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Michele Calos

Professor of Genetics, Emerita

CONTACT INFORMATION

- **Alternate Contact**

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Bio

ACADEMIC APPOINTMENTS

- Emeritus Faculty, Acad Council, Genetics
- Member, Bio-X
- Member, Cardiovascular Institute
- Member, Maternal & Child Health Research Institute (MCHRI)

ADMINISTRATIVE APPOINTMENTS

- Chair, School of Medicine Appointments and Promotions Committee, (2008-2010)

HONORS AND AWARDS

- Blue Flame Award, ADDGENE (2017)
- Outstanding Inventor Award, Stanford Office of Technology Licensing (2015)
- Searle Scholar Award, Searle Family Foundation (1986)
- Graduate Fellowship, National Science Foundation (1979)

BOARDS, ADVISORY COMMITTEES, PROFESSIONAL ORGANIZATIONS

- President, American Society of Gene and Cell Therapy (2018 - 2019)
- President-Elect, American Society of Gene and Cell Therapy (2017 - 2018)
- Vice President, American Society of Gene and Cell Therapy (2016 - 2017)

PROFESSIONAL EDUCATION

- B.A., M.A., Oxford University, U.K. , Zoology
- Ph.D., Harvard University , Biochemistry & Molecular Biology
- Postdoc., University of Geneva, Switzerland , Biologie Moleculaire

COMMUNITY AND INTERNATIONAL WORK

- null
- Member, Board of Directors, American Society of Gene and Cell Therapy
- Advisory Committee, United States Food and Drug Administration, Bethesda, Maryland

PATENTS

- Michele Calos, Ruby Yanru Tsai, Fangfang Zhu, Matthew Gamboa, Alfonso Farruggio, Simon Hippenmeyer, Bosiljka Tasic, Birgit Schuele. "United States Patent 9,932,607 Site-specific integration of transgenes into human cells", Leland Stanford Junior University, Mar 20, 2018
- Michele Calos. "United States Patent pending Gene therapy for muscle improvement", Leland Stanford Junior University, Oct 30, 2017
- Michele P. Calos. "United States Patent 8,420,395 Methods of unidirectional, site-specific integration into a genome, compositions and kits for practicing the same", Leland Stanford Junior University, Apr 16, 2013
- Michele P. Calos. "United States Patent 8,304,233 Methods of unidirectional, site-specific integration into a genome, compositions and kits for practicing the same", Leland Stanford Junior University, Nov 6, 2012
- Michele P. Calos. "United States Patent 8,227,249 Methods and Compositions for Genomic Modification", Leland Stanford University, Jul 24, 2012
- Michele P. Calos. "United States Patent 7,842,503 Hybrid recombinases for genome manipulation", Poetic Genetics LLC, Nov 30, 2010
- Michele P. Calos, Christopher R. Sclimenti. "United States Patent 7,732,585 Altered recombinases for genome modification", Leland Stanford Junior University, Jun 8, 2010
- Michele P. Calos. "United States Patent 7,361,641 Methods and compositions for genomic modification", Leland Stanford Junior University, Apr 22, 2008
- Michele P. Calos,, Christopher R. Sclimenti. "United States Patent 7,141,426 Altered recombinases for genome modification", Leland Stanford Junior University, Nov 28, 2006
- Michele P. Calos, Christopher R. Sclimenti. "United States Patent 6,808,925 Altered recombinases for genome modification", Leland Stanford Junior University, Oct 26, 2004
- Michele P. Calos. "United States Patent 6,632,672 Methods and Compositions for Genomic Modification", Leland Stanford Junior University, Oct 14, 2002
- Michele P. Calos. "United States Patent 5,707,830 Autonomous replication system for mammalian cells", Leland Stanford Junior University, Jan 13, 1998
- Michele P. Calos. "United States Patent 4,753,874 Rapid mutation testing system", Leland Stanford Junior University, Jun 28, 1988
- Thomas W. Chalberg, Mark Blumenkrantz, Daniel V. Palanker, Alexander Vankov, Philip Huie, Michael F. Marmor, Michele P. Calos. "United States Patent 8,101,169 Ocular gene therapy using avalanche-mediated transfection", Leland Stanford Junior University, Jan 24, 0012

LINKS

- My Lab Site: https://web.stanford.edu/~calos/

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

Our research is focused on development of novel strategies for gene and cell therapy, using gene therapy and regenerative medicine approaches. We are working to improve the clinical condition of patients suffering from genetic disorders like Duchenne muscular dystrophy and limb girdle muscular dystrophy types 2A, 2B, and 2D.

To develop a stem cell therapy for muscular dystrophy, we are using induced pluripotent stem cells (iPSC) derived from patients, using non-integrating reprogramming methods. We carry out precise genome engineering to edit mutations and add therapeutic sequences to the iPSC genome, using CRISPR/Cas9, homologous recombination, and phage integrases to mediate sequence-specific gene editing and genomic integration. The corrected cells are differentiated into muscle precursors and transplanted back to the patient, where they can engraft and produce healthy muscle fibers.

We are also developing methods to add therapeutic genes and correct mutations directly in the target muscle tissue. We have demonstrated delivery of naked plasmid DNA to muscles through the vascular system and by electroporation. We are attempting to perform genetic engineering on muscle stem cells while they are resident in the tissue.

We are currently testing these approaches in mouse models of muscular dystrophy. If successful, these types of therapies will provide new options for patients suffering from muscular dystrophy and other genetic diseases. They may also provide new possibilities for treatment of other common diseases and conditions, including normal aging.

Teaching

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Cancer Biology (Phd Program)
- Genetics (Phd Program)

Publications

PUBLICATIONS

- **Nucleofection of phiC31 Integrase Protein Mediates Sequence-Specific Genomic Integration in Human Cells.** *Journal of molecular biology*
  Guha, T. K., Calos, M. P.
  2020
- **Plasmid-Mediated Gene Therapy in Mouse Models of Limb Girdle Muscular Dystrophy.** *Molecular therapy. Methods & clinical development*
  Guha, T. K., Pichavant, C., Calos, M. P.
  2019; 15: 294-304
- **Lack of RAC.** *Molecular therapy : the journal of the American Society of Gene Therapy*
  Calos, M. P.
  2018
- **Genomic integration of the full-length dystrophin coding sequence in Duchenne muscular dystrophy induced pluripotent stem cells** *BIOTECHNOLOGY JOURNAL*
  Farruggio, A. P., Bhakta, M. S., du Bois, H., Ma, J., Calos, M. P.
  2017; 12 (4)
- **Genome Editing Techniques and Their Therapeutic Applications** *CLINICAL PHARMACOLOGY & THERAPEUTICS*
  Calos, M. P.
  2017; 101 (1): 42-51
- **Knock-in Blunt Ligation Utilizing CRISPR/Cas9** *bio-protocol*
  Geisinger, J. M., Calos, M. P.
  2017; 7 (05, Mar 05, 2017)
- **Three novel immune-deficient mouse models of muscular dystrophy** *PLOS Currents Muscular Dystrophy*
  Pichavant, C., Bjornson, C. R., Gallagher, T., Neal, T. L., du Bois, H., Bhakta, M., Calos, M. P.
  2017
- **Use of the DICE (Dual Integrase Cassette Exchange) System.** *Methods in molecular biology (Clifton, N.J.)*
  Farruggio, A. P., Bhakta, M. S., Calos, M. P.
  2017; 1642: 69–85
- **DNA-Mediated Gene Therapy in a Mouse Model of Limb Girdle Muscular Dystrophy 2B.** *Molecular therapy. Methods & clinical development*
  Ma, J. n., Pichavant, C. n., du Bois, H. n., Bhakta, M. n., Calos, M. P.
  2017; 7: 123–31
- **In vivo blunt-end cloning through CRISPR/Cas9-facilitated non-homologous end-joining** *NUCLEIC ACIDS RESEARCH*
  Geisinger, J. M., Turan, S., Hernandez, S., Spector, L. P., Calos, M. P.
  2016; 44 (8)
- **The CRISPR Way to Think about Duchenne's** *NEW ENGLAND JOURNAL OF MEDICINE*

Calos, M. P.
2016; 374 (17): 1684-1686

- **Precise Correction of Disease Mutations in Induced Pluripotent Stem Cells Derived From Patients With Limb Girdle Muscular Dystrophy.** *Molecular therapy : the journal of the American Society of Gene Therapy*
  Turan, S., Farruggio, A. P., Srifa, W., Day, J. W., Calos, M. P.
  2016; 24 (4): 685-696

- **Phage Integrases for Genome Editing** *GENOME EDITING: THE NEXT STEP IN GENE THERAPY*
  Calos, M. P.
  2016; 895: 81-91

- **Using phage integrases in a site-specific dual integrase cassette exchange strategy.** *Methods in molecular biology (Clifton, N.J.)*
  Geisinger, J. M., Calos, M. P.
  2015; 1239: 29-38

- **Nonverbal genome modification strategies for gene therapy: Transposon, integrase, and nuclease systems** *Gene and Cell Therapy Therapeutic Mechanisms and Strategies*
  Woodard, L. E., Calos, M. P.
  CRC Press.2015; 4: 675–699

- **Recombinase-Mediated Reprogramming and Dystrophin Gene Addition in mdx Mouse Induced Pluripotent Stem Cells** *PLOS ONE*
  Zhao, C., Farruggio, A. P., Bjornson, C. R., Chavez, C. L., Geisinger, J. M., Neal, T. L., Karow, M., Calos, M. P.
  2014; 9 (4)

- **DICE, an efficient system for iterative genomic editing in human pluripotent stem cells.** *Nucleic acids research*
  Zhu, F., Gamboa, M., Farruggio, A. P., Hippenmeyer, S., Tasic, B., Schüle, B., Chen-Tsai, Y., Calos, M. P.
  2014; 42 (5)

- **Serine integrase chimeras with activity in E. coli and HeLa cells.** *Biology open*
  Farruggio, A. P., Calos, M. P.
  2014; 3 (10): 895-903

- **Generating Dystrophin plus Myogenic Cells from mdx Fibroblasts by Using a Triple-Recombinase iPS Cell-Based Strategy** *16th Annual Meeting of the American-Society-of-Gene-and-Cell-Therapy (ASGCT)*
  Geisinger, J. M., Zhao, C., Farrugio, A. P., Chavez, C. L., Bjornson, C. R., Neal, T. L., Calos, M. P.
  NATURE PUBLISHING GROUP.2013: S68–S69

- **Translating the Genomics Revolution: The Need for an International Gene Therapy Consortium for Monogenic Diseases** *MOLECULAR THERAPY*
  Tremblay, J. P., Xiao, X., Aartsma-Rus, A., Barbas, C., Blaus, H. M., Bogdanove, A. J., Boycott, K., Brauns, S., Breakefield, X. O., Bueren, J. A., Buschmann, M., Byrne, B. J., Calos, et al
  2013; 21 (2): 266-268

- **Translating the genomics revolution: the need for an international gene therapy consortium for monogenic diseases.** *Molecular therapy : the journal of the American Society of Gene Therapy*
  Tremblay, J. P., Xiao, X., Aartsma-Rus, A., Barbas, C., Blau, H. M., Bogdanove, A. J., Boycott, K., Braun, S., Breakefield, X. O., Bueren, J. A., Buschmann, M., Byrne, B. J., Calos, et al
  2013; 21 (2): 266-268

- **Site-Specific Recombination Using PhiC31 Integrase** *Site-directed Insertion of Transgenes*
  Geisinger, J. M., Calos, M. P.
  Springer Science+Business Media Dordrecht.2013: 211–239

- **Efficient reversal of phiC31 integrase recombination in mammalian cells** *BIOTECHNOLOGY JOURNAL*
  Farruggio, A. P., Chavez, C. L., Mikell, C. L., Calos, M. P.
  2012; 7 (11)

- **Safe Genetic Modification of Cardiac Stem Cells Using a Site-Specific Integration Technique** *Meeting of the American-Heart-Association*
  Lan, F., Liu, J., Narsinh, K. H., Hu, S., Han, L., Lee, A. S., Karow, M., Nguyen, P. K., Nag, D., Calos, M. P., Robbins, R. C., Wu, J. C.
  LIPPINCOTT WILLIAMS & WILKINS.2012: S20-?

- **Recombinase Strategies To Make and Modify iPS Cells** *15th Annual Meeting of the American-Society-of-Gene-and-Cell-Therapy (ASGCT)*
  Chavez, C. L., Zhao, C., Farruggio, A. P., Geisinger, J., Karow, M., Bjornson, C., Neal, T., Calos, M. P.
  NATURE PUBLISHING GROUP.2012: S174–S174
- **Site-specific integration with bacteriophage FC31 integrase.** *Cold Spring Harbor protocols*
  Hillman, R. T., Calos, M. P.
  2012; 2012 (5)
- **Long-Term Expression of Human Coagulation Factor VIII in a Tolerant Mouse Model Using the phi C31 Integrase System** *HUMAN GENE THERAPY*
  Chavez, C. L., Keravala, A., Chu, J. N., Farruggio, A. P., Cuellar, V. E., Voorberg, J., Calos, M. P.
  2012; 23 (4): 390-398
- **Site-Specific Recombinase Strategy to Create Induced Pluripotent Stem Cells Efficiently with Plasmid DNA** *STEM CELLS*
  Karow, M., Chavez, C. L., Farruggio, A. P., Geisinger, J. M., Keravala, A., Jung, W. E., Lan, F., Wu, J. C., Chen-Tsai, Y., Calos, M. P.
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- **The therapeutic potential of phiC31 integrase as a gene therapy system** *EXPERT OPINION ON BIOLOGICAL THERAPY*
  Karow, M., Calos, M. P.
  2011; 11 (10): 1287-1296
- **Therapeutic Applications of the PhiC31 Integrase System** *CURRENT GENE THERAPY*
  Chavez, C. L., Calos, M. P.
  2011; 11 (5): 375-381
- **Long-term phenotypic correction in factor IX knockout mice by using phiC31 integrase-mediated gene therapy** *GENE THERAPY*
  Keravala, A., Chavez, C. L., Hu, G., Woodard, L. E., Monahan, P. E., Calos, M. P.
  2011; 18 (8): 842-848
- **Site-specific integration of transgene targeting an endogenous lox-like site in early mouse embryos** *JOURNAL OF APPLIED GENETICS*
  Ito, M., Yamanouchi, K., Naito, K., Calos, M. P., Tojo, H.
  2011; 52 (1): 89-94
- **Kinetics and Longevity of phi C31 Integrase in Mouse Liver and Cultured Cells** *HUMAN GENE THERAPY*
  Chavez, C. L., Keravala, A., Woodard, L. E., Hillman, R. T., Stowe, T. R., Chu, J. N., Calos, M. P.
  2010; 21 (10): 1287-1297
- **Impact of Hydrodynamic Injection and phiC31 Integrase on Tumor Latency in a Mouse Model of MYC-Induced Hepatocellular Carcinoma** *PLOS ONE*
  Woodard, L. E., Keravala, A., Jung, W. E., Wapinski, O. L., Yang, Q., Felsher, D. W., Calos, M. P.
  2010; 5 (6)
- **Effect of nuclear localization and hydrodynamic delivery-induced cell division on phi C31 integrase activity** *GENE THERAPY*
  Woodard, L. E., Hillman, R. T., Keravala, A., Lee, S., Calos, M. P.
  2010; 17 (2): 217-226
- **DNA integrating vectors (transposon, integrase)** *A Guide to Human Gene Therapy*
  Woodard, L. E., Calos, M. P.
  World Scientific Publishing Co..2010: 123–138
- **PhiC31 Integrase-Mediated Gene Transfer into Mesoangioblast Stem Cells for Amelioration of Muscular Dystrophy** *12th Annual Meeting of the American Society of Gene Therapy*
  Keravala, A., Woodard, L. E., Jung, W. E., Mosely, N. L., Calos, M. P.
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- **Mutational Derivatives of PhiC31 Integrase With Increased Efficiency and Specificity** *MOLECULAR THERAPY*
  Keravala, A., Lee, S., Thyagarajan, B., Olivares, E. C., Gabrovsky, V. E., Woodard, L. E., Calos, M. P.
  2009; 17 (1): 112-120
- **Factoring nonviral gene therapy into a cure for hemophilia A** *CURRENT OPINION IN MOLECULAR THERAPEUTICS*
  Gabrovsky, V., Calos, M. P.
  2008; 10 (5): 464-470

- **Long-term transgene expression in mouse neural progenitor cells modified with phi C31 integrase** *JOURNAL OF NEUROSCIENCE METHODS*
  Keravala, A., Ormerod, B. K., Palmer, T. D., Calos, M. P.
  2008; 173 (2): 299-305

- **Site-specific chromosomal integration mediated by phiC31 integrase.** *Methods in molecular biology (Clifton, N.J.)*
  Keravala, A., Calos, M. P.
  2008; 435: 165-173

- **Creating transgenic Drosophila by microinjecting the site-specific phi C31 integrase mRNA and a transgene-containing donor plasmid** *NATURE PROTOCOLS*
  Fish, M. P., Groth, A. C., Calos, M. P., Nusse, R.
  2007; 2 (10): 2325-2331

- **The phi C31 integrase system for gene therapy** *CURRENT GENE THERAPY*
  Calos, M. P.
  2006; 6 (6): 633-645

- **Gene transfer to rabbit retina with electron avalanche transfection** *INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE*
  Chalberg, T. W., Vankov, A., Molnar, F. E., Butterwick, A. F., Huie, P., Calos, M. P., Palanker, D. V.
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- **A diversity of serine phage integrases mediate site-specific recombination in mammalian cells** *MOLECULAR GENETICS AND GENOMICS*
  Keravala, A., Groth, A. C., Jarrahian, S., Thyagarajan, B., Hoyt, J. J., Kirby, P. J., Calos, M. P.
  2006; 276 (2): 135-146

- **Long-term increase in mVEGF164 in mouse hindlimb muscle mediated by phage phi C31 integrase after nonviral DNA delivery** *HUMAN GENE THERAPY*
  Portlock, J. L., Keravala, A., Bertoni, C., Lee, S., Rando, T. A., Calos, M. P.
  2006; 17 (8): 871-876

- **PhiC31 integrase mediates integration in cultured synovial cells and enhances gene expression in rabbit joints** *JOURNAL OF GENE MEDICINE*
  Keravala, A., Portlock, J. L., Nash, J. A., Vitrant, D. G., Robbins, P. D., Calos, M. P.
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- **Phage phi C31 integrase-mediated genomic integration of the common cytokine receptor gamma chain in human T-cell lines** *JOURNAL OF GENE MEDICINE*
  Ishikawa, Y., Tanaka, N., Murakami, K., Uchiyama, T., Kumaki, S., Tsuchiya, S., Kugoh, H., Oshimura, M., Calos, M. P., Sugamura, K.
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- **Integration specificity of phage phi C31 integrase in the human genome** *JOURNAL OF MOLECULAR BIOLOGY*
  Chalberg, T. W., Portlock, J. L., Olivares, E. C., Thyagarajan, B., Kirby, P. J., Hillman, R. T., Hoelters, J., Calos, M. P.
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  Bertoni, C., Jarrahian, S., Wheeler, T. M., Li, Y. N., Olivares, E. C., Calos, M. P., Rando, T. A.
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- **Plasma-mediated transfection of RPE** *16th Conference on Ophthalmic Technologies*
  Palanker, D., Chalberg, T., Vankov, A., Huie, P., Molnar, F. E., Butterwick, A., Calos, M., Marmor, M., Blumenkranz, M. S.
  SPIE-INT SOC OPTICAL ENGINEERING.2006

- **phi C31 integrase confers genomic integration and long-term transgene expression in rat retina** *INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE*
  Chalberg, T. W., Genise, H. L., Vollrath, D., Calos, M. P.
  2005; 46 (6): 2140-2146

- **In vivo correction of murine hereditary tyrosinemia type I by phi C31 integrase-mediated gene delivery** *MOLECULAR THERAPY*
  Held, P. K., Olivares, E. C., Aguilar, C. P., Finegold, M., Calos, M. P., Grompe, M.
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- **Site-Specific Integration with phi C31 Integrase for Prolonged Expression of Therapeutic Genes** *NON-VIRAL VECTORS FOR GENE THERAPY, SECOND EDITION: PART 2*

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- **Site-specific integration for high-level protein production in mammalian cells.** *Methods in molecular biology (Clifton, N.J.)*
  Thyagarajan, B., Calos, M. P.
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- **Nucleofection of muscle-derived stem cells and myoblasts with phi C31 integrase: Stable expression of a full-length-dystrophin fusion gene by human myoblasts** *MOLECULAR THERAPY*
  Quenneville, S. P., Chapdelaine, P., Rousseau, J., Beaulieu, J., Caron, N. J., Skuk, D., Mills, P., Olivares, E. C., Calos, M. P., Tremblay, J. P.
  2004; 10 (4): 679-687

- **Development of a novel helper-dependent adenovirus-Epstein-Barr virus hybrid system for the stable transformation of mammalian cells** *JOURNAL OF VIROLOGY*
  Dorigo, O., Gil, J. S., Gallaher, S. D., Tan, B. T., Castro, M. G., Lowenstein, P. R., Calos, M. P., Berk, A. J.
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- **Site-specific integration enhances expression of DNA introduced into skeletal muscle** *7th Annual Meeting of the American-Society-of-Gene-Therapy*
  Wheeler, T. M., Jarrahian, S., Bertoni, C., Olivares, E. C., Doyle, T., Contag, C. H., Calos, M. P., Rando, T. A.
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- **Construction of transgenic Drosophila by using the site-specific integrase from phage phi C31** *GENETICS*
  Groth, A. C., Fish, M., Nusse, R., Calos, M. P.
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- **Site-specific genomic integration produces therapeutic Factor IX levels in mice** *NATURE BIOTECHNOLOGY*
  Olivares, E. C., Hollis, R. P., Chalberg, T. W., Meuse, L., Kay, M. A., Calos, M. P.
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- **Stable nonviral genetic correction of inherited human skin disease** *NATURE MEDICINE*
  Ortiz-Urda, S., Thyagarajan, B., Keene, D. R., Lin, Q., Fang, M., Calos, M. P., Khavari, P. A.
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  Stoll, S. M., Ginsburg, D. S., Calos, M. P.
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  Sclimenti, C. R., Thyagarajan, B., Calos, M. P.
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  Olivares, E. C., Hollis, R. P., Calos, M. P.
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  Stoll, S. M., Sclimenti, C. R., Baba, E. J., Meuse, L., Kay, M. A., Calos, M. P.
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  Thyagarajan, B., Olivares, E. C., Hollis, R. P., Ginsburg, D. S., Calos, M. P.
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  Sclimenti, C. R., Baba, E. J., Calos, M. P.
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