BIOGRAPHICAL SKETCH

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NAME: Yu, Lei

eRA COMMONS USER NAME (credential, e.g., agency login): yulei1

POSITION TITLE: Distinguished Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Jiangnan University, Wuxi, China	B.S.	07/1979	Ind. Fermentation
Institute of Genetics, Beijing, China	M.S.	06/1981	Molecular Genetics
California Institute of Technology, Pasadena, CA	Ph.D.	04/1987	Biology
California Institute of Technology, Pasadena, CA	Postdoctoral	08/1988	Biology

A. Personal Statement

My research area is in the molecular and genetic bases of nervous system disorders, including pain and drug addiction. I have extensive experience in this area. My group was the first to report the molecular cloning of the mu opioid receptor, the cellular target for opioid drugs such as morphine and heroin, and a key molecule for opioid-mediated pain relief and opioid addiction.

B. Positions and Honors

Positions and Employment

1981-1987 California Foundation for Biochemical Research Predoctoral Fellow, California Institute of Technology, Pasadena, California
1987-1988 Del Webb Postdoctoral Fellow, California Institute of Technology, Pasadena, California
1988-1993 Assistant Professor, Indiana University School of Medicine, Indianapolis, Indiana
1993-1995 Associate Professor, Indiana University School of Medicine, Indianapolis, Indiana
1995-1997 Professor, Indiana University School of Medicine, Indianapolis, Indiana
1997-2005 Professor, University of Cincinnati College of Medicine, Cincinnati, Ohio
2005- Distinguished Professor, Rutgers University, Piscataway, New Jersey

Other Experience and Professional Memberships

1994-1995 Extramural Science Advisory Board, NIDA, National Institutes of Health
1996-1997 Blue Ribbon Panel for Review of Intramural Research at NIDA, National Institutes of Health
1996-1999 National Advisory Council on Drug Abuse, National Institutes of Health
1996-1999 Board of Scientific Counselors as the Representative of NIDA Council, Intramural Research Program, National Institute on Drug Abuse, National Institutes of Health
1997- Member, American College of Neuropsychopharmacology

2002-2003 Special Molecular Imaging Study Section, Center for Scientific Review, National Institutes of Health
2005 General Clinical Research Center Site Visit Committee, National Center for Research Resources, National Institutes of Health
2006 NIDA Program Project Review Panel, NIDA, National Institutes of Health
2006-2015 NIDA Center Grant Review Committee, NIDA, National Institutes of Health

C. Contributions to Science

1. *Opioid receptor signaling:* My group was the first to report the molecular cloning of the mu opioid receptor — the molecular target for morphine, heroin, and other opioids. Also, we were the first to report OPRM1 A118G SNP and its potential cellular impact. My laboratory has been studying opioid analgesic properties, tolerance, dependence, and addiction, at cellular, molecular, behavioral, and genetic levels.

a. Chen, Y., Mestek, A., Liu, J., Hurley, J.A., and Yu, L. (1993) Molecular cloning and functional expression of a mu-opioid receptor from rat brain. *Mol. Pharmacol. 44*:8-12.
b. Mestek, A., Hurley, J.H., Bye, L.S., Campbell, A., Chen, Y., Tian, M., Schulman, H. and Yu, L. (1995) The human mu opioid receptor: Modulation of functional desensitization by calcium/calmodulin-dependent protein kinase and protein kinase C. *J. Neurosci. 15*:2396-2406.
c. Tian, M., Broxmeyer, H.E., Fan, Y., Lai, Z., Zhang, S., Aronica, S., Cooper, S., Bigsby, R.M., Steinmetz, R., Engle, S.J., Mestek, A., Pollock, J.D., Lehman, M.N., Jansen, H.T., Ying, M., Stambrook, P.J., Tischfield, J.A., and Yu, L. (1997) Altered hematopoiesis, behavior, and sexual function in mu opioid receptor-deficient mice. *J. Exp. Med. 185*:1517-1522.
d. Bond, C., LaForge, K.S., Tian, M., Melia, D., Zhang, S., Borg, L., Gong, J., Schluger, J., Strong, J.A., Leal, S.M., Tischfield, J.A., Kreek, M.J., and Yu, L. (1998) Single-nucleotide polymorphism in the human mu opioid receptor gene alters β-endorphin binding and activity: Possible implications for opiate addiction. *Proc. Natl. Acad. Sci. USA 95*:9608-9613.

2. *Mechanism of neuropathic pain and molecular components:* My group has been studying molecular mechanisms involved in pain sensation, particularly those for neuropathic pain, because a lack of adequate understanding of neuropathic pain mechanisms has hindered the development of effective therapies for neuropathic pain. Through behavioral screening, we have identified a number of molecular entities that played a key role in the development and maintenance of neuropathic pain. These studies have led to patents for targeting the molecular entities for drug development.

a. Moalem, G., Xu, K., and Yu, L. (2004) T lymphocytes play a role in neuropathic pain following peripheral nerve injury in rats. *Neuroscience 129*:767-777.
b. Xie, W., Strong, J.A., Meij, J.T.A., Zhang, J.-M., and Yu, L. (2005) Neuropathic pain: early spontaneous afferent activity is the trigger. *Pain 116*:243-56.
c. Wang, X., Zhang, Y., Kong, L., Xie, Z., Lin, Z., Guo, N., Strong, J.A., Meij, J.T., Zhao, Z., Jing, N., and Yu, L. (2005) RSEP1 is a novel gene with functional involvement in neuropathic pain behavior. *Eur. J. Neurosci. 22*:1090-1096.
d. Zhang, Y.-Q., Guo, N., Peng, G., Han, M., Raincrow, J., Chiu, C., Coolen, L.M., Wenthold, R.J., Zhao, Z.-Q., Jing, N., and Yu, L. (2009) Role of SIP30 in the development and maintenance of peripheral nerve injury-induced neuropathic pain. *Pain 146*:130-140.

3. *Molecular mechanism of drug abuse, alcoholism, and potential treatment:* In an effort to explore drug abuse, alcoholism, and potential treatment, my group has been studying molecular mechanisms related to drug abuse and alcoholism in both human and rodent model systems. In addition, we have collaborated with chemists to develop novel opioid-containing compounds with strong analgesic efficacy and with reduced abuse potential.

a. Smelson, D.A., Yu, L., Buyske, S., Gonzalez, G., Tischfield, J.A., Deutsch, C.K., Ziedonis, D. (2012) Genetic association of GABA-A receptor alpha-2 and mu opioid receptor with cocaine cue-reactivity: Evidence for inhibitory synaptic neurotransmission involvement in cocaine dependence. *Am. J. Addictions 21*:411-415.

b. Wang K, Song H, Jin M, Xiao H, Zhao G, Zou H, Yu L (2014) Chronic alcohol consumption from adolescence-to-adulthood in mice — Hypothalamic gene expression changes in insulin signaling pathway. *Alcohol 48*:571-578.
c. Zou H, Wang K, Gao Y, Song H, Xie Q, Jin M, Zhao G, Xiao H, Yu L (2014) Chronic alcohol consumption from adolescence-to-adulthood in mice — Hypothalamic gene expression changes in the dilated cardiomyopathy signaling pathway. *BMC Neuroscience 15*:61.
d. Lax NC, Chen R, Leep SR, Uhrich KE, Yu L, Kolber BJ (2017) PolyMorphine provides extended analgesic-like effects in mice with spared nerve injury. *Mol. Pain 13*:1-12.

4. *Using long-tailed macaque monkeys (Macaca fascicularis) as non-human primate models to study pain and behavior:* In an effort to develop neuropathic pain models and behavioral measurements in a non-human primate species, we worked with cynomolgus monkeys (long-tailed macaque, also known as crab-eating macaque).

a. Guo N, Gu X, Zhao J, Zhao G, Jin M, Zou H, Zhang Y, Zhao Z, Jin GJ, Yu L (2012) Maxillary nerve compression in cynomolgus monkey *Macaca fascicularis*: Altered somatic sensation and peripheral nerve firing. *BMC Neuroscience 13*:150.
b. Guo N, Gu X, Xie Y, Zhao J, Xie Q, Zhao G, Jin M, Zhao Z, Zou H, Zhang Y, Jin GJ, Yu L (2014) Sciatic nerve neuropathy in cynomolgus monkey *Macaca fascicularis*: Altered leg usage and peripheral nerve firing. *J. Neurol. Neurophysiol. 5(6)*:247.
c. Zou H, Luan Y, Liu M, Agre LA, Buyske S, Xie Q, Cheng Z, Zhao G, Jin M, Guo N, Jin GJ, Yu L (2015) Differential behavior patterns in cynomolgus monkey *Macaca fascicularis* in home cage in response to human gaze. *J. Med. Primatol. 44*:1-11.
d. Zou H, Liu M, Luan Y, Xie Q, Cheng Z, Zhao G, Jin M, Guo N, Jin GJ, Yu L (2017) Pattern of novel object exploration in cynomolgus monkey *Macaca fascicularis*. *J. Med. Primatol. 46*:19-24.

5. *Intellectual property development for analgesic innovation:* Ever since my group's 1993 work of opioid receptor genetics, and the accompanying patent filing by the university, I have been cognizant of the responsibility of using public funding source for public good. In the case of biomedical research funded by NIH grants, I have worked closely with my university technology office to apply for patents, as the effort to develop intellectual property rights for subsequent commercialization possibilities. To date, I have seven issued US patents, four of which are listed below, per NIH biosketch requirement of maximum four listing per topic section.

a. Yu L "Polynucleotide encoding mu opioid receptor." US Patent 6103492 (issued August 15, 2000).
b. Yu L "Nucleic acid encoding mammalian mu opioid receptor." US Patent 6235496 (issued May 22, 2001).
c. Yu L "Methods for screening for substances that bind opioid receptors." US Patent 7097988 (issued August 29, 2006).
d. Yu L, Guo N, Zhang YQ, Zhao ZQ, Jing NH "Compositions and methods for treatment of neuropathic pain." US Patent 9068984 (issued June 30, 2015).

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