Walter J. Lukiw, BS, MS, PhD
Associate Professor of Neuroscience & Ophthalmology LSU Neuroscience Center, Louisiana State University Health Sciences Center, New Orleans, LA 70112 (email: wlukiw@lsuhsc.edu)

Education
1988-1992 PhD, University of Toronto, Toronto, ON 1986-1987 MS, York University, NY Research Institute, Staten Island, NY 1983-1985 BS, University of Toronto, Toronto, ON

Positions
2003 – present: Associate Professor of Neuroscience and Ophthalmology 1999-2002: Assistant Professor, LSU Neuroscience Center, New Orleans, LA 1993-1998: Postdoctoral fellow, LSU Neuroscience Center, New Orleans, LA

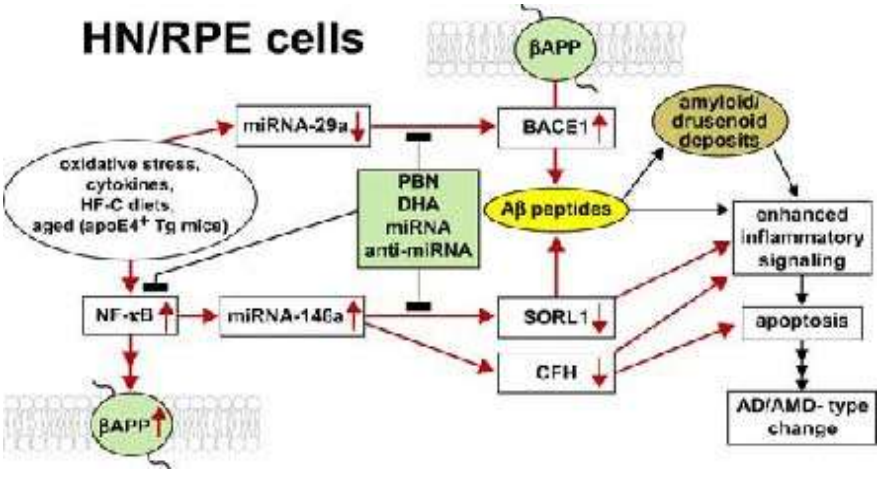
Current Research
Molecular-genetic mechanisms involved in pathological signaling in age-related macular degeneration (AMD), Alzheimer's disease (AD), glioblastoma multiforme (GBM); potential drug strategies for the clinical improvement of these neurological disorders.

Research Interests and Goals
Alzheimer's disease, bioinformatics, brain gene transcription, chromatin structure, complexity, DNA polymorphisms, environmental health, genetic, evolution, genotoxicity, inflammation, memory, neurodegeneration, neurological disorders, neurotoxicity, messenger RNA, oxidative stress, sleep cycles, small RNA, trace metals.

Awards/Recognitions/Invited Lectures (last 4 years)
Editorial Board: ***Cell. & Molec. Neurobiol.; Neurochem. Research***, ***Molec. Neurobiol., Journal of Alzheimer's Disease*** 2009- Plenary speaker, 9th Annual International Keele Meeting on Trace Metals, Prague, CZECH REPUBLIC2009- Platform speaker, Asia-ARVO 2nd Annual Meeting, Hyderabad, INDIA2008- Symposium speaker, Laurentian University Department of Biochemistry, Sudbury, CANADA2008- Platform, Association for Research in Vision & Ophthalmology (ARVO), Ft. Lauderdale, FL, USA2008- Plenary speaker, 11th International Congress of Alzheimer's Disease, Chicago IL, USA 2008- Platform speaker, Wyeth Nutritional Pharmaceuticals Symposium, Madison, NJ, USA 2007- Plenary, Seventh International Keele Meeting on Trace Metals in the Brain, Uxmal, MEXICO 2007- 'Retina Symposium' Speaker, Asia-ARVO 2007 General Meeting, SINGAPORE2006- Platform, Association for Research in Vision & Ophthalmology (ARVO), Ft. Lauderdale, FL, USA2006- Plenary, Neurodegeneration and Neuroprotection Symposium, Munster, GERMANY2006- Platform, Society for Neuroscience Annual Meeting, Atlanta, GA, USA 2005-Plenary, Sixth International Keele Meeting on Trace Metals in the Brain, Busaco, PORTUGAL 2005- Platform, Association for Research in Vision & Ophthalmology (ARVO), Ft. Lauderdale, FL, USA 2005- Platform, Joint ISN-ESN Satellite Meeting on Neurodegeneration, Warsaw, POLAND

Research Summary
Our major research interests are the elucidation of inflammatory signaling circuitsin Alzheimer's disease (AD) and in age-relatedmacular degeneration (AMD). *AD and AMD represent common, progressive degenerative disorders of human neural (HN) and retinal pigment epithelial (RPE) cells, respectively. Oxidative stress, cytokines, high fat-cholesterol (HF-C) diets, the lipid transporter apolipoprotein E4 (apoE4), and aging, are prominent risk factors for the development of AD and AMD (oval at middle left). These risk factors up-regulate a set of stress-sensitive transcription factors that include, prominently, NF-κB. Promoter mapping of the regulatory regions of the gene encoding beta-amyloid precursor protein (βAPP), is enriched in NF-κB binding sites. Micro RNAs (miRNAs) act as highly effective post-transcriptional repressors of gene expression. NF-κB also up-regulates miRNA-146a expression with resultant down-*

regulation of sortilin-1 (SORL1) and CFH. SORL1 and CFH down-regulation are associated with increased Aβ peptide generation and Aβ peptide-mediated pathogenic events that (1) contributes to amyloid and drusenoid deposition, (2) enhances inflammatory signaling and apoptosis and (3) drives AD/AMD-type change. In a parallel pathogenic circuit miRNA-29a down-regulation induces up-regulation of betaamyloid cleavage enzyme 1 (βACE1) expression. βACE1-mediated cleavage of the polytopic membrane spanning protein βAPP (green ovals) ultimately increases Aβ peptide abundance that further contributes to amyloid and drusen formation and enhanced inflammatory signaling. Vertical up- or down-arrows within boxes indicate up- or down-regulation, respectively; filled light green box indicates potential blocking compounds – highly penetrant antioxidants such as phenyl butyl nitrone (PBN), the essential omega-3 fatty acid DHA, and miRNA and anti-miRNA strategies. We hypothesize that these specific pathways of genetic mis-regulation in human brain and retinal cells lead to an inflammatory response, resulting in apoptotic changes that are direct precursors to early pathological change in both AD and AMD.



Recent Peer-Reviewed Publications (last 4 years; from ~116 total)

Prerna S and **Lukiw WJ.** Micro-RNA (miRNA) abundance and stability in human brain & retina, RNA Journal, under revision (2009).

Culicchia F, Cui JG, Zhao Y, **Lukiw WJ**. Up-regulation of micro-RNA 221 (miRNA-221) and caspase 3 accompanies down-regulation of survivin-1 (NAIP) anti-apoptotic protein in advanced GBM, J. Neurooncology 89:255-262 (2009).

Lukiw WJ. Docosahexaenoic acid (DHA) and amyloid-beta (Aβ) peptide signaling in Alzheimer's disease (AD). World Review of Nutrition & Diet 99:55-70 (2009).

Dufault R, Leblanc B, Schnoll R, Cornett C, Schweitzer L, Patrick L, Hightower J, Wallinga D, **Lukiw WJ**. Mercury from chlor-alkali plants: measured concentrations in food product sugar. Environmental Health 8:2-12 (2009).

Kruck TP, Percy ME, **Lukiw WJ**. Metal sulfate-mediated induction of pathogenic genes and repression by phenyl butyl nitrone (PBN) and Feralex-G (FXG). Neuroreport 19:245-249 (2008).

Lukiw WJ. Aβ-peptide modulators for Alzheimer's disease, Expert Opinion Emerging Drugs 13:255-271 (2008).

Hill JM, Ball MJ, Neumann DM, Azcuy AM, Bhattacharjee PS, Bouhanik S, Clement C, **Lukiw WJ**, Foster TP, Kumar M, Kaufman HE, Thompson HW. High prevalence of HSV1 in human trigeminal ganglia is not a function of age. J. Virology 82:8230-8234 (2008).

Lukiw WJ and Bazan NG. Docosahexaenoic acid (DHA) in brain aging. J. Nutrition, 138:2510-2514 (2008).

Lukiw WJ, Cui JG, Zhao JG. An NF-κB-sensitive microRNA-146a-mediated inflammatory circuit in Alzheimer's disease and in stressed human brain cells, J. Biol Chemistry 283:31315-31322 (2008).

J Cui JG, Hill JM, Zhao Y, **Lukiw WJ**, Expression of inflammatory genes in the primary visual cortex of late-stage Alzheimer's disease, Neuroreport 18:115-9 (2008).

Lukiw WJ. Micro RNA speciation in fetal, aged and Alzheimer hippocampus, Neuroreport 18:297-300 (2007).

Lukiw WJ, Pogue AI. Induction of specific micro-RNA (miRNA) species by ROS-generating metal sulfates in primary human brain cells. J. Inorg Biochem. 101:1265-1269 (2007).

Lukiw WJ. 100 years of AD research; are we any closer to a cure? Aging Health 3:279-282 (2007).

Zhao Y, J Cui JG, Hill JM, **Lukiw WJ.** Reduction of sortilin-1 in Alzheimer hippocampus and in cytokine-stressed human brain cells. Neuroreport 18:1187-1191 (2007).

Boetkjaer A, Boedker M, Cui JG, Zhao Y, **Lukiw WJ**. Synergism in the repression of COX-2- and TNFalpha-induction in platelet activating factor-stressed human neural cells. Neuroscience Letters 426:59-63 (2007).

Lukiw WJ. Cholesterol and 24S-hydroxycholesterol trafficking in Alzheimer's disease. Expert Rev. Neurotherapeutics 6:683-693 (2007).
Zhao Y, Cui JG, **Lukiw WJ.** Natural secretory products of human neural and microvessel endothelial cells; implications in pathogenic 'spreading' in Alzheimer's disease, Molecular Neurobiology, 34:181-192. (2006).
Lukiw WJ, Bazan NG. Survival signaling in Alzheimer's disease. Biochem Soc Trans 34:1277-1282 (2006).
Lukiw WJ, Cui JG, Marcheselli VL, Bodker M, Botkjaer A, Bazan NG. A role for DHA-derived neuroprotectin D1 in neural cell survival and Alzheimer disease. J. Clinical Investigation 115:2774-2783 (2005).
Cui JG, Zhao Y, **Lukiw WJ**. Isolation of high spectral quality RNA using run-on gene transcription: application to gene expression profiling, Cellular & Molecular Neurobiology 25:789-794 (2005).
Alexandrov PN, Zhao Y, Pogue AI, Tarr MA, Kruck TP, Percy ME, Cui JG, **Lukiw WJ**. Synergistic effects of iron and aluminum on stress-related gene expression. J. Alzheimer's Dis. 2005 8:117-127 (2005).
Lukiw WJ, Pappolla MA, Peleaz RP and Bazan NG. Alzheimer's disease – A dysfunction of cholesterol and brain lipid metabolism, Cellular & Molecular Neurobiology 25:475-483 (2005).
Cui JG, Salehi-Rad S, Rogaeva E, **Lukiw WJ.** Functional analysis of a cyclooxygenase-2 -765G->C promoter polymorphism in human neural cells, Neuroreport 16:575-579*,* (2005).
Lukiw WJ. Gene expression profiling in fetal, aged and Alzheimer hippocampus – a continuum of stress-related signaling. Neurochemical Research, 29:1287-1297 (2005).

Funding
"Microarray gene expression bi-clustering using associative pattern mining"; Investigators - Prerna Sethi andWalter J. Lukiw; Agency - Louisiana Biotechnology Research Network (LBRN).
"Gene expression patterns in glioblastoma multiforme (GBM)"; Investigators - Walter J. Lukiw; Agency - Translational Research Initiative (TRI), Louisiana State University Board of Reagents.
"Mentoring Neuroscience in Louisiana: A biomedical program to enhance neuroscience" (COBRE); ProjectDirector – Nicolas G. Bazan; Mentor – Walter J. Lukiw; Agency - NIH, NCRR
"Rule-based data mining for knowledge discovery in Alzheimer's disease using Microarray Databases";Investigators - Prerna Sethi and Walter J. Lukiw; Agency – Louisiana-INBRE program (pending).
"miRNA signaling in Alzheimer's disease (AD)"; Investigator - Walter J. Lukiw; Agency NIH, NIA (pending).