Jeffrey L. Noebels, M.D., Ph.D.

- **Professor of Neurology, Neuroscience, and Molecular & Human Genetics**
  Baylor College of Medicine
- **Director, Blue Bird Circle Developmental Neurogenetics Laboratory**
  Baylor College of Medicine
- **Vice-Chair for Research, Department of Neurology**
  Baylor College of Medicine
- **Graduate Program Faculty, Integrative Molecular and Biomedical Sciences; Translational Biology & Molecular Medicine**
  Baylor College of Medicine
- **Cullen Trust for Health Care Endowed Chair in Neurogenetics**
  Baylor College of Medicine

CONTACT INFORMATION

Jeffrey L. Noebels, M.D., Ph.D.
Baylor Neurology
Baylor College of Medicine Medical Center, McNair Campus
7200 Cambridge St., 9th Floor, MS: BCM302
Houston, Texas 77030

Tel: 713-798-5860
Fax: 713-798-7528
Email: jnoebels@bcm.edu

PROFESSIONAL STATEMENT

The principal research strategy in the Developmental Neurogenetics Laboratory is to apply mutational analysis to learn how genes regulate neuronal excitability and network synchronization within the mammalian central nervous system. Spontaneous and transgenic mutations that express neurological phenotypes in the mouse provide a valuable opportunity to identify excitability genes and examine their role in synaptic plasticity in the developing brain. Brain wave (EEG) phenotypes emerge from altered neuronal signaling properties, and are of special interest. Six mouse mutants causing spike-wave synchronization of the neocortex have been discovered in our laboratory, and four (tottering, lethargic, ducky, and stargazer) are linked to mutations of subunits of neuronal voltage-gated calcium ion channels. Study of these mice have led to the identification of novel members of the gene family, and a new understanding of how related molecules rescue function and determine selective vulnerability within thalamocortical pathways. Other new mouse models for human epilepsy syndromes involving mutant ion channel, receptor, and synaptic vesicle proteins are being analyzed to pinpoint the neural network and specific electrophysiological abnormalities characteristic of the human disorder. We also explore the presynaptic release process and activity-induced changes of downstream gene expression in epileptic brain to identify regulatory pathways that are critical mechanisms of disease progression.

At present, mutant mouse models of inherited disorders in neuronal excitability are under investigation using in vitro cell physiology and optical fluorescence measurements of ion channel activity and exocytosis in presynaptic terminals of mouse brain slices, as well as molecular anatomical techniques including laser-capture microspcopy and realtime quantitative PCR, in situ hybridization and immunohistochemistry, and microarray analysis of seizure-activated mRNAs. These studies form the basis for development of strategies to selectively correct the tissue expression of neuronal gene errors early in development.

In collaboration with the Baylor Human Genome Sequencing Center, a large-scale translational genomic research study examining variants in human ion channel genes is currently in progress. The Human Channelopathy Project will evaluate the contribution of SNP profiles in several hundred ion channel subunit genes to the complex inheritance of neurological excitability disorders such as epilepsy.

CERTIFICATION

- American Board of Psychiatry and Neurology, Neurology

EDUCATION

- M.D., Yale University, Conn.
- Ph.D., Stanford University, Stanford, Calif.
- B.A., Reed College, Ore.
- Residency, Neurology, Massachusetts General Hospital, Boston, Mass.
- Fellowship, , Harvard University, Mass.

CONSULT

713-798-7528

CLINICAL INTERESTS

Epilepsy and inherited neurological disease

RESEARCH INTERESTS

- Gene control of neuronal excitability within the developing mammalian CNS
- Inherited neurological diseases
- Epilepsy

GRANTS (NIH FUNDING)

- Noebels JL (Principal Investigator). Excitability and plasticity in developing epileptic brain. National Institute of Neurological Disorders and Stroke R01 grant (PA-13-302); $6,840,145 awarded in direct costs, Sept. 1, 1991–Aug. 31, 2019.
- Noebels JL (Principal Investigator). SUDEP research alliance: cardiac gene and circuit mechanisms; application 7 of 7. National Institute of Neurological Disorders and Stroke U01 grant (RFA-NS-14-004); $1,290,000 awarded in direct costs, Sept. 30, 2014–July 31, 2019.
- Noebels JL (Principal Investigator). In vivo recruitment of neocortical neurons in stargazer absence seizures. National Institute of Neurological Disorders and Stroke R21 grant (PA-13-303); $125,000 awarded in direct costs, May 1, 2015–April 30, 2017.
- Noebels JL (Principal Investigator). Predictive Genes, Mechanisms, and Clinical Biomarkers of SUDEP. National Institute of Neurological Disorders and Stroke P20 grant (RFA-NS-11-006); $1,301,318 awarded in direct costs, Sept. 26, 2011–Aug. 31, 2014.
- Noebels JL (Principal Investigator). Parallel Sequence Profiling of Ion Channels in Epilepsy. National Institute of Neurological Disorders and Stroke R01 grant (PAS-03-092); $5,109,546 awarded in direct costs, Aug. 15, 2004–May 31, 2011.
- Noebels JL (Principal Investigator). Course Development in the Neurobiology of Disease. National Institute on Aging R25 grant (RFA-MH-05-011); $116,531 awarded in direct costs, Sept. 30, 2005–Aug. 31, 2008.
- Noebels JL (Principal Investigator). Neurophysiology Database of Inbred Mutant Strains. National Institute of Neurological Disorders and Stroke R01 grant (RFA-MH-99-006); $619,087 awarded in direct costs, Sept. 30, 1999–June 30, 2004.

JOURNAL PUBLICATIONS

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2. Aiba I, Ning Y, Noebels JL. A hyperthermic seizure unleashes a surge of spreading depolarizations in Scn1a-deficient mice. JCI Insight. 2023;8(15):e170399. PMID: 37551713.
3. Curry RN, Aiba I, Meyer J, Lozzi B, Ko Y, McDonald MF, et al. Glioma epileptiform activity and progression are driven by IGSF3-mediated potassium dysregulation. Neuron. 2023;111(5):682-95 e9. PMID: 36787748.
4. Goethe EA, Deneen B, Noebels J, Rao G. The role of hyperexcitability in gliomagenesis. Int J Mol Sci. 2023;24(1):. PMID: 36614191.
5. Huang-Hobbs E, Cheng YT, Ko Y, Luna-Figueroa E, Lozzi B, Taylor KR, et al. Remote neuronal activity drives glioma infiltration via Sema4f. bioRxiv. 2023;:. PMID: 36993539.
6. Huang-Hobbs E, Cheng YT, Ko Y, Luna-Figueroa E, Lozzi B, Taylor KR, et al. Remote neuronal activity drives glioma progression through SEMA4F. Nature. 2023;619(7971):844-50. PMID: 37380778.

7. Hussain T, Sanchez K, Crayton J, Saha D, Jeter C, Lu Y, et al. WWOX P47T partial loss-of-function mutation induces epilepsy, progressive neuroinflammation, and cerebellar degeneration in mice phenocopying human SCAR12. Prog Neurobiol. 2023;223:102425. PMID: 36828035.
8. Okoh J, Mays J, Bacq A, Oses-Prieto JA, Tyanova S, Chen CJ, et al. Targeted suppression of mTORC2 reduces seizures across models of epilepsy. Nat Commun. 2023;14(1):7364. PMID: 37963879.
9. Villacres JE, Riveira N, Kim S, Colgin LL, Noebels JL, Lopez AY. Abnormal patterns of sleep and waking behaviors are accompanied by neocortical oscillation disturbances in an Ank3 mouse model of epilepsy-bipolar disorder comorbidity. Transl Psychiatry. 2023;13(1):403. PMID: 38123552.
10. Aloi MS, Thompson SJ, Quartapella N, Noebels JL. Loss of functional System x-c uncouples aberrant postnatal neurogenesis from epileptogenesis in the hippocampus of Kcna1-KO mice. Cell Rep. 2022;41(8):111696. PMID: 36417872.
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12. Ning Y, Noebels JL, Aiba I. Emx1-Cre is expressed in peripheral autonomic ganglia that regulate central cardiorespiratory functions. eNeuro. 2022;9(5):. PMID: 36192157.
13. Aiba I, Noebels JL. Kcnq2/Kv7.2 controls the threshold and bihemispheric symmetry of cortical spreading depolarization. Brain. 2021;144(9):2863-78. PMID: 33768249.
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identified by foramen ovale electrodes in Alzheimer's disease. Nat Med. 2017;23(6):678-80. PMID: 28459436.

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POSTER and PLATFORM PRESENTATIONS

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