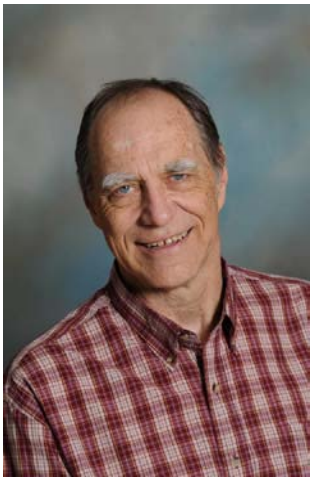

James Cleary, PhD.
• **Associate Director for Research**, GRECC, Minneapolis VA Health Care System, Minneapolis, MN
• **Member,** N. Bud Grossman Center for Memory Research, University of Minnesota, Minneapolis, MN
• **ETS Walton Visiting Scholar,** Trinity College Dublin, Ireland (2007-8)
• **Associate Professor,** Department of Neurology, University of Minnesota, Minneapolis, MN
• **Adjunct Associate Professor,** Department of Psychology, University of Minnesota, Minneapolis, MN

Research Interests:

Our research is focused on Alzheimer's disease (AD), its molecular causes, symptoms, and treatment. Major areas of interest are the neurotoxic and behavioral effects of the soluble fragments of the amyloid precursor protein, including amyloid beta peptide (Aβ). Aβ is the major component of the plaques found in brains of patients suffering from Alzheimer's disease, and is implicated in the cascade of neurological events leading to neural and behavioral pathogenesis. We have recently focused on small soluble conformations of the Aβ peptide that produce memory loss in animals. We developed sensitive bioassays for AD-like cognitive changes and which allow us to inject oligomers of Aβ, or other soluble amyloid fragments, directly into the brains of rats while they perform memory assessment tasks. We use these assays to help understand the mechanisms of memory loss. These results allow us to test potentially therapeutic drugs for Alzheimer's disease.

We also use transgenic mouse models to assess contributions of mutant proteins in neurodegenerative disease and to test potential therapeutic interventions. We use single, double and triple mutant models of neurodegenerative disease as well as models which allow regulation of the mutant protein expression. We characterize the behavior of these mouse models under several behavioral protocols, including those for motivation, attention, perception and memory. We track the cognitive changes over time and compare the neurodegeneration using biochemistry and immunohistochemistry.

Recent Publications:

Cleary, J.P., Walsh, D.M., Hofmeister, J.J., Shankar, G.M., Kuskowski, M.A., Selkoe, D.J., & Ashe, K.H. (2005) Natural oligomers of the amyloid-β protein specifically disrupt cognitive function. Nature *Neuroscience, 8:* 79-84.

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McDaid DG, Kim E-M, Reid RE, Leslie J.C, **Cleary J,** O'Hare E. (2005) Parenteral antioxidant treatment preserves temporal discrimination following intrahippocampal aggregated a-beta (1-42) injections. *Behavioral Pharmacology*, 16*:* 237-242.

Walsh DM, Klyubin I, Shankar GM, Townsend M, Fadeeva JV, Betts V, Podlinsny MB, **Cleary JP,** Ashe KH, Rowan MJ, & Selkoe DJ. (2005) The role of cell-derived oligomers of Aβ in Alzheimer's disease and avenues for therapeutic intervention. *Biochem Soc Trans, 33:* 1087-1090.
Townsend M*, **Cleary JP*,** Mehta T, Hofmeister J, Lesne S, O'Hare E, Walsh DM, & Selkoe DJ. (2006) Orally available compound prevents deficits in memory caused by the Alzheimer amyloid-β oligomers. *Ann of Neurology, 60:* 668-676.
Cleary JP, Johannsdottir R, Hofmeister J, Forster C, SantaCruz K, & Ashe KH (2006) Cognitive and pathological effects of regulatable tau in adult mice. Alzheimer's and Dementia: *The Journal of the Alzheimer's Association 2:* 37. (Archived abstract).
Kotilinek AL, Westerman MA, Wang Q, Panizzon K, Lim GP, Simonyi A, Lesne S, Falinska A, Younkin LH, Younkin SG, Rowan MJ, **Cleary JP,** Wallis RA, Sun GY, Cole G, Frautschy S, Anwyl R, and Ashe KH. (2008) Cyclooxygenase-2 inhibition improves amyloid-β-mediated suppression of memory and synaptic plasticity. *Brain 131(3):* 651-664.
Poling A, Paisley-Morgan K, Panos JJ, Kim E-M, O'Hare E, **Cleary JP,** Lesne S, Ashe KH, Porritt M, & Baker LE. (2008) Oligomers of the amyloid-beta protein disrupt working memory: confirmation with two behavioral procedures. *Behavioural Brain Research, 193(2):* 230-234.
Klyubin I, Wang O, Reed , MN, Irving EA, Upton N, Hofmeister J, **Cleary JP,** Anwyl R, & Rowan MJ. (2009). Protection against Aß-mediated rapid disruption of synaptic plasticity and memory by memantine. *Neurobiology of Aging,* (19446369: Epub ahead of print).
Reed MM, Hofmeister JJ, Jungbauer L, Welzel AT, Yu C, Sherman M, Lesné S, LaDu MJ, Walsh DM, Ashe KH, **Cleary JP.** (2009) Cognitive effects of cell-derived and synthetically-derived Aß oligomers. *Neurobiology of Aging,* (PMID: 200312784: Epub ahead of print).
O'Nuallain, B, Klyubin, I., McDonald, JM, Barry, A, Dykoski, RK, **Cleary, JP**, Martijn F.B.G. Gebbink, MF, Michael J. Rowan, MJ, and Walsh, DM. (2011) A monoclonal antibody against synthetic AB-□dimer assemblies neutralizes brain-derived synaptic plasticity-disrupting Abeta*. American Journal of Neurochemistry, 119:* 189-201, 2011, PMCID: PMC3174526

Current Funding

BX001639 (PI Cleary, J) 07/01/2012—6/30/2015
Department of Veterans Affairs Merit Review Program
"Cognitive Dysfunction in Transgenic Mouse Model of Alpha-Synucleinopathy"
Project assesses cognition and neurodegeneration in a mouse model of Parkinson's disease
There is no scientific or budgetary overlap with the current proposal

Honors

E.T.S Walton Visiting School, Trinity College, Dublin Ireland 2007-2008
Top cited article in Alzheimer's disease, Nature Medicine, 2005-2006
Distinguished Alumni Award, Western Michigan University, 1998
National Research Service Award 1982-1984

Collaborations:

Grossman Center for Memory Research & Care, University of Minnesota, Minneapolis, MN
Conway Institute, University College Dublin, Dublin Ireland
Department of Pharmacology and Therapeutics, Trinity College Dublin, Dublin, Ireland
Trinity College Institute for Neuroscience, Trinity College Dublin, Dublin, Ireland
Department of Psychology, Western Michigan University, Kalamazoo, MI

Education:

- **BA Psychology –** University of Wisconsin, Eau Claire, WI, 1977
- **MA Psychology –** Western Michigan University, Kalamazoo, MI, 1980
- **PhD Psychology –** Western Michigan University, Kalamazoo, MI, 1982
- **Postdoctoral Fellow –** University of Minnesota, Minneapolis, MN 1983

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