitors.
- Demonstrated the feasibility of utilizing MTC-MRI to investigate osmotic changes in human sugar cataracts.
- Demonstrated that altered redox changes associated with sorbitol dehydrogenase inhibitors, and non-enzymatic glycosylation and advanced glycosylation endproducts (AGEs) form sugar cataracts that are secondary to aldose reductase initiated cataract formation.
- Discovered that a group of compounds derived from a known sorbitol dehydrogenase inhibitor delay advanced sugar cataracts through a mechanism independent of the polyol pathway.
- Synthesized novel multifunctional antioxidants and demonstrated that they accumulate in the lens and retina and delay cataract formation.

Enzyme Studies

- Purified and characterized aldose reductase from human placenta, rat, and dog lenses. Developed antibodies against these enzymes and then localized the enzyme in various tissues by immuno

- Purified and characterized aldehyde reductase in rat and dog lenses.
- Purified and characterized a separate NADPH-dependent reductase not related to aldose or aldehyde reductase in dog thyroid.
- Confirmed that the production of sorbitol, galactitol and xylitol is enzymatic in nature and not due to "auto-oxidation".
- Defined flux changes in the metabolism of glucose by aldose reductase, sorbitol dehydrogenase and glucose, galactose and xylose oxidase in tissues and cells associated with diabetic complications.

Aldose Reductase Inhibitors

- Defined mechanisms of action and pharmacophore requirements of aldose reductase inhibitors.
- Demonstrated feasibility of utilizing affinity labeled analogs of aldose reductase inhibitors to identify reactive regions on the enzyme.
- Using affinity labels, demonstrated the feasibility of an alternate inhibitor site on the enzyme.
- Using molecular modeling and quantum mechanical calculations, defined binding and potential mechanism of action of inhibitors in the substrate binding site.
- Defined differences in the susceptibility to inhibition of aldose reductase inhibitors with aldose versus aldehyde reductase.
- Discovered an intrinsic inhibitor of aldose reductase in mammalian tissues.

Retina

- Defined the progression of retinal lesions in the galactose-fed dog model and demonstrated that it begins with the selective degeneration of retinal capillary pericytes.
- Developed computer assisted method for quantifying retinal capillary changes and demonstrated that inhibition of aldose reductase in the early stages can arrest the development of retinal lesions.
- Demonstrated aldose reductase inhibitors prevent the onset of retinopathy in a dose-dependent manner and demonstrated that removal of galactose diet (equivalent to inhibition of aldose reductase) at the early stages of retinopathy where pericyte ghosts and microaneurysms occur also prevents the further progression of retinopathy.
- Demonstrated that aldose reductase inhibitors can inhibit capillary basement membrane thickening associated with diabetes.
- Demonstrated that retinal capillaries with thickened basement membranes do not increase in permeability as commonly believed.

Other Ocular Tissues:

- Demonstrated that corneal epithelium and endothelium changes are associated with aldose reductase in the rat and dog, respectively.
- Demonstrated that aldose reductase inhibitors prevent delayed pupil dilation changes associated with neuropathy and histological changes of the iris that results in fibrosis.
- Demonstrated that galactose-fed dogs undergo autoimmune thyroid changes similar to those clinically observed in diabetics and that these are linked to aldose reductase.
- Determined structure of asteroid hyalosis in vitreous

Animal Models:

- Developed two strains of a Philly mouse cataract model, one that developed early hereditary cataracts at approximately 3 weeks and one that developed hereditary cataracts at approximately 8 weeks after birth.
- Refined and extensively investigated the galactose-fed dog model. Demonstrated that this dog develops retinal lesions that are clinically and histochemically similar to human diabetic retinopathy from the background stage of dot and blot microaneurysms to the proliferative end stage. Also demonstrated that the dog develops the ocular changes of iris vessel leakage, cataract, keratopathy and asteroid hyalosis. In

nephropathy and cardiac myopathy does develop in the latter stages.

- Developed a mouse models that contains green fluorescent protein and human aldose reductase in vascular cells containing smooth muscles, including retinal capillary pericytes.
- Developed natural diabetic mouse models that containing green fluorescent protein and human aldose reductase in vascular cells containing smooth muscles, including retinal capillary pericytes.

Other Tissues:

- Demonstrated that aldose reductase inhibitors prevent alveolar bone loss in periodontal disease.
- In diabetic rats, verified that motor nerve conduction is normalized by a number of aldose reductase inhibitors and demonstrated that MNC reduction was directly linked to sorbitol formation.
- Demonstrated that both diabetic and galactosemic rats produced proteinuria that can be prevented by aldose reductase inhibitors. Also demonstrated that aldehyde reductase rather than aldose reductase was primarily involved in proteinuria.
- Demonstrated that unlike man or rat, neuropathy is absent in galactose-fed dogs. MNC remains normal despite that fact that galactitol levels are elevated, myoinositol levels are decreased and the lactate/pyruvate levels, indicative of redox changes are abnormal. Moreover, no morphological changes occur in the dog nerve, suggesting that an unknown preventative factor is present in dog nerve.
- Demonstrated that aldose reductase was involved in norepinephrine metabolism.

Professional Societies:

American Chemical Society
Medicinal Chemical Division, American Chemical Society
Association for Ocular Pharmacology and Therapeutics
Association for Research in Vision and Ophthalmology
American Association of Pharmaceutical Scientists
American Diabetes Association
European Association for the Study of Diabetes
European Vision and Eye Research
International Diabetes Federation
International Society for Eye Research
Sigma Xi Research Society
European Vision and Eye Research
United Health Coucil

Awards Received

Vision Research Related (chronological)

Rohto Foundation Cataract Research Award, recipient, May, 1981
Foundation for the Advancement of Science Fellow sponsored by Ayerst Research Laboratories, Inc., 1983-1984; 1984-1985.
Alcon Foundation Research Award, recipient April, 1986
Juvenile Diabetes Foundation Research Award, 1986
Juvenile Diabetes Foundation Research Award, 1987
Kinoshita Lectureship, National Foundation for Eye Research, Kona, Hawaii, November, 1995.
Foundation for the Advancement of Science Research Award sponsored by Pfizer Pharmaceuticals, 1998.
Fellow, American Association of Pharmaceutical Scientists, November 2004
Japanese Cataract Cooperative Research Group Award, November 2005
Fellow, Association for Research in Vision and Ophthalmology, 2010
Distinguished Scientist, University of Nebraska Medical Center, 2010

Other (chronological)

Columbus Technical Council Science Student of the Year, 1968
International Science Fair, Detroit MI, Fourth Award, 1968
Ford-Future Scientists of America Regional Award, 1968
Central Ohio Heart Association Undergraduate Research Scholarship
"Effect of Various Honeybee Extracts on Black Bee Disease", 1970-71
Central Ohio Heart Association Undergraduate Research Scholarship
"O-Alkyldiglyceride Analysis in Rat Adipose Tissue", 1971-72
National Institutes of Health Pre-doctoral Trainee in Medicinal Chemistry, 1972-76
Alumni Achievement Award of Capital University, May 1990
Jack Beal Postbaccalaureate Alumni Achievement Award, Ohio State University College of Pharmacy, Columbus, Ohio, May, 1992
Bundesverdienstkreuz (Federal Cross of Merit) from the German Government, German Embassy, Washington, DC. November, 1994

Other Professional Activities

Executive Vice-President of the National Foundation for Eye Research, January, 1996 - present.
Trustee of the Association for Ocular Pharmacology and Therapeutics (AOPT), 1995 – 2001; 2011-present
President of Ocular Pharmacology and Therapeutics (AOPT), 2004-2011.
Member, U.S. Cataract Cooperative Research Group Planning Board, 1994 - present
Consultant on cataract drug development, Shojin Research Associates, Studio City, CA 1990-2001
Expert Committee Member, US Pharmacopeia, 2000-2006
Consultant on ocular toxicology, Merck & Co., Inc. 2001- 2006
Consultant, MedVet Columbus 2007-2008.
Consultant on ocular toxicology, Eli Lilly and Company 2007-2009.
Consultant on ocular toxicology, Johnson and Johnson Company 2009-2010.
Scientific Advisory Board, Encore Vision 2007-2010.
Scientific Advisor, Aventix Animal Health 2010-present
Scientific Advisory Board, Merz Pharmaceuticals GmbH 2011-2012.
Consultant and Expert Witness, Rakoczy Molino Mazzochi Siwik LLP Patent Attorneys 2012-present.
Consultant, IPExperts, LLC, 2014- present
Consultant on ocular toxicology, Vertex Pharmaceutical Company 2014-2015
Consultant and Expert Witness, Covington and Burling LLP 2016-present.

Continuing Education Courses

Conducting Clinical Trials, National Eye Institute, 1984
Using Molecular Biology for Drug Discovery; American Chemical Society, 2001
Bioinformatics, Rensselaer Polytechnical Institute, 2000
Managing Government Employees, Brookings Institute 1998

Requested Editing

Editorial Board Member, Journal Ocular Pharmacology and Therapeutics, 1997 – 2000; 2008 - current
Co-editor Polyol Pathway and its Role in Diabetic Complications, Excerpta Medica, International Congress Series 760
Co-editor Current Concepts of Aldose Reductase and its Inhibitors Excerpta Medica, International Congress Series 913

Journal Reviews

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