Prof. dr hab. Krzysztof Palczewski – informacja biograficzna

Działalność naukowa – osiągnięcia

Wśród najważniejszych osiągnięć profesora Palczewskiego znajduje się niekwestionowany udział w zrozumieniu funkcjonowania oka poprzez badania nad metabolizmem witaminy A. Profesor Palczewski odkrył i scharakteryzował m.in. grupę dehydrogenaz witaminy A (RDHs) – bierze ona istotny udział w skomplikowanym mechanizmie regeneracji rodopsyny, który umożliwia izomeryzację retinalu z postaci all-trans w 11-cis. Wspomniane dehydrogenazy – poza ich rolą w przemianach metabolicznych siatkówki – spełniają także rolę w ochronie fotoreceptorów. Ich rola jest ogromna, gdyż zapobiegają kumulacji retinalu, czyli reaktywnej formy retinoidu powodującego obumieranie fotoreceptorów. Przełomem stało się stworzenie mysich modeli degeneracyjnych chorób siatkówki, które posiadały wybrane z dehydrogenaz zmutowane geny kodujące. Ten moment pozwolił otworzyć całkiem nowy, a zarazem kluczowy rozdział w badaniach nad zapobieganiem obumieraniu komórek światłoczułych – pozwolił więc dać nadzieję milionom pacjentów cierpiących z powodu zwyrodnienia plamki żółtej związanego z wiekiem (AMD). Dzięki Profesorowi powstało jedno z najistotniejszych narzędzi badawczych, służące opisaniu fizjologicznej roli acylotransferazy lecytyna:retinol (LRAT) – specyficznego dla oka transportera retinalu z grupy ABCA – i wielu innych. Profesor Palczewski opracował także obowiązujący obecnie model, który wyjaśnia mechanizm enzymatycznego przekształcenia izomeru all-trans witaminy A w 11-cis – tym samym jest inicjatorem i pionierem badań nad mechanizmem izomeryzacji retinoidów.

Kaskada przekazywania sygnałów i regeneracja purpury wzrokowej – badania strukturalne nad białkami biorącymi w nich udział

Rok 2000 okazał się dla profesora Palczewskiego i światowej nauki wielkim odkryciem – wtedy właśnie opisał on strukturę rodopsyny. W tym czasie Palczewski wraz ze swoim zespołem skupił uwagę i włożył wiele wysiłku w projekty służące opisowi struktur białek błonowych. Przyniosło to efekt w postaci kilkunastu publikacji w najważniejszych światowych czasopismach naukowych (w tym w Nature, Science i PNAS) – prace dotyczyły m.in. aktywowanej przez światło formy rodopsyny i kompleksu rodopsyny z białkiem G, a także specyficznego dla nabłonka barwnikowego siatkówki enzymu katalizującego izomeracje retinoidów, RPE65. Nadmienić trzeba, że jedna z form RPE5 została wykrystalizowana w sposób umożliwiający utrzymanie jej aktywnej konformacji. Nie można również nie wspomnieć o najnowszych sukcesach profesora Palczewskiego, którymi niewątpliwie są badania nad strukturą ABCA4, czyli specyficznego dla retinalu transportera izolowanego z dysków fotoreceptorów, oraz nad acetylotransferazami lecytynowymi.

Obrazowanie siatkówki in vivo – wyzwania profesora Palczewskiego

Wydawałoby się, że oko to narząd łatwo dostępny badaniom obrazowym – nie jest pokryte powłokami ani nie przykrywa go żaden inny narząd. I jakkolwiek okuliści z dużym powodzeniem potrafią je badać, na potrzeby nauki XXI wieku konieczne są dużo bardziej precyzyjne metody. Dziś chcemy już nie tylko oglądać powierzchnie narządów, tkanek i błon – potrzebujemy narzędzi umożliwiających ocenę warstw komórek, komórek i w końcu ich organelli. Właśnie dzięki tym technikom, pozwalającym na ocenę struktury komórkowej siatkówki, możliwe

jest dalsze poznawanie mechanizmów funkcjonowania oka. Jednym z priorytetów profesora Palczewskiego stały się nieinwazyjne metody obrazowania komórek dna oka. Kolejnym przełomem, w którym miał on swój udział, było zastosowanie mikroskopii dwufotonowej do wizualizacji fotoreceptorów i komórek nabłonka barwnikowego siatkówki in vivo. W ten sposób udało się odkryć specyficzne dla retinoidów struktury komórkowe zwane retinosomami oraz obserwować zmiany w przepływie retinoidów w trakcie naświetlania i adaptacji do ciemności. Metody te już dziś wykorzystywane są w laboratoriach do oceny stanu siatkówki w chorobach degeneracyjnych – następnym krokiem będzie ich wykorzystanie w gabinetach okulistycznych.

Wkład Profesora Palczewskiego w badania podstawowe pozwala myśleć o rzeczywistym i praktycznym wykorzystaniu tej wiedzy w terapii chorób zwyrodnieniowych oka. Jednym z największych wyzwań stojących przed naukowcami zajmującymi się tematyką chorób oczu jest leczenie zwyrodnienia plamki żółtej (AMD), które prowadzi do utraty wzroku. Choroba ta dotyka 20 mln osób na świecie i pomimo dużego nakładu pracy, jej patofizjologia o wieloczynnikowej etiologii nadal nie jest do końca poznana. Dyskretne zmiany w przemianach witaminy A i regeneracji purpury wzrokowej skutkują gromadzeniem ubocznych metabolitów. Te z kolei nieuchronnie prowadzą do dysfunkcji nabłonka barwnikowego i fotoreceptorów. Model mysi odwzorowujący AMD, opracowany przez profesora Palczewskiego, jak i wspomniane nowe metody diagnostyczne umożliwiają selekcję najbardziej obiecujących i najskuteczniejszych leków.

Podsumowując, uwaga profesora Krzysztofa Palczewskiego skupia się obecnie zarówno na rozpoznawaniu, jak i opracowywaniu nowych, skutecznych terapii. Omówione sukcesy dają realne nadzieje chorym, jak na razie nieefektywnie leczonym.

Życiorys naukowy

Position Professor and Chair
Department of Pharmacology, School of Medicine, Case Western Reserve University
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Education

1980 M.S. in Organic Chemistry, University of Wroclaw, Poland

1983 (Feb–July) Research Assistant, Southern Illinois University, Carbondale, IL. Training in protein sequencing

1980–1986 Junior/Senior Research Fellow, Department of Biochemistry, Technical University of Wroclaw, Poland

1986 Ph.D. in Biochemistry, Technical University of Wroclaw, Poland: Topography of the active site and the mononucleotide binding site of aldolase fructose–1.6– P2. (Preceptor: Prof. Dr. M. Kochman)

Postgraduate training

1986–1988 Postdoctoral Fellow, University of Florida, Gainesville, FL. Topic: Rhodopsin phosphorylation, phosphorylation of synthetic peptides, rhodopsin kinase and phosphatase, properties of arrestin. (Preceptor: Dr. Paul A. Hargrave)

Faculty positions held (including professional experience)

1988–1989 Assistant Research Scientist, Department of Ophthalmology, University of Florida, Gainesville, FL

1990–1992 Assistant Scientist II, R.S. Dow Neurological Sciences Institute and Dept of Ophthalmology, Good Samaritan Hospital & Medical Center, Portland, OR

1990–1992 Assistant Professor of Biochemistry and Molecular Biology, Oregon Health Sciences University, Portland, OR

1990–2008 Courtesy Assistant Scientist, Department of Ophthalmology, University of Florida, Gainesville, FL

1990–1992 Research Assistant Professor of Ophthalmology, Oregon Health Sciences University, Portland, OR

1991–1992 Associate Scientist I, Robert S. Dow Neurological Sciences Institute, Good Samaritan Hospital and Medical Center, Portland, OR

1992–1994 Assistant Professor, Department of Ophthalmology, Adjunct, Pharmacology; University of Washington, Seattle, WA

1992–2005 Affiliate, Center on Human Development and Disability (CHDD); University of Washington, Seattle, WA

1994–1997 Associate Professor of Ophthalmology, Adjunct, Pharmacology; University of Washington, Seattle, WA

1997–2005 Professor of Ophthalmology; University of Washington, Seattle, WA

1997–2005 Professor (Adjunct) of Pharmacology; University of Washington, Seattle, WA

1998–2005 Professor (Joint) of Chemistry; University of Washington, Seattle, WA
2003–2005 Interim Research Director; University of Washington, Seattle, WA
1999–2005 Research Affiliate, Regional Primate Research Center; University of Washington, Seattle, WA
1999–2005 E.K. Bishop Professor, Department of Ophthalmology; University of Washington, Seattle, WA
2005– Professor and Chair, Department of Pharmacology; Case Western Reserve University, Cleveland, OH
2005– John H. Hord Professor; Case Western Reserve University, Cleveland, OH
2008– Professor, Center for Proteomics and Bioinformatics; Case Western Reserve University, Cleveland, OH

Honors and awards

Polish Academy of Science (1978, 1985)
Polish Ministry of Education (1986)
Jules and Doris Stein Research to Prevent Blindness Professor (1992–1999)
Cogan Award, Association for Research in Vision and Ophthalmology (1996)
Humboldt Research Award for Senior U.S. Scientists (2000)
Trustee Award, The Foundation Fighting Blindness (2000)
Senior Scientific Investigator, Research to Prevent Blindness, Inc. (2001)
Alcon Research Institute Award (2001)
Tom and Sandy Trudell Research Award, The Foundation Fighting Blindness (2007)
Sayer Lecture and Award Series at the National Eye Institute (2007)
Senior Fellow of the American Asthma Foundation (2007–2011)
Knight's Cross of the Order of Merit of the Republic of Poland Sep 22, 2011. New York from the President of Poland Bronislaw Komorowski
The Roger H Johnson Macular Degeneration Award, the Department of Ophthalmology, University of Washington, June 16 2012
The John S. Diekhoff Award 2012 Nominee "Excellence in Graduate Mentoring"
Recipient of 2012 Award from Foundation for Polish Science (highest ranking research award in Poland)
The CWRU Faculty Distinguished Researcher Award (2013)
The Friedenwald Award 2014 from The Association for Research in Vision and Ophthalmology
Distinguished Fellow of Polish-American Scientists Honored by Kosciuszko Foundation's Collegium of Eminent Scientists
The 2014 Maurice Saltzman Award, Mt. Sinai Health Care Foundation, Cleveland
The 2014 Beckman - Argyros Award in Vision Research (intended to reward individuals who are making significant transformative breakthroughs in vision research)

Professional organizations

American Society for Biochemistry and Molecular Biology
Association for Research in Vision and Ophthalmology (ARVO)
Member, Award Committee (1998–2003)
Federation of American Societies for Experimental Biology (FASEB)

Teaching responsibilities

2001–2004 Chemistry, Chemical Biology 532
1996–2001 Graduate School Supervisory Committee for Susan Carol Stankewitz-Frey (PhD student).
1997–2001 Graduate School Supervisory Committee for Terry Cook PhD student, Pharmacology)
1998–2001 Graduate School Supervisory Committee for Gary Meints (PhD student, Chemistry)
1999–2004 Supervisor for Joshua McBee (PhD student, Chemistry)
2002–2004 Graduate School Supervisory Committee for Joseph Tsung – Yo Ho (PhD student, Neurobiology and Biology, Neurosurgery)
2002–2004 Graduate School Supervisory Committee for Jeremy Celver (PhD student, Pharmacology)
2002–2005 Graduate School Supervisory Committee for Gary E. Oerli (PhD student, Molecular and Cellular Biology, Genetics)
2002–2005 Graduate School Supervisory Committee for James Francis Carey (PhD student, Molecular and Cellular Biology)
2002–2006 Supervisor for Li Zhu (PhD student, Chemistry)
2005–2006 Supervisor for Xiaomeng Zhou (PhD student, Pharmacology)
2005–2010 Supervisor for Philip Kiser (PhD student, Pharmacology)
2010 Promoter PhD committee Anja Mohr (Supervisor, Prof. Dr. Andreas Plückthum) Universität Zürich "Selection of specific binding designed ankyrin repeat proteins for the adenosine receptor 2A via different phage display strategies"
2008–2013 Supervisor for Debarshi Mustafi (M.D., Ph.D. program, Pharmacology)
2007 MSTP mentor
2007 Supervisor for Teresa Capristo (SURP student)
2007–2013 Graduate School Supervisory Committee for Alexander Veenstra (PhD student, Pharmacology)
2008 Supervisor for Xuewu Sui (PhD student, Pharmacology)
2008 Graduate School Supervisory Committee for Seth Villarreal (PhD student, Pharmacology)
2008 Graduate School Supervisory Committee for Darwin Babino (PhD student, Pharmacology)
2012 Graduate School Supervisory Committee for Michele Mumaw (PhD student, Pharmacology)
2013 Supervisor for Lukas Hofmann (PhD student, Pharmacology, Ph.D. program)
2013 Supervisor for Sahil Guliati (with Phoebe Stewart; PhD student, Pharmacology, Ph.D. program)

Editorial responsibilities (current)

Editorial Board (Advisory Board)
Journal of Biological Chemistry (2007–2012; 2013–2018)
FASEB Journal (2008–)
Investigative Ophthalmology & Visual Science (1999–)

Biochemistry	(2005–2016)
Acta Biochimica Polonica (Polish Biochemical Society, Polish Academy of Sciences)	(2001–)
Drug Discovery Today: Disease Models	(2002–)
Central European Journal of Biology (CEJB)	(2005–)
The Open Pharmacology Journal	(2007–)
Molecular and Cellular Pharmacology	(2008–)

Editorial responsibilities (past)

Annexins	(2003–2006)
Molecular Pharmacology	(2002–2012)

Book and series editor

Methods in Enzymology, volumes 315 and 316, "Phototransduction and the Visual Cycle" Academic Press (2000)

Photoreceptors and Calcium: Advances in Experimental Medical and Biology, vol. 514. Edited by W. Baehr and **K. Palczewski**. Copyright © 2002 Kluwer Academic/Plenum Publishers and Landes Bioscience

Thematic mini–reviews in J Biol Chem (6 articles) Focus on Vision. 2011

Thematic mini–reviews in Chemical Reviews (5 articles) Chemistry and Biology of Retinoids and Carotenoids. 2014

Patents issued

1. "Method for identifying and purifying a cancer associated retinopathy autoantigen, and testing patient serum for the autoantibody to the autoantigen"; US patent 5,405,749; (with Dr. Arthur Polans).
2. "Purified protein for identifying a cancer–associated retinopathy autoantibody"; US patent 5,753,522; (with Dr. Arthur Polans).

3–4. "Methods for assessing a physiological state of a mammalian retina"; US patents: 7,706,863 and 8,346,345; (with Drs. Eric Seibel, Bryan Sires, Yoshikazu Imanishi).

5. "Methods for the treatment and prevention of age–related retinal dysfunction"; US patent 8,324,270; (with Drs. Tadao Maeda, David Saperstein).
6. "Retinal derivatives and methods for the use thereof for the treatment of visual disorders"; US patent 7,951,841; (with Mr. Matthew Batten).
7. "Methods for treating metabolic diseases"; US patent 8,338,394; (with Drs. Alex Moise, Vladimir Kuksa).
8. "Compounds and methods of treating ocular disorders" US patent 8,722,669 (with Drs. Akiko Maeda, and Marcin Golczak).

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1983–2009 numer of published papers: 286
2010–2014 number of published papers: 123

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