

## X. William Yang, M.D., Ph.D.

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### PERSONAL HISTORY

#### *Business Address*

Center for Neurobehavioral Genetics,  
Jane and Terry Semel Institute for Neuroscience and Human Behavior  
Department of Psychiatry and Biobehavioral Sciences  
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### EDUCATION

- **M.S./B.S.**, Molecular Biophysics & Biochemistry, 1991, **Yale University**, New Haven, CT (**M.S. Advisor: Joan A. Steitz**).
- **Doctor of Philosophy (Ph.D.)**, 1998, **Rockefeller University (MSTP Program; Advisor: Nathaniel Heintz)**, New York, NY.
- **Doctor of Medicine (M.D.)**, 2000, **Weill Medical College of Cornell University (MSTP Program)**, New York, New York.
- **Medicine Internship**, 2000-2001, **New York-Presbyterian Hospital/Cornell Medical Center**, New York, New York.
- **Postdoctoral Fellowship**, 1998-1999; 2001-2002. Laboratory of Molecular Biology (**Advisor: Nathaniel Heintz**), **Rockefeller University**, New York, New York.

### PROFESSIONAL LICENSE

New York State Medicine (Physician) License #223628

### PROFESSIONAL EXPERIENCE

- 2019-present The Terry Semel Chair in Alzheimer's Disease Research and Treatment,  
Department of Psychiatry & Biobehavioral Sciences  
David Geffen School of Medicine  
University of California at Los Angeles
- 2011-present Full Professor (Tenured)  
Department of Psychiatry & Biobehavioral Sciences  
Center for Neurobehavioral Genetics, Semel Institute for Neuroscience & Human Behavior  
Brain Research Institute  
David Geffen School of Medicine  
University of California at Los Angeles
- 2008-2011 Associate Professor (Tenured), Department of Psychiatry & Biobehavioral Sciences  
Center for Neurobehavioral Genetics, Semel Institute for Neuroscience & Human Behavior  
Brain Research Institute

David Geffen School of Medicine  
University of California at Los Angeles

2002-2008 Assistant Professor, Department of Psychiatry & Biobehavioral Sciences  
Center for Neurobehavioral Genetics, Semel Institute for Neuroscience & Human Behavior  
Brain Research Institute  
David Geffen School of Medicine  
University of California at Los Angeles

## PROFESSIONAL ACTIVITIES

### *Committee Service*

2003-2004 Director, Gonda Vivarium Faculty Users' Committee  
2003-2006 Co-founder and Faculty Coordinator, Neurogenetics Affinity Group,  
Brain Research Institute, UCLA  
2003-2011 UCLA Chancellor's Campus Vivarium Faculty Advisory Committee  
2003-2010 Curriculum Committee, Neuroscience Inter-departmental Graduate Program  
2004- Member, UCLA MSTP Admission Committee  
2013-2015 Co-director, Transgenic & Genome Editing Core, UCLA  
2014-2016 Member, Faculty Advisory Committee to the UCLA Accelerator  
2015-2017 Co-leader, Genome Editing Affinity Group, UCLA Brain Research Institute

### *Community Service*

2008-2011 Chartered Member, **NIH Chronic Neurodegeneration Study Section (CDIN-D)**  
2008 Program Committee Member, **2009 Gordon Conference on CAG Triplet Repeat Disorders**  
2005-2007 *Ad hoc* reviewer, **NIH Chronic Neurodegeneration Study Section (CDIN-D)**  
2005-2009 Scientific Advisory Board Member, **Hereditary Disease Foundation**  
2011- Scientific Advisory Board Member, **Hereditary Disease Foundation**  
2011 *Ad hoc* reviewer, **NIH Cellular and Molecular Biology of Neurodegeneration Study Section (CMND)**  
2013 *Ad hoc* reviewer, **NIH Chronic Dysfunction and Integrative Neurodegeneration (CDIN) Study Section.**  
2011-2014 Clinical Consulting Board Member, **NIH Nanomedicine Center**  
2015-2021 Chartered Member, **NIH Cellular and Molecular Biology of Neurodegeneration Study Section (CMND)**  
2003-present Peer reviewer for journals including: *Science, Cell, Neuron, Nature Neuroscience, Nature Medicine, Nature Chemical Biology, Science Translational Medicine, Cell Stem Cell, Cell Reports, PNAS, Journal of Neuroscience, Gene & Development, Trends in Neuroscience, PLOS Biology, PLOS Genetics, eLife, Neurology, Molecular Neurodegeneration, Journal of Clinical Investigation, Neurobiology of Disease, Human Molecular Genetics, Genome Research, etc.*

### *Professional Associations and Scholarly Societies*

2002- Society for Neuroscience  
2005- American Association for Advancement of Science  
2005- Chinese Biological Investigators Society

### *Editorial Service*

2005- Editorial Board Member, **Molecular Neurodegeneration**  
2005- Faculty Member, Neurogenetics Section, **Faculty of 1000**

2012-

Editorial Member, **Journal of Huntington's Disease**

## **HONORS AND SPECIAL AWARDS**

- *Summa cum laude*; distinction in the major, Yale University (1991).
- Michael J. Fox Foundation for Parkinson's Research: Rapid Response Innovation Award (2008)
- McKnight Neuroscience of Brain Disorders Award (2009)
- Interviewed on NBC Nightly News for the Discovery of Molecular Switch for HD (May 10, 2010)
- The Carol Moss Spivak Scholar in Neuroscience from UCLA Brain Research Institute (2011-2016)
- Center for Excellence in Education Outstanding Alumni in STEM and Business (2013)
- The Most Influential Huntington's Disease Research Paper of 2014, Huntington's Disease Study Group/HD Insights (2014)
- BRAIN Initiative Award from NIH: Tools for Cells and Circuits (2014)
- Leslie Gehry Brenner Prize for Innovation in Science, Hereditary Disease Foundation (2014)
- The Most Influential Huntington's Disease Research Paper of 2015, Huntington's Disease Study Group/HD Insights (2015)
- Elected Member, American Society for Clinical Investigation (2017)
- BRAIN Initiative Award from NIH: Cell Census Network (2018)
- The Terry Semel Chair in Alzheimer's Disease Research and Treatment, Department of Psychiatry & Biobehavioral Sciences, David Geffen School of Medicine at UCLA (2019).

## **RESEARCH GRANTS RECEIVED**

*Agency:* National Institute of Mental Health/BRAIN Initiative (U01MH117079)

*Date:* September 2018-May 2023

*Title:* Dendritome mapping of genetically-defined and sparsely-labeled cortical and striatal projection neurons

*Joint-PIs:* Yang (Contact PI) & Hongwei Dong (USC)

*Agency:* National Institute of Aging (RF1AG056114)

*Date:* 04/01/2017 – 03/31/2022

*Title:* BAC transgenic mouse models of TREM2 to study neuroprotective mechanisms in AD

*PI:* Yang

*Agency:* National Institute of Neurological Disease and Stroke (R01NS113612)

*Date:* 07/01/2019 – 06/30/2024

*Title:* Novel Mouse Genetic Models to Study Modifiers of Huntington's Disease

*PI:* Yang

*Agency:* CHDI Foundation, Inc.

*Date:* 07/01/2013 – 06/30/2021

*Title:* CHDI-UCLA Collaborative Research on Huntington's Disease Systems Biology

*PI:* Yang

*Agency:* National Institute on Drug Abuse (2P50DA005010)

*Date:* 07/01/2007 – 06/30/2022

*Title:* Center for Study of Opioid Receptors and Drugs of Abuse (CSORDA) - "Molecular and Genetic Analyses of the Striatal Indirect Pathway Neuronal Circuit in Mediating Opiate Withdrawl-Induced Aversive Behavior"

*PI:* Evans *Component I PI:* Yang

*Agency:* Hereditary Disease Foundation

*Date:* 07/15/2017 – 12/14/2020

Title: Novel Fan1 knockin mice to facilitate Huntington's disease genetic modifier research  
PI: Yang

## BIBLIOGRAPHY

### RESEARCH PAPERS (PEER REVIEWED)

1. Baserga, S.J., **Yang, X.**, Steitz, J.A. Three pseudogenes for human U13 snRNA belong to class III. *Gene* 107, 347-348 (1991).
2. Baserga, S.J., **Yang, X.**, Steitz, J.A. An intact box C sequence in the U3 snRNA is required for binding of fibrillarin, the protein common to the major family of nucleolar snRNPs. *EMBO J.* 10, 2645-2651 (1991).
3. Baserga, S.J., Gilmore-Hebert, M., **Yang, X.** Distinct molecular signals for nuclear import of the nucleolar snRNA, U3. *Genes & Development* 6, 1120-1130 (1992).
4. **Yang, X.W.**, Zhong, R., Heintz, N. Granule cell specification in the developing mouse brain as defined by expression of the zinc finger transcription factor Ru49. *Development* 122: 555-566 (1996).
5. **Yang, X.W.**, Model, P., Heintz, N. Homologous recombination based modification in *E.Coli* and germline transmission in transgenic mice of an 131kb Bacterial Artificial Chromosome (BAC). *Nature Biotechnology* 15, 859-865 (1997).
6. **Yang, X.W.**, Wynder, C., Doughty, M.L., Heintz, N. BAC mediated gene-dosage analysis reveals a role for *Zipro1*(Ru49/Zfp38) in progenitor cell proliferation in cerebellum and skin. *Nature Genetics* 22, 327-335 (1999).
7. Misulovin, Z., **Yang, X.W.**, Yu, W., Heintz, N., Merfre, E. A rapid method for targeted modification and screening of recombinant Bacterial Artificial Chromosome. *J. Immuno. Methods* 257, 99-105 (2001).
8. Gong, S., **Yang, X.W.**, Li, C., Heintz, N. Highly efficient modifications of Bacterial Artificial Chromosomes (BACs) using novel shuttle vectors containing the R6Kg origin of replication. *Genome Research* 12, 1992-1998 (2002).
9. Gu, X., Li, C., Wei, W., Lo, V., Gong, S., Li, S., Iwasato, T., Itohara, S., Li, X., Mody, I., Heintz, N., **Yang, X.W.** Pathological cell-cell interactions elicited by a neuropathogenic form of mutant Huntingtin critically contribute to cortical pathogenesis in vivo. *Neuron* 46:433-444 (2005).
10. Yang, Z., Jiang, H., Chachainasakul, T., Gong, S., **Yang, X.W.**, Heintz, N., Lin, S. Modified Bacterial Artificial Chromosomes for zebrafish transgenesis. *Methods* 39, 183-188 (2006).
11. Lobo, M.K., Karsten, S.L, Gray, M., Geschwind, D.H., **Yang, X.W.** FACS-array profiling of striatal projection neuron subtypes in juvenile and adult mouse brains. *Nature Neuroscience* 9, 443-452 (2006).
12. Gu, X., Andre, V.M., Cepeda, C., Li, S.H., Li, X.J., Levine, M.S., **Yang, X.W.** Pathological cell-cell interactions are necessary for striatal pathogenesis in a conditional mouse model of Huntington's disease. *Molecular Neurodegeneration* 2, 8 (2007).
13. Lobo, M.K., Cui, Y., Ostlund, S.B., Balleine, B.W.\*, **Yang, X.W.\*** Genetic control of instrumental conditioning by striatopallidal neuron-specific S1P receptor Gpr6. *Nature Neuroscience* 10, 1395-1397. (2007) (\* co-corresponding authors).

14. Lobo, M.K., Yeh, C., **Yang, X.W.** Pivotal role of early B-cell factor 1 in development of striatonigral medium spiny neurons in the matrix compartment. *J Neurosci Res.* 86, 2134-2146 (2008).
15. Gray, M., Shirasaki D., Cepeda, C., Andre, V.M., Wilburn, B., Lu, X.H., Tao, J., Yamazaki, Y., Li, S.H., Sun, Y.E., Li, X.J., Levine, M.S., **Yang, X.W.** Full length human mutant Huntingtin with a stable polyglutamine repeat can elicit progressive and selective neuropathogenesis in BACHD mice. *J Neuroscience* 28, 6182-6195 (2008).
16. Spanpanato, J., Gu, X., **Yang, X.W.\***, Mody, I.\* Progressive synaptic pathology of motor cortical neurons in a BAC transgenic mouse model of Huntington's disease. *Neuroscience* 157, 606-620 (2008) (\* co-corresponding authors).
17. Hutnick, L.K., Golshani, P., Namihira, M., Xue, Z., Matynia, A., **Yang, X.W.**, Silva, A.J., Schweizer, F.E., Fan, G. DNA hypomethylation restricted to the murine forebrain induces cortical degeneration and impairs postnatal neuronal maturation. *Hum Mol Genet.* 18, 2875-2888 (2009).
18. Menalled, L., El-Khodori, B.F., Patry, M., Suarez-Farinas, M., Orenstein, S., Zahasky, B., Ragland, N., Leahy, C., **Yang, X.W.**, McDonald, M., Morton, J., Bates, J., Signer, E., Tobin, A., Leeds, J., Park, L., Howland, D., and Brunner, D. Systematic behavioral evaluation of Huntington's disease transgenic and knock-in mouse models. *Neurobiology of Disease* 35, 319-336 (2009).
19. Lu, X.H., Fleming, S.M., Meurers, B., Ackerson, C.A., Mortazavi, F., Lo, V., Hernandez, D., Sulzer, Z., Jackson, G.R., Maidment, N.T., Chesselet, M.F., **Yang, X.W.** BAC mice with a truncated mutant Parkin exhibit age-dependent hypokinetic motor deficits, dopaminergic neuron degeneration, and accumulation of proteinase K-resistant alpha Synuclein. *J Neuroscience* 29, 1962-1976 (2009).
20. Gu, X., Greiner, E.R., Mishra, R., Kodali, R., Osmand, A., Finkbeiner, S., Steffan, J.S., Thompson, L.M., Wetzel, R., and **Yang, X.W.** Serines 13 and 16 are critical determinants of full-length human mutant huntingtin induced disease pathogenesis in HD mice. *Neuron* 64:828-840 (2009).
21. Pouladi, M.A., Xie, Y., Skotte, N.H., Ehrnhoefer, D.E., Graham, R.K., Kim, J.E., Bissada, N., **Yang, X.W.**, Paganetti, P., Friedlander, R.M., Leavitt, B.R., Hayden, M.R. Full-length huntingtin levels modulate body weight by influencing insulin-like growth factor 1 expression. *Hum Mol Genet.* 19, 1528-1538 (2010).
22. André, V.M., Cepeda, C., Cummings, D.M., Jocoy, E.L., Fisher, Y.E., **Yang, X.W.**, Levine, M.S. Dopamine modulation of excitatory currents in the striatum is dictated by the expression of D1 and D2 receptors and modified by endocannabinoids. *Eur J Neurosci.* 31, 14-28 (2010).
23. Graham, R.K., Deng, Y., Carroll, J., Vaid, K., Cowan, C., Pouladi, M.A., Metzler, M., Bissada, N., Wang, L., Faull, R.L., Gray, M., **Yang, X.W.**, Raymond, L.A., Hayden, M.R. Cleavage at the 586 amino acid caspase-6 site in mutant huntingtin influences caspase-6 activation *in vivo*. *J Neuroscience* 30,15019-15029 (2010).
24. André, V.M., Cepeda, C., Fisher, Y.E., Huynh, M., Bardakjian, N., Singh, S., **Yang, X.W.**, Levine, M.S. Differential electrophysiological changes in striatal output neurons in Huntington's disease. *J Neuroscience* 31, 1170-1182 (2011).
25. Tao, J., Wu, H., Lin, Q., Wei, W., Lu, X.H., Cantle, J.P., Ao, Y., Olsen, R.W., **Yang, X.W.**, Mody, I., Sofroniew, M.V., Sun, Y.E. Deletion of astroglial dicer causes non-cell-autonomous neuronal dysfunction and degeneration. *J Neuroscience* 31, 8306-8319 (2011).

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32. Southwell, A.L., Warby, S.C., Carroll, J.B., Doty, C.N., Skotte, N.H., Zhang, W., Villanueva, E.B., Kovalik, V., Xie, Y., Pouladi, M.A., Collins, J.A., **Yang, X.W.**, Franciosi, S., Hayden, M.R. A fully humanized transgenic mouse model of Huntington disease. *Hum Mol Genet.* 22:18-34 (2013).
33. Wang, N., Lu, X.H., Sandoval, S.V., **Yang, X. W.** An Independent Study of the Preclinical Efficacy of C2-8 in the R6/2 Transgenic Mouse Model of Huntington's Disease. *J. Huntington's Dis.* 2: 443-451 (2013).
34. Cui, Y., Ostlund, S.B., James, A., Park, C.S., Ge, W., Roberts, K.W., Mittal, N., Murphy, N.P., Cepeda, C., Kieffer, B.L., Levine, M.S., Jentsch, J.D., Walwyn, W.M., Sun, Y.E., Evans, C.J., Maidment, N.T., **Yang, X.W.** Targeted expression of  $\mu$ -opioid receptors in a subset of striatal direct-pathway neurons restores opiate reward. *Nature Neuroscience* 17:254-261 (2014).
35. Haustein, M.D., Kracun, S., Lu, X.H., Shih, T., Jackson-Weaver, O., Tong, X., Xu, J., **Yang, X.W.**, O'Dell, T.J., Marvin, J.S., Ellisman, M.H., Bushong, E.A., Looger, L.L., Khakh, B.S. Conditions and constraints for astrocyte calcium signaling in the hippocampal mossy fiber pathway. *Neuron* 82: 413-429 (2013).

36. Wang, N., Gray, M., Lu, X.H., Cattle, J.P., Holley, S.M., Greiner, E., Gu, X., Shirasaki, D., Cepeda, C., Li, Y., Dong, H.W., Levine, M.S., **Yang, X.W.** Neuronal targets of mutant huntingtin genetic reduction to ameliorate Huntington's disease pathogenesis in mice. *Nature Medicine* 20: 536-541 (2014).
37. Lu, X.H., Mattis, V.B., Wang, N., Al-Ramahi, I., van den Berg, N., Fratantoni, S.A., Waldvogel, H., Greiner, E., Osmand, A., Elzein, K., Xiao, J., Dijkstra, S., de Pril, R., Vinters, H., Faull, R., Signer, E., Kwak, S., Marugan, J.J., Botas, J., Fischer, D.F., Svendsen, C.N., Munoz-Sanjuan, I., **Yang, X.W.** Targeting ATM ameliorates mutant Huntingtin toxicities in cell and animal models of Huntington's disease. *Science Translational Medicine* 6: 268ra178 (2014).
38. Peñagarikano, O., Lázaro, M.T., Lu, X.H., Gordon, A., Dong, H., Lam, H.A., Peles, E., Maidment, N.T. Murphy, N.P., **Yang, X.W.**, Golshani, P., Geschwind, D.H. Exogenous and evoked oxytocin restores social behavior in the Cntnap2 mouse model of autism. *Science Translational Medicine* 7:271ra8 (2015).
39. Gu, X., Cattle, J.P., Greiner, E. C.Y. Lee, C.Y.D., Barth, A.M., Gao, F., Park, C.S., Zhang, Z., Sandoval, S., Zhang, R., Diamond, M., Mody, I., Coppola, G., **Yang, X.W.** N17 Modifies Mutant Huntingtin Nuclear Pathogenesis and Severity of Disease in HD BAC Transgenic Mice. *Neuron* 85: 726-741 (2015).
40. Estrada-Sanchez, A., Burroughs, C., Cavaliere, S., Barton, S., Chen, S., **Yang, X.W.**, Rebec, G. Cortical Efferents Lacking Mutant huntingtin Improve Striatal Neuronal Activity and Behavior in a Conditional Mouse Model of Huntington's Disease. *J. Neuroscience* 35: 4440-4451 (2015).
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43. Chandra, A., Sharma, A., Calingasan, N.Y., White, J.M, Shurubor, Y., **Yang, X.W.**, Beal, M.F., Johri, A. Enhanced mitochondrial biogenesis ameliorates disease phenotype in a full-length mouse model of Huntington's disease. *Hum Mol Genet.* pii: ddw095 (2016).
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47. Xu, J., Bernstein, A.M., Wong, A., Lu, X.H., Khoja, S., **Yang, X.W.**, Davies, D.L., Micevych, P., Sofroniew, M.V., Khakh, B.S. P2X4 Receptor Reporter Mice: Sparse Brain Expression and Feeding-Related Presynaptic Facilitation in the Arcuate Nucleus. *J Neurosci.* 36: 8902-8920 (2016).

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49. Lu, X.H., **Yang, X.W.** Genetically-directed Sparse Neuronal Labeling in BAC Transgenic Mice through Mononucleotide Repeat Frameshift. *Sci Rep.* 7:43915 (2017).
50. Yau, R.G., Doerner, K., Castellanos, E.R., Haakonsen, D., Werner, A., Wang, N., **Yang, X.W.**, Matsumoto, M.L., Vishva M. Dixit, V.M., Rape, M. Assembly and Function of Heterotypic Ubiquitin Chains in Cell Cycle and Protein Quality Control. *Cell* 171:918-933 (2017).
51. Langfelder, P., Gao, F., Wang, N., Howland, D., Kwak, S., Vogt, T.F., Aaronson, J.S., Rosinski, J., Coppola, G., Horvath, S., **Yang, X.W.** MicroRNA signatures of endogenous Huntingtin CAG repeat expansion in mice. *PLoS One* 13:e0190550 (2018).
52. Victor, M.B., Richner, M., Olsen, H.E., Lee, S.W., Monteys, A.M., Ma, C., Huh, C.J., Zhang, B., Davidson, B.L., **Yang, X.W.**, Yoo, A.S. Striatal neurons directly converted from Huntington's disease patient fibroblasts recapitulate age-associated disease phenotypes. *Nature Neurosci.* 21:341-352 (2018).
53. Lee, C.Y., Daggett, A., Gu, X., Jiang, L.L., Langfelder, P., Li, X., Wang, N., Zhao, Y., Park, C.S., Cooper, Y., Ferando, I., Mody, I., Coppola, G., Xu, H., **Yang, X.W.** Elevated TREM2 gene dosage reprograms microglia responsivity and ameliorates pathological phenotypes in Alzheimer's disease models. *Neuron* 97:1032-48 (2018).
54. Li, R., Zhu, M., Li, J., Bienkowski, M.S., Foster, N.N., Xu, H., Ard, T., Bowman, I., Zhou, C., **Yang, X.W.**, Hintiryan, H., Zhang, J., Dong, H.-W. Precise segmentation of densely interweaving neuron clusters using G-Cut. *Nature Communications* 10: 1549 (2019).
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## PATENTS

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2. Heintz, N., Jiang, W., and **Yang, X.W.** Methods of performing gene trapping in bacterial and bacteriophage-derived artificial chromosomes and use thereof. Rockefeller University. US Pat. No.6,485,912
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