David J. Segal, Ph.D.

Research/Academic Interests

Dr. Segal's research, together with the labs of Kyle Fink and Jill Silverman, focuses on developing molecular therapies for neurologic disorders. We use programable DNA- or RNA-binding platforms (Zinc finger, TALE, CRISPR/Cas9, Cas12, Cas13) to cause long-term changes in the expression of disease genes. This approach avoids problematic double-strand breaks. We use a variety of delivery systems (protein, AAV, lipo-particles, stem cells) to treat the brain in animal models of disease, which are extensively characterized on a molecular and behavioral level. A flagship project is Angelman syndrome, for which the therapeutic strategy is to reactivate a silenced gene in the brain. We collaborate with groups around the world to de-risk genetic therapies for this and several other related disorders.

Title

Professor

Specialty

Neurodevelopmental Disorders

Department

Biological Chemistry and Molecular Medicine

Division

Biological Chemistry

Center/Program Affiliation

Genome Center
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Genome and Biomedical Sciences Building, Genome & Biomedical Sciences Facility, 451 Health Sciences Dr Davis, CA 95616
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Education

Ph.D., Biochemistry, University of Utah, Salt Lake City UT 1996
B.S., Biology, Cornell University, Ithaca NY 1989

Professional Memberships

American Society for Gene and Cell Therapy

Honors and Awards

Foundation for Angelman Syndrome Therapeutics Accelerator Award, 2021

Select Recent Publications

See: Complete List of Publications

Saha K, Sontheimer EJ, Brooks PJ, Dwinell MR, Gersbach CA, Liu DR, Murray SA, Tsai SQ, Wilson RC, Anderson DG, Asokan A, Banfield JF, Bankiewicz KS, Bao G, Bulte JWM, Bursac N, Campbell JM, Carlson DF, Chaikof EL, Chen ZY, Cheng RH, Clark KJ, Curiel DT, Dahlman JE, Deverman

UCDAVIS HEALTH

David J. Segal, Ph.D.

BE, Dickinson ME, Doudna JA, Ekker SC, Emborg ME, Feng G, Freedman BS, Gamm DM, Gao G, Ghiran IC, Glazer PM, Gong S, Heaney JD, Hennebold JD, Hinson JT, Khvorova A, Kiani S, Lagor WR, Lam KS, Leong KW, Levine JE, Lewis JA, Lutz CM, Ly DH, Maragh S, McCray PB Jr, McDevitt TC, Mirochnitchenko O, Morizane R, Murthy N, Prather RS, Ronald JA, Roy S, Roy S, Sabbisetti V, Saltzman WM, Santangelo PJ, Segal DJ, Shimoyama M, Skala MC, Tarantal AF, Tilton JC, Truskey GA, Vandsburger M, Watts JK, Wells KD, Wolfe SA, Xu Q, Xue W, Yi G, Zhou J; SCGE Consortium. The NIH Somatic Cell Genome Editing program. Nature. 2021 Apr;592(7853):195-204. doi:10.1038/s41586-021-03191-1. Epub 2021 Apr 7. PMID:33828315.

Halmai JANM, Deng P, Gonzalez CE, Coggins NB, Cameron D, Carter JL, Buchanan FKB, Waldo JJ, Lock SR, Anderson JD, O'Geen H, Segal DJ, Nolta J, Fink KD. Artificial escape from XCI by DNA methylation editing of the CDKL5 gene. Nucleic Acids Res. 2020 Jan 11;48:2372-2387. doi: 10.1093/nar/gkz1214.

O'Geen H, Bates SL, Carter SS, Nisson KA, Halmai J, Fink KD, Rhie SK, Farnham PJ, Segal DJ. Ezh2-dCas9 and KRAB-dCas9 enable engineering of epigenetic memory in a context-dependent manner. Epigenetics Chromatin. 2019 may 3;12:26. doi:10.1186/s13072-019-0275-8.

Bailus BJ, Pyles B, McAlister MM, O'Geen H, Lockwood SH, Adams AN, Nguyen JT, Yu A, Berman RF, Segal DJ. Protein Delivery of an Artificial Transcription Factor Restores Widespread Ube3a Expression in an Angelman Syndrome Mouse Brain. Mol Ther. 2016 Mar;24(3):548-55. doi: 10.1038/mt.2015.236. Epub 2016 Jan 4. PMID:26727042.

Fink KD, Deng P, Gutierrez J, Anderson JS, Torrest A, Komarla A, Kalomoiris S, Cary W, Anderson JD, Gruenloh W, Duffy A, Tempkin T, Annett G, Wheelock V, Segal DJ, Nolta JA. Allele-Specific Reduction of the Mutant Huntingtin Allele Using Transcription Activator-Like Effectors in Human Huntington's Disease Fibroblasts. Cell Transplant. 2016;25(4):677-86. doi:10.3727 /096368916X690863. Epub 2016 Feb 4. PMID:26850319.

O'Geen H, Henry IM, Bhakta MS, Meckler JF, Segal DJ. A genome-wide analysis of Cas9 binding

David J. Segal, Ph.D.

specificity using ChIP-seq and targeted sequence capture. Nucleic Acids Res. 2015 Mar 31;43(6): 3389-404. doi:10.1093/nar/gkv137. Epub 2015 Feb 20. PMID:25712100.

Johnson LM, Du J, Hale CJ, Bischof S, Feng S, Chodavarapu RK, Zhong X, Marson G, Pellegrini M, Segal DJ, Patel DJ, Jacobsen SE. SRA- and SET-domain-containing proteins link RNA polymerase V occupancy to DNA methylation. Nature. 2014 Mar 6;507(7490):124-128. doi:10.1038 /nature12931. Epub 2014 Jan 22. Erratum in: Nature. 2017 Mar 2;543(7643):136. PMID: 24463519.

Segal DJ, Carroll D. Endonuclease-induced, targeted homologous extrachromosomal recombination in Xenopus oocytes. Proc Natl Acad Sci U S A. 1995 Jan 31;92(3):806-10. doi: 10.1073/pnas.92.3.806. Erratum in: Proc Natl Acad Sci U S A. 1995 Apr 11;92(8):3632. PMID: 7846056.

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