

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel in the order listed for Form Page 2.  
Photocopy this page or follow this format for each person.

NAME Neil William Kowall		POSITION TITLE Professor of Neurology and Pathology	
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of British Columbia, Canada	BS	1975	Physiology
University of British Columbia, Canada	MD	1979	Medicine
Beth Israel Deaconess Medical Center, Boston	Fellow	1981	Internal Medicine
Massachusetts General Hospital, Boston	Fellow	1984	Neurology

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. If the list of publications in the last three years exceeds two pages, select the most pertinent publications.

1979 Hamber Prize & Medal (Top of graduating class) U.B.C. Faculty of Medicine  
 1979-81 Residency & Fellowship, Internal Medicine, B.I. Deaconess, Harvard Med. School, Boston  
 1981-87 Residency & Fellowship (Clin&Res), Neurology, Mass. General Hosp., Harvard Med. School, Boston  
 1987-93 Asst Neurologist, Pathologist & Asst Prof Neurology, Mass General & Harvard Med School, Boston  
 1988,90 Moore Award, Best Paper Clinicopathological Correlation, Amer. Assoc. Neuropathologists  
 1993- Associate Professor to Professor Neurology & Pathology, Boston University School of Medicine  
 1993- Director, New England VA Geriatric Research Education and Clinical Center, Bedford & Boston MA  
 1997 Zenith Award (Alzheimer's Association)  
 1998-2002 Member and Chair, Med Research Adv Group (Neurological/Sensory Disorders) Dept Veterans Affairs  
 1999- Member, Brain Disorders and Clinical Neurosciences 3 special emphasis panel (study section), NIH

**Original Reports: (from a total of 113 peer reviewed)**

Ferrante RJ, Kowall NW, Beal MF, Richardson EP Jr., Bird ED, Martin JB. Selective sparing of a class of striatal neurons in Huntington's disease. *Science* 1985;230:561-563.  
 Beal MF, Kowall NW, Ellison DW, Mazurek MF, Swartz KJ, Martin JB. Replication of the neurochemical characteristics of Huntington's disease by quinolinic acid. *Nature* 1986;321:168-171.  
 Kowall NW, Kosik KS. Axonal disruption and aberrant localization of tau protein characterize the neuropil pathology of Alzheimer's disease. *Ann Neurol* 1987;22:639-643.  
 Kowall NW, Beal MF. Cortical somatostatin, neuropeptide Y, and NADPH diaphorase neurons: normal anatomy and alterations in Alzheimer's disease. *Ann Neurol* 1988;23:105-114.  
 Kowall NW, Mueller MG. NADPH diaphorase neurons in human brainstem. *Neuroscience* 1988; 26:645-654.  
 Kowall NW, Beal MF. Galanin-like immunoreactivity is present in the human substantia innominata and in senile plaques in Alzheimer's disease. *Neurosci. Lett.* 1989; 98:118-123.  
 Kelley M, Kowall NW. CRF neurons persist in Alzheimer's disease. *Brain Res* 1989;501:392-396  
 McKee AC, Kosik KS, Kennedy MB, Kowall NW. Hippocampal neurons predisposed to neurofibrillary tangle formation are enriched in Type II CaM Kinase. *J Neuropath Exptl Neurol* 1990; 49:49-63.  
 Sangruchi T, Kowall NW. NADPH diaphorase in the human hypothalamus. *Neuroscience* 1991; 40:713-724.  
 Quigley BJ, Kowall NW. Substance P neurons depleted in Alzheimer's disease. *Neuroscience* 1991;41:41-60.  
 Kowall NW, Beal MF. Glutamate, glutaminase and taurine neurons develop neurofibrillary tangles in Alzheimer's disease. *Ann Neurol* 1991; 29:162-167.  
 Beal, MF, Swartz KJ, Finn SF, Mazurek MF, Kowall NW. Neurochemical characterization of excitotoxic lesions in cerebral cortex. *J Neurosci* 1991; 11:147-158.  
 McKee AC, Kosik KS, Kowall NW. Neuritic pathology and dementia in Alzheimer's. *Ann Neurol* 1991; 30:156-165.  
 Kowall, NW, Beal MF, Busciglio J, Duffy, LK, Yankner, BA. Neurodegenerative effects of beta amyloid in the adult rat brain and protection by substance P. *Proc Natl Acad Sci.USA* 1991; 88:7247-51.

- Nihei K, Kowall NW. Neurofilament & NCAM histochemistry of Huntington's. *Ann Neurol* 1992; 31:59-63.
- Leifer D, Kowall NW. Thy-1 in hippocampus: normal anatomy and neuritic growth in Alzheimer's disease. *J Neuropathol Exptl Neurol* 1992; 51:133-141.
- Yokota M, Peterson JW, Kaoutzanis M, Kowall NW. The histochemical distribution of protein kinase C isozymes is differentially altered in ischemic gerbil hippocampus, *Brain Res* 1992;587: 123-129.
- Kowall NW, McKee AC, Yankner BA, Beal MF. In vivo neurotoxicity of beta amyloid [ $\beta(1-40)$ ] and the  $\beta(25-35)$  fragment. *Neurobiol. Aging* 1992;13:537-542.
- Nihei K, McKee AC, Kowall NW. Patterns of neuronal degeneration in the motor cortex of amyotrophic lateral sclerosis patients, *Acta Neuropathol* 1993; 86:55-64.
- Kowall NW, Quigley BJ Jr, Krause JE, Lu F, Kosofsky BE, Ferrante RJ. Substance P and substance P receptor histochemistry in human neurodegenerative diseases. *Regulatory peptides* 1993; 46:174-185.
- Nihei K and Kowall NW. Involvement of neuropeptide Y neurons in the cerebral cortex of amyotrophic lateral sclerosis patients. *Neurosci Lett* 1993; 159:67-70.
- Leifer D, Kowall NW. Immunohistochemical patterns of selective cellular vulnerability in human cerebral ischemia. *J Neurol Sci* 1993; 119:217-228.
- Giordano T, Pan JB, Monteggia LM, Holzman TF, Snyder SW, Krafft G, Ghanbari H, Kowall NW. Similarities between  $\beta$  amyloid peptides 1-40 and 40-1: effects on aggregation, toxicity *in vitro*, and injection in young and aged rats. *Exptl Neurology* 1994; 125: 175-182
- Lo EH, Pan Y, Matsumoto K, Kowall NW. Blood-brain barrier disruption in experimental focal ischemia: comparison between *in vivo* MRI and immunocytochemistry. *Magn Reson Imaging* 1994; 12:403-411.
- Storey E, Cipolloni PB, Ferrante RJ, Kowall NW, Beal MF. Movement disorder following excitotoxin lesions in primates. *NeuroReport* 1994;5:1259-1261.
- Rosen DR, Bowling AC, Patterson D, Usdin TB, Sapp P, Mezey E, O'Regan J, McKenna-Yasek D, Ferrante RJ, Brownstein MJ, Kowall NW, Beal MF, Horvitz HR, Brown RH Jr. A frequent Ala 4 to Val mutation in exon 1 of SOD1 gene: associated with rapidly progressive familial ALS. *Hum Molec Gen* 1994;3:981-987
- Volicer L, Hurley AC, Lathi DC, Kowall NW. Measurement of severity in Advanced Alzheimer's disease. *J Gerontol* 1994; 49:M223-M226.
- Matsumoto K, Lo EH, Pierce AR, Wei H, Garrido L, Kowall NW. Role of vasogenic edema and tissue cavitation in ischemic evolution or diffusion-weighted imaging: comparison with multiparameter MR and immunocytochemistry. *Am J Neuroradiol* 1995; 16:1107-1115
- Brouillet E, Hantraye P, Ferrante RJ, Dolan R, Kowall NW, Beal MF. Chronic energy impairment produces selective striatal degeneration and abnormal choreiform movements in primates. *PNAS (USA)* 1995; 92:7105-7109
- Leifer D, Speliotis L, Kowall NW. MEF2C in human brain development. *Neuroscience* 1995; 63:1067-1079.
- Beal MF, Ferrante RJ, Henshaw R, Mathews RT, Chan PH, Kowall NW, Epstein CJ, Schulz JB. 3-Nitropropionic acid neurotoxicity is attenuated in SOD transgenic mice. *J Neurochem* 1995; 65:919-922.
- Schulz JB, Mathews RT, Jenkins BG, Ferrante RJ, Siwek D, Henshaw DR, Cipolloni PB, Kowall NW, Rosen BR, Beal MF. Blockade of neuronal nitric oxide synthase protects against excitotoxicity. *J Neurosci* 1995;15:8419-29.
- Smith MA, Perry G, Richey PL, Sayre LM, Anderson VE, Beal MF, Kowall NW. Oxidative damage in Alzheimer's. *Nature* 1996;382:120-121.
- Reaume AG, Elliot JL, Hoffman EK, Kowall NW, Ferrante RJ, Siwek DF, Wilcox HM, Flood DG, Beal MF, Brown, RH Jr, Scott RW, Snider WD. Motor neurons in Cu/Zn superoxide dismutase-deficient mice develop normally but exhibit enhanced cell death after axonal injury. *Nature genetics* 1996;13:43-47
- Ferrante RJ, Schulz JB, Matthews RT, Thomas CE, Kowall NW, Gurney, M, Beal MF. Increased 3-NT and oxidative damage in mice with human Cu, Zn superoxide dismutase mutation. *Ann Neurol* 1997; 42:326-334
- Beal MF, Ferrante RJ, Browne SE, Mathews RT, Kowall, NW, Brown, RH Jr. Increased 3-nitrotyrosine in both sporadic and familial amyotrophic lateral sclerosis. *Ann Neurol* 1997;42:646-654
- Ferrante RJ, Browne SE, Shinobu LA, Bowling AC, Baik MJ, MacGarvey U, Kowall NW, Brown RH Jr, Beal MF. Evidence of increased oxidative damage in sporadic and familial ALS. *J Neurochem* 1997;69:2064-2074.
- McKee AC, Kowall NW, Schumacher JS, Beal MF. The neurotoxicity of A $\beta$  in aged primates *Amyloid* 1998;5:1-9.
- Hanlon EB, Itzkan I, Dasari RR, Feld MS, Ferrante RJ, McKee AC, Lathi D, Kowall NW. Near infrared fluorescence spectroscopy detects Alzheimer's disease *in vitro* *Photochem Photobio*, 1999;70:236-42
- Volicer L, Wells JM, McKee AC, Kowall NW. Enhanced inhibition of free radical-induced deoxyribose breakdown by Alzheimer brain homogenates. *Neurosci Lett* 1999; 270:169-72.

Shefner JM, Reaume AG, Flood DG, Scott RW, Kowall NW, Ferrante RJ, Siwek DF, Upton-Rice M, Brown RH Jr. Mice lacking cytosolic copper/zinc SOD display a distinctive motor axonopathy. *Neurology* 1999;53:1239-46.

Kowall NW, Hantraye P, Brouillet E, Beal MF, McKee AC, Ferrante RJ. MPTP induces alpha-synuclein aggregation in the substantia nigra of baboons. *Neuroreport* 2000;11:211-3.

Montine TJ, Shinobu L, Montine KS, L. J. Roberts LJ II, Kowall NW, Beal MF, Morrow JD. No difference in plasma or urine F<sub>2</sub>-isoprostanes among Huntington's disease or Alzheimer's disease, and controls. *Ann Neurol*, 2000;48:950.

Andreassen, OA, Ferrante, RJ, Klivenyi, P, Klein AM, Dedeoglu A, Albers DS, Kowall, NW, Beal, MF. Transgenic ALS mice show increased vulnerability to mitochondrial toxins MPTP and 3NP. *Exp Neurol*. 2001;168:356-63

Malin DH, Crithers MK, Lake JR, Goyarzu P, Plotner RE, Garcia, SA. Spell SH, Tomsic BJ, Giordano T, Kowall NW. Hippocampal A $\beta$  1-40 impair subsequent one-trial/day reward learning. *Neurobiol Learn Mem*, 2001; 76: 125-37

Kiechle T, Dedeoglu A, Kubilus J, Kowall NW, Beal MF, Friedlander RM, Hersch SM, Ferrante RJ. Cytochrome C and Caspase-9 Expression in Huntington's Disease *NeuroMol Med*. 2002;1:183-195

Dedeoglu A, Kubilus JK, Jeitner TM, Matson SA, Bogdanov M, Kowall NW, Matson WR, Cooper AJ, Ratan RR, Beal MF, Hersch SM, Ferrante RJ. Therapeutic effects of cystamine in a murine model of Huntington's disease. *J Neurosci*. 2002;22:8942-50.

Albright CD, Siwek DF, Craciunescu CN, Mar MH, Kowall NW, Williams CL, Zeisel SH. Choline availability alters the localization of calretinin in developing and aging mouse hippocampus. *Nutr Neurosci*. 2003;6:129-34.

McKeon-O'Malley C, Siwek D, Lamoureux JA, Williams CL, Kowall NW. Prenatal choline deficiency decreases the cross-sectional area of cholinergic neurons in the medial septal nucleus. *Brain Res*. 2003;977:278-83.

Sheridan PL, Solomont J, Kowall N, Hausdorff, JM. Influence of Executive Function on Locomotor Function: Divided Attention Increases Gait Variability in Alzheimer's Disease *J Amer Ger Soc* 2003; 51:1633-37

Ferrante RJ, Kubilus JK, Lee J, Ryu H, Beesen A, Zucker B, Smith K, Kowall NW, Ratan RR, Luthi-Carter R, Hersch SM. Histone deacetylase inhibition by sodium butyrate chemotherapy ameliorates the neurodegenerative phenotype in Huntington's disease mice. *J Neurosci*. 2003;23:9418-27.

#### Currently Funded Projects:

##### **NIH, 1 P30 AG13846, funding 7/01/96 to 6/30/06. Principal Investigator: Neil W. Kowall, M.D.**

“Alzheimer's Disease Core Center Grant”

The major goals are to: 1) To promote research on Alzheimer's disease (AD) at Boston University; 2) To establish a longitudinal clinical database on patient and caregiver populations; 3) To perform detailed postmortem analysis of human brains with AD; and 4) To provide a comprehensive information and education program for AD.

##### **NIH, P01 AG09525, funding 4/15/99 to 3/31/04. Principal Investigator: Jan K. Blusztajn, Ph.D.**

“Aging of Brain: Effect of Perinatal Choline Exposure” (Investigator)

The goal is to determine how the prenatal availability of choline and folate affect brain structure throughout the lifespan of rats and mice development through old age

##### **NIH, 1P01 AG12922, funding 04/01/00 to 3/31/05. Principal Investigator: Robert H. Brown, M.D.**

“The Role of Superoxide Dismutase In Aging and Brain Degeneration” (Investigator)

The aims of this project are to characterize the pathology of animal lesions and changes produced by manipulation of SOD expression and to perform detailed postmortem analysis on human brains studied in the center.

##### **NIH, R01 ES11343, funding 6/1/01 to 5/31/06. Principal Investigator: Konstantin Khrapko, Ph.D.**

"Role of Somatic mtDNA Mutations in Late-Onset Neurodegeneration" (Investigator)

The major goal of this project is to explore the role of homoplasmic somatic mtDNA mutations in predisposing particular neuronal populations to neurodegeneration in the late-onset neurodegenerative disease.