BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Amy Lee	Associate Professor
eRA COMMONS USER NAME (credential, e.g., agency login) amyl2e	

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 Michigan, Ann Arbor, MI	B.S.	1986-90	Biology
University of Connecticut, Storrs, CT		1991-92	Neurobiology
University of Virginia, Charlottesville, VA	Ph.D.	1992-97	Neuroscience
University of Washington, Seattle, WA		1998-02	Neuroscience

A. Personal statement

My lab is interested in mechanisms regulating voltage-gated Ca^{2+} channels in the nervous and cardiovascular systems. We have been working on novel mechanisms controlling the expression, function, and trafficking of Ca^{2+} channels in various neuronal cell-types including cerebellar Purkinje neurons, retinal photoreceptors, and cochlear inner hair cells. We are extending this research to discovering novel protein interaction networks that control neuronal excitability. We use a variety of experimental approaches including patch clamp recording of neurons in slice and in dissociated preparations, fluorescent imaging of Ca^{2+}, and biochemical and immunohistochemical analysis of Ca_v channel localization. Despite moving our lab from Emory University to the University of Iowa between 2008-2009, my lab has maintained a relatively continuous record of publications, all focused on Ca_v channel regulation. Since I participated in the initial characterization of $Ca_v2.1$ channel regulation by Ca^{2+}/CaM (A. Lee et al., 1999, *Nature* 399:155-159) and CaBP1 (A. Lee et al., 2002, *Nat Neurosci*, 5:210-217), I have been particularly dedicated to unraveling the mechanisms by which CaBP1 and related proteins regulate Ca^{2+}-dependent feedback regulation of Ca_v channels. My independent lab has published 14 papers on this topic and our work continues to motivate research in the field. Through these experiences, I have gained the necessary insight to be principal investigator on this application.

B. Positions and honors

Positions and employment

1998-02 Senior fellow, Dept. of Pharmacology, University of Washington
2002-08 Assistant Professor, Dept. of Pharmacology, Emory University
2008-present Associate Professor, Depts. of Molecular Physiology & Biophysics, Otolaryngology, and Neurology, University of Iowa
2009-10 Co-Instructor, Ion Channels Course, Cold Spring Harbor Laboratories

Other experience and professional memberships

1996-present Society for Neuroscience, member
2008-present Association for Research in Otolaryngology
2011-present Neurotransporters, receptors, and calcium signaling NIH study section, member
2012-present Biophysical Society, member

Honors

1986 University of Michigan Alumni Scholarship
1995 Individual pre-doctoral NRSA F31 MH11074
1996-present Member, Society for Neuroscience
1997 Eric Lothman Award for Outstanding Achievement in the Neurosciences, University of Virginia
1998 Individual post-doctoral NRSA F32 NS10645
2002 PhRMA Foundation Research Starter Award
2007 Teaching Excellence Award, Emory University School of Medicine

2011-present NIH study section (NTRC) member
2012-present Editorial Board, Molecular Pharmacology
2012 Carver Research Program of Excellence
2012 Elected to Biophysical Society Council

C. Selected peer-reviewed publications (of 37 total)

Most relevant to the current application

1. Haeseleer, F. Imanishi, Y., Maeda, T., Possin, D., Maeda, A., **Lee, A**., Rieke, F., and K. Palczewski. (2004) Essential role of Ca^{2+}-binding protein 4, a $Ca_v1.4$ channel regulator, in photoreceptor synaptic function. *Nat. Neurosci.* 7: 1079-1087. PMC1352161
2. Zhou, H., Kim, S.-A., Kirk, E.A., Tippens, A. L., Sun, H., Haeseleer, F., and **A. Lee**. (2004) Ca^{2+}-binding protein-1 facilitates and forms a postsynaptic complex with $Ca_v1.2$ (L-type) Ca^{2+} channels. *J. Neurosci.* 24:4698-4708.
3. Zhou, H., Yu, K., McCoy, K.L., and **A. Lee** (2005) Molecular mechanism for divergent regulation of $Ca_v1.2$ Ca^{2+} channels by calmodulin and Ca^{2+}-binding protein-1. *J. Biol. Chem.* 280:29612-29619. http://www.jbc.org/content/280/33/29612.long
4. Kreiner, L. and **A. Lee** (2006) Endogenous and exogenous Ca^{2+} buffers differentially modulate Ca^{2+}-dependent inactivation of $Ca_v2.1$ Ca^{2+} channels. *J. Biol. Chem.* 281: 4691-4698. http://www.jbc.org/content/281/8/4691.long
5. Tippens, A.L. and **A. Lee** (2007) Caldendrin: a neuron-specific modulator of $Ca_v1.2$ (L-type) Ca^{2+} channels. *J. Biol. Chem*. 282:8464-8473. http://www.jbc.org/content/282/11/8464.long
6. Cui, G., Meyer, A.C., Calin-Jageman, I., Neef, J., Haeseleer, F., Moser, T. and **A. Lee.** (2007) Ca^{2+}-binding proteins tune Ca^{2+}-feedback to $Ca_v1.3$ channels in auditory hair cells. *J. Physiol.* 585: 791-803. PMC2375505
7. **Lee , A.**, Jimenez, A., Cui, G., and F. Haeseleer (2007). Phosphorylation of CaBP4 by protein kinase C zeta in photoreceptors. *J. Neurosci.* 27:12743-12754. PMC2703458
8. Tippens, A.L., Pare, J.-F., Moosmang, S., Milner, T.A., Smith, Y., and **A. Lee.** (2008) Ultrastructural evidence for pre- and post-synaptic localization of $Ca_v1.2$ L-type Ca^{2+} channels in the rat hippocampus. *J.Comp.Neurol.* 506:569-583.
9. Rieke, F., **Lee, A**., and F. Haeseleer. (2008) Characterization of Ca^{2+}-binding protein 5 knockout mouse retina. *Invest Ophthalmol Vis Sci* 49:5126-5135.
10. Kreiner, L., Christel, C.J., Benveniste, M., Schwaller, B., and **A. Lee**. (2010) Compensatory regulation of $Ca_v2.1$ Ca^{2+} channels in cerebellar Purkinje neurons lacking parvalbumin and calbindin D-28k. *J. Neurophysiol.* 103:371-381.
11. Jenkins, M.A., Christel, C.J., Jiao,Y., Abiria, S., Kim, K.Y., Usachev, Y.M., Obermair, G.J., Colbran, R.J. and **A. Lee**. (2010) Ca^{2+}-dependent facilitation of $Ca_v1.3$ Ca^{2+} channels by densin and Ca^{2+}/calmodulin-dependent protein kinase II. *J. Neurosci.* 30: 5125-5135.
12. Oz, S., Tsemakhovich, V., Christel, C.J., **Lee, A.,** Dascal, N. (2011) CaBP1 regulates voltage dependent inactivation and activation of $Ca_v1.2$ (L-type) calcium channels. *J. Biol. Chem.* 286:13945-13953.
13. Schrauwen, I., Helfmann, S., Inagaki, A., Wolk, F., Tabatabaiefar, M.A., Picher M.M., Sommen, M., ZazoSeco, C., Kremer, H., Dheedene, A., Claes, C., Fransen,E., Reimnitz, F., Diederichsen, U., HashemzadehM., Couke, P., **Lee, A**., Moser, T., Van Camp, G. A mutation in CABP2, expressed in cochlear hair cells, causes autosomal recessive hearing impairment. *Am. J. Hum. Genet.* (in press)
14. Christel, C.J., Schaer, R., Wang, S., Henzi, T., Kreiner, L., Grabs, D., Schwaller, B., and **A. Lee.** Calretinin regulates Ca^{2+}-dependent inactivation and facilitation of $Ca_v2.1$ Ca^{2+} channels through a direct interaction with the $_1$2.1 subunit. *J. Biol. Chem.* (in press)

Additional recent publications of importance to the field

3. Calin-Jageman, I., Yu, K., Hall, R.A., Mei, L., and **A. Lee**. (2007) Erbin enhances voltage-dependent facilitation of $Ca_v1.3$ Ca^{2+} channels through relief of an autoinhibitory domain in the $Ca_v1.3$ $_1$ subunit. *J. Neurosci*: 27:1374-1385. http://www.jneurosci.org/cgi/content/full/27/6/1374
4. Calin-Jageman, I. and **A. Lee**. (2008) Ca_v1 L-type Ca^{2+} channel signaling complexes in neurons *J.Neurochem*. 105: 573-583.
5. Yu, K., Xiao, Q., Cui G., **Lee, A.** and H. C. Hartzell. (2008) The Best Disease-Linked Cl Channel hBest1 Regulates Ca_v1 (L-type) Ca^{2+} Channels Via SH3-binding Domains. *J. Neurosci.* 28:5660-5670.

6. Frank,T., Rutherford, M.A., Strenzke, N., Neef, A., Pangršič, T., Khimich, D., Fetjova, A., Gundelfinger, E.D., Liberman, M.C., Harke, B., Bryan, K.E., **Lee, A**., Egner, A., Riedel, D., and T. Moser. (2010) Bassoon and the Synaptic Ribbon Organize Ca^{2+} Channels and Vesicles to Add Release Sites and Promote Refilling. *Neuron* 68: 724-738.
7 Gregory, F.D., Pangrsic, T., Bryan, K.E., Calin-Jageman, I.E., Moser, T., and **A. Lee.** (2011) Harmonin inhibits presynaptic $Ca_v1.3$ channels in mouse inner hair cells. *Nat. Neurosci.*14:1109-1111.
8. Lee, A.S., Ra, S. Rajadhyaksha, A.M., Britt, J.K., Moosmang, S., Hofmann, F., **Lee, A.**, Pieper, A.A., Rajadhyaksha, A.M. (2012) Forebrain elimination of *CACNA1C* mediates anxiety-like behavior in mice. *Mol. Psychiatry* (in press, doi: 10.1038/mp.2012.71)
9. Christel, C.J., Cardona, N., Mesirca, P., Herrmann, S., Hofmann, F., Striessnig, J., Ludwig, A., Mangoni, M.E.,and **A. Lee.** Distinct localization and modulation of $Ca_v1.2$ and $Ca_v1.3$ L-type Ca^{2+} channels in mouse sinoatrial node. *J. Physiol.* (in press)

D. Research Support

<u>Ongoing research support</u>:

R01 DC009433: *Regulation of auditory calcium channels* (PI: Amy Lee, 4.8 cal months) 12/01/08-11/30/13
The goal of this project is to characterize the importance of two proteins, CaBP1 and harmonin, for the function of voltage-gated Ca^{2+} channels in auditory inner hair cells.

R01 HL087120 *Modulation of Cav 1.3 L-type Ca^{2+} channels by PDZ-protein interactions* (PI: Amy Lee, 2.4 cal months) 05/01/09-4/30/13
The goal of this project is to characterize the mechanisms by which proteins containing PDZ domains interact with and regulate Cav1.3 Ca^{2+} channels in neurons and in cardiac myocytes. **This grant will not be renewed if the current application is funded.**

R01 EY020850 *Regulation of L-type calcium channels by CaBP4* (PI: F. Haeseleer, collaborator: Amy Lee, 2.4 cal months) 9/1/10-9/30/14
The goal of this project is to elucidate the physiological role of CaBP4 in regulating photoreceptor Ca^{2+} channels and synapse organization in the retina.

<u>Research support completed during the last 3 years</u>:

Israel Binational Science Foundation Research Grant (*Inactivation of L-type Ca^{2+} channels: Regulation by Ca^{2+}-binding proteins*; co PI: Amy Lee) 9/01/06-8/30/10
The goal of this project is to elucidate the molecular determinants by which calmodulin and CaBP1 influence Ca^{2+}-dependent inactivation of Ca_v1 Ca^{2+} channels.