

BIOGRAPHICAL SKETCH

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NAME Robert D. Moir, Ph.D.	POSITION TITLE		
eRA COMMONS USER NAME (credential, e.g., agency login)	Assistant Professor		
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
University of Western Australia, Australia	B. Sc. (Hon)	1985	Honors Biochemistry
University of Melbourne, Australia	Ph.D.	1995	Medical Biochemistry

NOTE: The Biographical Sketch may not exceed four pages. Follow the formats and instructions on the attached sample.

B. Positions and Honors

1986 Research Assistant, Endocrinology Department, King Edward Memorial Hospital, Australia
 1987 Tutor (part-time) Biochemistry Department, University of Western Australia, Australia
 1987-1989 Lecturer (part-time), Pharmacology Department, Curtin University of Technology, Australia
 1994-1997 Research Fellow, Harvard Medical School/Massachusetts General Hospital, USA
 1997-2006 Assistant Geneticist in Neurology, Massachusetts General Hospital (Neurology Service MGH)
 1997-2006 Instructor in Neurology, Department of Neurology, Harvard Medical School
 2006-present Assistant Professor, Harvard Medical School/Massachusetts General Hospital, USA

Other Experience and Professional Memberships

1995- Member, Society for Neuroscience
 2008- Editor, International Journal of Biomedical Nanoscience and Nanotechnology

Honors:

1990 Mental Health and Research Institute of Victoria Alzheimer's Disease Research Scholarship
 1994 Postdoctoral Scholarship - University of Melbourne
 1997 Postdoctoral Fellowship Award - Massachusetts General Hospital Fund for Medical Discovery

C. Selected Peer-reviewed Publications (from 50)**Additional recent publications of importance to the field (in chronological order)**

- 1 Moir RD and Stokes GB. A spectrophotometric assay for 6-phosphogluconolactonase using immobilized enzymes to prepare the labile 6-phosphogluconolactone, *Biochem. J.* 1988; 256: 69-73.
- 2 Ratajczak T, Comber M, Moir RD and Hahnel R. The amino-terminal sequence for the 85-90 KD nonhormone binding component of the molybdate-stabilized estradiol receptor from calf uterus. *Biochem. Biophys. Res. Comm.* 1987; 143: 218-224.
- 3 Bush AI, Martins RN, Rumble B, Moir RD, Fuller SJ, Milward EA, Currie J, Ames D, Weidemann A, Fischer P, Multhaup G, Beyreuther K and Masters CL. The amyloid precursor protein of Alzheimer's disease is released by human platelets. *J. Biol. Chem.* 1990; 265: 15977-15983.
- 4 Small DH, Moir RD, Fuller SJ, Michaelson S, Bush AI, Li Q-X, Milward EA, Hilbich C, Weidemann A, Beyreuther K and Masters CL. A protease activity associated with acetylcholinesterase releases the membrane-bound form of the amyloid precursor protein of Alzheimer's disease. *Biochemistry* 1991; 30: 10795-10799.
- 5 Moir RD, Martins RN, Small DH, Bush AI, Milward EA, Multhaup G, Beyreuther K and Masters CL. Human brain β A4 amyloid protein precursor (APP) of Alzheimer's Disease: purification and partial characterization. *J. Neurochemistry* 1992; 59: 1490-1498.

- 6 Milward EA, Papadopoulos R, Fuller SJ, Moir RD, Small DH, Beyreuther K and Masters CL. The amyloid protein precursor of Alzheimer's disease is a mediator of the effects of nerve growth factor on neurite outgrowth. *Neuron* 1992; 9: 129-137.
- 7 Small DH, Nurcombe V, Moir RD, Michaelson S, Monard D, Beyreuther K and Masters CL. Association and release of the amyloid protein precursor of Alzheimer's disease from chick brain extracellular matrix. *J. Neurosci.* 1992;12: 4143-4150.
- 8 Bush AI, Multhaup G, Moir RD, Williamson TG, Small DH, Rumble B, Pollwein P, Beyreuther K and Masters CL. A novel zinc(II) binding site modulates the function of the β A4 amyloid protein precursor of Alzheimer's disease. *J. Biol. Chem.* 1993; 268: 16109-16112.
- 9 Small DH, Nurcombe V, Reed G, Clarris H, Moir RD, Beyreuther K and Masters CL. A heparin-binding domain in the amyloid protein precursor of Alzheimer's disease is involved in the regulation of neurite outgrowth. *J. Neuro. Chem.* 1994; 14: 2117-2127.
- 10 Bush AI, Moir RD, Rosenkranz KM and Tanzi RE. Zinc and Alzheimer's Disease. *Science* 1995; 268: 1921-1922.
- 11 Kounnas MZ, Moir RD, Rebeck CW, Bush AI, Argraves WS, Tanzi RE, Hyman BT and Strickland DK. LDL receptor-related protein, a multifunctional apolipoprotein E receptor, binds secreted β -amyloid precursor protein and mediates its degradation. *Cell* 1995; 82: 331-40.
- 12 Kovacs DM, Fausett HJ, Page KJ, Kim T-W, Moir RD, Merriam DE, Hollister RD, Hallmark OG, Mancini E, Felsenstein KM, Hyman BT, Tanzi RE and Wasco W. Alzheimer-associated presenilins 1 and 2: Neuronal expression in brain and localization to intracellular membranes in mammalian cells. *Nature Med.* 1996; 2: 224-229.
- 13 Kim T-W, Pettingell WH, Hallmark OG, Moir RD, Wasco W, and Tanzi RE. Endoproteolytic cleavage and proteasomal degradation of presenilin 2 in transfected cells. *J. Biol. Chem.* 1997; 272: 11006-11010.
- 14 Huang X, Atwood CS, Moir RD, Hartshorn MA, Vonsattel J-P, Tanzi RE and Bush AI. Zinc-induced Alzheimer's disease A β 1-40 aggregation is mediated by conformational factors. *J. Biol. Chem.* 1997; 272: 26464-26470.
- 15 Hock C, Golombowski S, Müller-Spahn F, Naser W, Beyreuther K, Mönning U, Schenk D, Vigo-Pelfrey C, Bush AI, Moir RD, Tanzi RE, Growdon JH and Nitsch RM. Cerebrospinal fluid levels of Amyloid Precursor Protein and amyloid β -peptide in Alzheimer's disease and major depression- Inverse correlation with dementia severity. *Eur. Neurol.* 1998; 29: 111-118.
- 16 Atwood CS, Moir RD, Huang X, Scarpa RC, Bacarra MN, Romano DM, Hartshorn MA, Tanzi RE and Bush AI. Dramatic aggregation of Alzheimer A β by Cu(II) is induced by conditions representing physiological acidosis. *J. Biol. Chem.* 1998; 273: 12817-12826.
- 17 Moir RD, Lynch T, Bush AI, Multhaup G, Whyte S, Tanzi RE, Small DH, Beyreuther, K and Masters, CL. Relative increase in Alzheimer's disease of soluble forms of cerebral A β amyloid protein precursor containing the Kunitz Protease Inhibitory domain. *J. Biol. Chem.* 1998; 273: 5013-5019.
- 18 Moir RD, Bush AI, Romano DM, Atwood CS, Huang X., Smith J and Tanzi RE. Differential effects of apolipoprotein E isoforms on metal-induced aggregation of A β under physiological conditions. *Biochemistry* 1999; 38: 4595-4603.
- 19 Huang X, Atwood CS, Hartshorn MA, Multhaup G, Goldstein LE, Scarpa RC, Cuajungco MP, Gray DN, Lim J, Moir RD, Tanzi RE and Bush AI. The A β peptide of Alzheimer's Disease directly produces hydrogen peroxide through metal ion reduction. *Biochemistry.* 1999; 38: 7609-7616.
- 20 Huang X, Cuajungco MP, Atwood CS, Hartshorn MA, Tyndall J, Hanson GR, Stokes KC, Multhaup G, Goldstein LE, Scarpa RC, Saunders AJ, Lim J, Moir RD, Glabe CG, Bowden EF, Masters CL, Fairlie DP, Tanzi RE and Bush AI. Cu(II) potentiation of Alzheimer A β neurotoxicity: correlation with cell-free hydrogen peroxide production and metal reduction. *J. Biol. Chem.* 1999; 274: 37111-37116.
- 21 Atwood CS, Scarpa RC, Huang X, Moir RD, Jones WD, Fairlie DP, Tanzi RE and Bush AI Characterization of Copper Interactions with Alzheimer A β Peptides- Identification of a Femtomolar Affinity Copper Binding Site on A β 1-42. *J. Neurochem.* 2000; 75: 1219-1233.
- 22 Liu Y, Jones M, Hingtgen, Bu G, Larabee N, Tanzi RE, Moir RD, Nath A and He J. Uptake of human immunodeficiency virus-1 Tat protein mediated by low-density lipoprotein receptor-related protein disrupts the neuronal metabolic balance of ligands for low-density lipoprotein-related protein. *Nature Med.* 2000; 6: 1380-1386.

- 23 Cherny RA, Atwood CS, Xilinas ME, Gray DN, Jones WD, Catriona A, McLean CA, Barnham BJ, Volitakis I, Fraser FW, Kim Y-S, Huang X, Goldstein LE, Moir RD, Lim JT, Zheng H, Tanzi RE, Masters CL and Bush AI. Treatment with a copper-zinc chelator markedly and rapidly inhibits β -amyloid accumulation in Alzheimer's disease transgenic mice. *Neuron*. 2001; 30: 665-676.
Rebeck GW, Moir RD, Mui S, Strickland DK, Tanzi RE, and Hyman BT. Association of membrane-bound amyloid precursor protein APP with the apolipoprotein E receptor LRP. *Mol. Brain Res*. 2001; 87: 238-245.
- 24 Rogers JT, Randall JD, Eder PS, Huang X, Bush AI, Tanzi RE, Venti A, Payton SM, Giordano T, Nagano S, Cahill CM, Moir RD, Lahiri DK, Greig N, Sarang SS and Gullans SR. Alzheimer's disease drug discovery targeted to the APP mRNA 5'untranslated region. *J. Mol. Neurosci*. 2002; 30: 77-82.
- 25 Opazo C, Huang X, Cherny RA, Moir RD, Roher AE, White AR, Cappai R, Masters CL, Tanzi RE, Inestrosa NC and Bush AI. Metalloenzyme-like activity of Alzheimer's disease β -amyloid: Cu-dependent catalytic conversion of dopamine, cholesterol and biological reducing agents to neurotoxic H_2O_2 . *J. Biol. Chem*. 2002; 277: 40302-40308.
- 26 Goldstein LE, Muffat JA, Cherny RA, Moir RD, Ericsson MH, Huang X, Mavros C, Coccia JA, Faget KY, Fitch KA, Masters CL, Tanzi RE, Chylack LT, Bush AI. Cytosolic β -amyloid deposition and supranuclear cataracts in lenses from people with Alzheimer's disease. *Lancet* 2003; 361: 1258-1265.
- 27 Atwood CS, Perry G, Zeng H, Kato Y, Jones WD, Ling KQ, Huang X, Moir RD, Wang D, Sayre LM, Smith MA, Chen SG, Bush AI. Copper Mediates Dityrosine Cross-Linking of Alzheimer's Amyloid- β . *Biochemistry*. 2004; 43: 560-568.
- 28 Xie Z, Moir RD, Romano DM, Tesco G, Kovacs DM, Tanzi RE. Hypocapnia Induces Caspase-3 Activation and Increases A β Production. *Neurodegenerative Dis*. 2004; 1: 29-37.
- 29 Nagano S, Huang X, Moir RD, Payton SM, Tanzi RE, Bush AI. Peroxidase activity of COX-2 cross-links A β and generates A β : COX-2 hetero-oligomers that are increased in Alzheimer's disease. *J Biol. Chem*. 2004; 279: 14673-14678.
- 30 Hutter-Paier B, Huttunen HJ, Puglielli L, Eckman CB, Kim DY, Hofmeister A, Moir RD, Domnitz SB, Frosch MP, Windisch M, Kovacs DM. The ACAT Inhibitor CP-113,818 Markedly Reduces Amyloid Pathology in a Mouse Model of Alzheimer's Disease. *Neuron* 2004; 44: 227-238.
- 31 Dedeoglu A, Cormier K, Payton SM, Tseitlin KA, Shen LF, Pearlmanf RS, Laig L, Lig X, Moir RD, Tanzi RE, Bush AI, Kowall NW, Rogers JT, Huang X. Preliminary studies of a novel bifunctional metal chelator targeting Alzheimer's amyloidogenesis. *Exp. Gerontol*. 2004; 39: 1641-1649.
- 32 Huang X, Atwood CS, Moir RD, Hatshorn MA, Tanzi RE, Bush AI. Trace metal contamination initiates the apparent auto-aggregation, amyloidosis, and oligomerization of Alzheimer's disease A β peptides. *J. Biol. Inorg. Chem*. 2004; 9: 954-960.
- 33 Moir RD, Tseitlin KA, Soscia S, Hyman BT, Irizarry MC, Tanzi RE. Autoantibodies to redox-modified oligomeric A β are attenuated in the plasma of AD patients. *J. Biol. Chem*. 2005; 280: 17458-17463.
- 34 Moir RD, Tanzi RE. LRP-mediated clearance of A β is inhibited by KPI-containing isoforms of APP. *Curr. Alzheimer Res*. 2005; 2: 269-273.
- 35 Xie Z, Dong Y, Maeda U, Moir RD, Xia W, Culley DJ, Crosby G, Tanzi RE. Inhalation anesthetic isoflurane induces a vicious cycle of apoptosis and A β generation. *J. Neurosci*. 2006; 27: 1247-54.
- 36 Xie Z, Dong Y, Maeda U, Moir RD, Inouye S, Culley DJ, Crosby G, Tanzi RE. Isoflurane-induced apoptosis: a potential pathogenic link between delirium and dementia. *J. Gerontol*. 2006 61:1300-6.
- 37 Zhang B, Dong Y, Zhang G, Moir RD, Xia W, Yue Y, Tian M, Culley DJ, Crosby G, Tanzi RE, Xie Z. The inhalation anesthetic desflurane induces caspase activation and increases amyloid β -protein levels under hypoxic conditions. *J. Biol. Chem*. 2008; 283:11866-75.
- 38 Xie Z, Culley DJ, Dong Y, Zhang G, Zhang B, Moir RD, Frosch MP, Crosby G, Tanzi RE. The common inhalation anesthetic isoflurane induces caspase activation and increases amyloid β -protein level in vivo. *Ann. Neurol*. 2008; 64: 618-27.
- 39 Myre MA, Washicosky K, Moir RD, Tesco G, Tanzi RE, Wasco W. Reduced amyloidogenic processing of the amyloid β -protein precursor by the small-molecule Differentiation Inducing Factor-1. *Cell Signal*. 2009; 21: 567-76.
- 40 Dong Y, Zhang G, Zhang B, Moir RD, Xia W, Marcantonio ER, Culley DJ, Crosby G, Tanzi RE, Xie Z. The common inhalational anesthetic sevoflurane induces apoptosis and increases β -amyloid protein levels. *Arch. Neurol*. 2009; 66: 620-31.

- 41 Soccia SJ, Kirby JE, Washicosky KJ, Tucker SM, Ingelsson M, Hyman B, Burton MA, Goldstein LE, Duong S, Tanzi RE, Moir RD. The Alzheimer's Disease-Associated Amyloid β -Protein Is an Antimicrobial Peptide. *PLoS ONE* 2010; 5(3): e9505.
- 42 Moncaster JA, Pineda R., Moir RD, Lu S, Burton MA, Ghosh JG, Ericsson M, Soccia SJ, Mocofanescu A, Folkerth RD, Robb RM, Kuszak JR, Clark JI, Tanzi RE, Hunter DG, Goldstein LE. Alzheimer's Disease Amyloid- β Links Lens and Brain Pathology in Down Syndrome. *PLoS ONE* 2010; In Press.

D. Research Support

Ongoing Research Support

Cure Alzheimer's Fund Research Grant 1/1/2009-6/31/2010
Potential for host cell cytotoxicity from microbially-derived A β oligomers
Our findings suggest the normal function of A β involves oligomerization in the presence of microbial organisms. This project investigates the potential direct and pro-cytokine pathological actions of microbially generated A β oligomers.

Role: PI

RO1 1R01AI081990-01A1 04/01/2010- 03/31/2015

The A β protein of Alzheimer's Disease is an antimicrobial peptide
Investigation of the role of A β in innate immunity as an antimicrobial peptide.

Role: PI

Helmsley Foundation 10/1/2010-9/31/2012

The amylin protein of diabetes mellitus is an antimicrobial peptide.
Amylin is a small peptide that forms amyloid deposits in the pancreas of patients with type II diabetes. This project investigates a novel role for amylin as a natural antibiotics functioning as part of the innate immune system to help fight infection.

Role: PI

Completed Research Support

Cure Alzheimer's Fund Research Grant 1/1/2008-12/31/2008

Neurotoxicity of cross-linked β -amyloid protein species
This project investigated conditions that promote the formation soluble of A β oligomers (CAPS) in the brain milieu, the chemical modifications that potentiate neurotoxicity, and what agents may be useful in ameliorating the pathogenic action of these modified species of A β .

Role: PI

R21 AG027800-01 07/01/06-6/30/08

Targeting cross-linked amyloid protein species as a therapy for AD.
The focus of this study was to identify the pathologically important soluble forms of β -amyloid.

Role: PI