University of Nebraska

August 16, 2021

Michael Baumgartner, Ph.D.
Executive Director
Coordinating Commission for Postsecondary Education
PO Box 95005
Lincoln, NE 68509-5005
mike.baumgartner@nebraska.gov

Dear Dr. Baumgartner:

Enclosed is a copy of the proposal to create the Genome Editing and Education Center-Nebraska in the Department of Pharmacology and Experimental Neuroscience in the College of Medicine at the University of Nebraska Medical Center. The proposal was approved by the Board of Regents at the August 13, 2021 meeting. Also enclosed is the Proposal for New Instructional Program Form 92-40.

Please do not hesitate to contact me if you have any questions.

With warmest personal regards,

Jeffrey P. Gold, M.D.
Executive Vice President and Provost

Enclosure

JPG/cr

cc: Jeffrey P. Gold, M.D., Chancellor
Dele Davies, M.D., Senior Vice Chancellor for Academic Affairs
Brad Britigan, M.D., Dean, College of Medicine
David Jackson, Ph.D., Vice Provost

Office of the Executive Vice President and Provost
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TO:	The Board of Regents	Addendum XI-A-7
	Academic Affairs Committee	
MEETING DATE:	August 13, 2021	
SUBJECT:	Establishment of Genome Editing and Education Center-Nebraska in the Department of Pharmacology and Experimental Neuroscience in the College of Medicine at the University of Nebraska Medical Center	
RECOMMENDED ACTION:	Approval to establish the Genome Editing and Education Center-Nebraska (GEEC-Nebraska) in the Department of Pharmacology and Experimental Neuroscience in the College of Medicine at the University of Nebraska Medical Center (UNMC)	
PREVIOUS ACTION:	None	
EXPLANATION:	The proposed UNMC Genome Editing and Education Center-Nebraska will transform its existing Mouse Genome Engineering Core Facility into a larger Academic Multidisciplinary Research Center. UNMC's current facility is used to create genetically engineered mouse models for researchers working to treat neurological and immunological dysfunctions, HIV and other viruses (including SARS-CoV-2), hearing and eye diseases, and various cancers. The core facility also supports many fields of basic science research. UNMC faculty and the core facility are recognized as global leaders in developing breakthrough genetic engineering technologies, some of which are used by the three major National Institutes of Health (NIH)-funded Knockout Mouse Phenotyping (KOMP) Centers (one located on each coast and one in Texas). The proposed Center will better position UNMC to scale up its scientific services to two to four times the number of investigators locally and globally, improve technologies further to address the problems of generating models for difficult-to-target genes, and perform these services for larger multi-disciplinary teams. One objective of the new Center will be to obtain an NIH KOMP Center designation, which will provide additional funding and identify the University as a primary resource for improving human and animal health in the Midwest and the world. This proposal has been reviewed by the Council of Academic Officers; it also has been reviewed by the Academic Affairs Committee.	
PROGRAM COST:	$591,000 for Year 1; $1,051,000 over five years	
SOURCE OF FUNDS:	Extramural support, UNMC internal support, and revenue from core services	
SPONSORS:	H. Dele Davies Senior Vice Chancellor for Academic Affairs Jeffrey P. Gold, Chancellor University of Nebraska Medical Center	

RECOMMENDED:

Jeffrey P. Gold, M.D.
Executive Vice President and Provost

DATE: July 16, 2021

May 12, 2021

Susan Fritz, Executive Vice President and Provost
University of Nebraska
3835 Holdrege Street
Lincoln, NE 68583
smfritz@nebraska.edu

Dear Provost Fritz:

I am forwarding you the materials relating to a proposed Genome Editing and Education Center- Nebraska (GEEC-Nebraska) to be administered by UNMC. This is a new application to transform UNMC's Mouse Genome Engineering Core Facility (MGECF) into an Academic Multidisciplinary Research Center. A major purpose of this proposal is to position UNMC to attract an NIH-designated KOMP/IMPC Center, of which there are none in the region. The current Core Facility is one of the leading laboratories in mouse genome editing technology development. Being in the mid-west region, a center designation will give UNMC a very high chance of attracting an NIH Center designation in the next few years.

Currently, similar to the KOMP centers, UNMC MGECF offers end-to-end services to develop mouse models for the scientific community within and outside of UNMC. Additionally, the UNMC MGECF has been outperforming other laboratories in terms of the number of models generated, and the number of investigators served when compared to the resources available at centers like KOMP. The center, once approved, will continue, expand, and improve current services and technologies.

This proposal has been reviewed, and it has my approval. I am requesting your review and approval and that it be reported to the Board of Regents at an upcoming meeting.

Sincerely,

Jeffrey P. Gold, M.D.
Chancellor

University of Nebraska Medical Center
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University of Nebraska Medical Center
New Academic Center

Academic Centers include bureaus and institutes

I. Descriptive Information

Name of Institution Proposing New Center
University of Nebraska Medical Center
Name of Proposed Center
Genome Editing and Education Center- Nebraska (GEEC-Nebraska)
Name of the Programs (majors) Involved
Genome Editing, Animal models, Molecular Genetics, Genomics.
Other Programs Offered in this Field by Institution
None
Administrative Unit(s) for the Proposed Center *[e.g. college, school, division, etc.]*
College of Medicine, Department: Pharmacology and Experimental Neuroscience
Physical Location, if applicable
DRC II Room 1014 + **Additional space to be allocated**
Date Approved by the Governing Board
Pending
Proposed Date the Center will be Initiated
Upon approval by the Coordinating Commission.

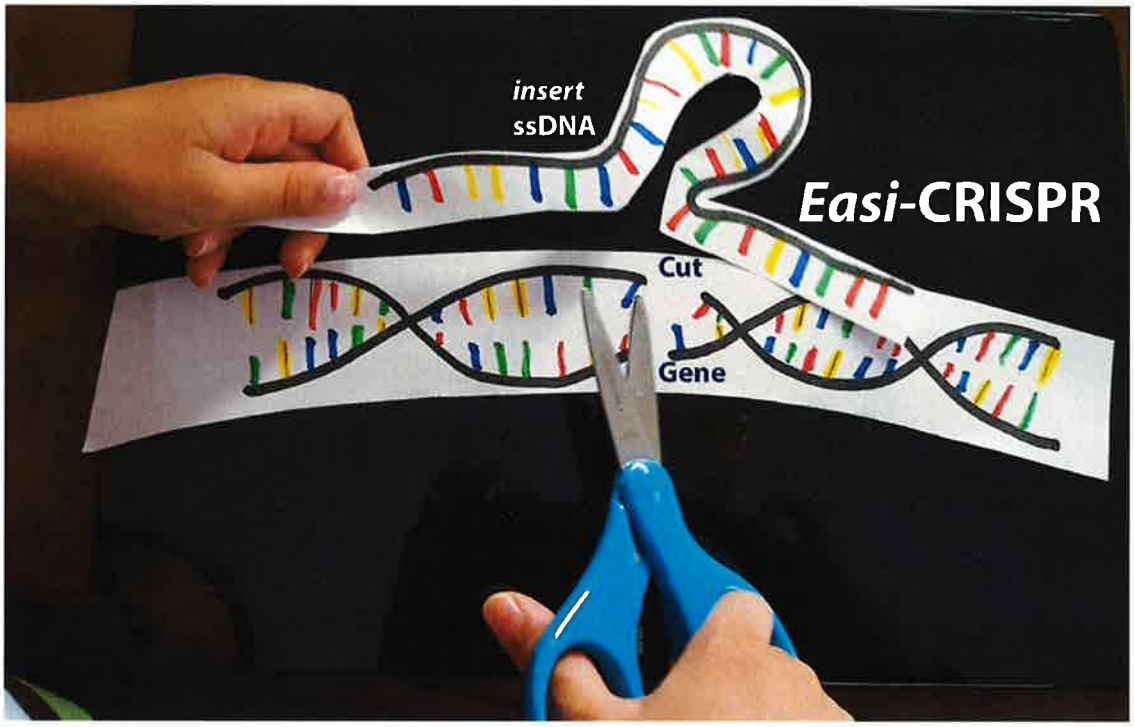
II. Review Criteria

A. Purpose and Context for the Center

Importance of animal models for understanding human physiology and for development of therapies for human and animal diseases. Invariably, all medicines approved for treating human and animal diseases have undergone prior testing in animal models. Experiments using animal models, such as mice, have also helped how our body works. Of all different laboratory animals, the mice are most predominantly used, because of the cost, their short life cycle and they also contain majority of the same type of genes that we humans have, and the molecular processes are highly similar between humans and mice. Nearly 70% of NIH funded research projects rely on mouse models. Another major reason why mouse has been a preferred laboratory animal species is that the genetic engineering technology to insert foreign genes into mice (called **transgenic mice**) or delete a gene of interest (called **knockout mice**) are well-established, and these technologies can create custom-made humanized mouse models suitable for studying numerous human diseases.

Several thousands of custom made mouse models have been developed so far, which are used for research to understand human physiology and disease. Here we provide two examples of custom made mouse models to emphasize their value for human health: *avatar mice and COVID19 mice*. **Avatar mice** represent miniature human cancer patients (termed "avatars"), wherein cancer cells from a patient are implanted into several groups of mice and each group of avatar mice are given different chemotherapy options to learn which chemotherapy works best against the patient's cancer cells, and the clinicians can use this information for deciding a suitable chemotherapy regimen for the patient. If human cancer cells are implanted into regular (wild type) mice, they reject the cells because they are foreign to mice and the mouse immune system attacks human cells. Avatar mice are created by deleting several mouse immunological genes and inserting human genes in (through genetic engineering technology), so that the mice do not reject human cells. **COVID19 mouse models**: research community quickly learnt that SARS-CoV-2 does not infect mice because the protein receptor that the virus attaches on to human cell surface (called Ace2) is different in mice and the virus is unable to enter mouse cells. Fortunately, however, genetic engineering technology in mice are so advanced that human Ace2 gene can be transferred to mice to create humanized Ace2 mice that can be used for infecting SARS-CoV-2 and test medicines and vaccines against COVID19.

UNMC has been a global leader in developing breakthrough genetic engineering technologies, particularly the latest advance in the field called CRISPR (Clustered Regularly Interspersed Palindromic Repeats)-Cas system. UNMC has established a transgenic mouse core facility to create custom made genetically engineered mouse models for researchers working in various diseases including cancer, neuroscience, immunology, HIV, hearing, eye diseases, COVID19 research and many fields of basic science research. More importantly, the core has accomplished much more in this area by developing newer technologies and has earned a worldwide recognition. Specifically, a far simpler and a most robust version of CRISPR called, ***Easi*-CRISPR (Efficient additions with ssDNA inserts CRISPR)**, was developed at UNMC, which is now adapted at hundreds of laboratories worldwide as the method of choice for creating mouse models.



This is a proposal to transform UNMC's Mouse Genome Engineering Core Facility (MGECF) into an Academic Multidisciplinary Research Center. The ultimate purpose of this proposal is to position UNMC to attract an NIH designated KOMP/IMPC Center. Specifics and additional details about the KOMP/IMPC program are described in section "I" (Constituencies to be Served), and we briefly describe the context of this application.

In April 2020, recognizing the outstanding accomplishments of the UNMC MGECF, Dr. Bradley Britigan (Dean of the UNMC College Of Medicine) and Dr. Howard Gendelman (Chairperson of the Pharmacology and Experimental Neuroscience Department) enthusiastically agreed to support the launch of a new Center for Genome Editing Technologies. The new center will leverage UNMC's outstanding position in CRISPR mouse genome editing.

The NIH initiated a large-scale project, in 2006, called KnockOut Mouse Project (KOMP) with a goal to create knockout mice for every single gene in mice. The KOMP project has continuously funded three centers in the US, all located along coasts (approximately $25-$30M per center per 5 year period). By 2010 the focus of KOMP shifted from complete KO mice to conditional KO mice where a given gene is knocked out only in specific cells and at a certain stage of life in mice. In 2013, when CRISPR technology was first published, the mouse genetics community thought that it could radically change the mouse model generation workflow. However, many transgenic facilities worldwide, including the KOMP centers, were unable to use CRISPR technology for creating conditional KO mice. **The Easi-CRISPR technology developed at UNMC solved the major problem in the field which was the length of time it took to create a usable mouse model. The Easi-CRISPR method has now been adopted at the three NIH KOMP centers and is currently being used to develop important mouse models. Several of UNMC's scientific contributions (published in over a dozen articles in the past 5 years) have drawn significant attention from the NIH and from the transgenic mouse community worldwide, bringing attention to UNMC's strengths and capabilities.** The Director of MGECF was also awarded a unique type of grant called the Outstanding Investigator Award from the National Human Genome Research Institute (NHGRI) for further improvement of the CRISPR technologies used for developing mouse models.

Workforce development: Currently the staff at UNMC MGECF is the director, two technicians (3 FTEs) and a part time administrator. This core offers end-to-end services (including designing, construct generation, microinjection, genotyping up to germ line transmission, and breeding) while most cores offer mainly microinjection services. Excluding phenotyping and our mouse repository services, MGECF core already operates similar to a mini-KOMP center. In the next three to four years, we aim to demonstrate to the NIH that: (a) we have infrastructure and capabilities on par with the existing KOMP centers, and; (b) that our unique technical capabilities will be particularly useful for the KOMP operations. Our specific plans to achieve KOMP status would be: (i) to recruit a few more technical personnel to the core which will allow us to develop new techniques and provide more services, (ii) this will increase our critical mass and provide the technical personnel necessary to compete for a center grant, and; (iii) to develop high throughput technologies and tools appropriate for plugging-in to the on-going operations of KOMP (through the use of the currently funded R35 grant to Dr. Gurumurthy).

In order to take the UNMC MGECF's success to the next level (attracting a KOMP center to Nebraska, for example), MGECF will need to achieve four major things: 1) scaling up of its scientific services by doubling or tripling in the next couple years, 2) offering those services to two to four times the number of investigators locally and globally, 3) improve technologies further to address the problems of generating models for difficult-to-target genes and 4) **more importantly perform these activities as part of a designated center at the University with multi-disciplinary teams of expertise utilizing and overseeing its services**. These activities should demonstrate to the funding agencies, such as NIH, that UNMC has exceptional faculty, well organized and functioning teams, plus the infrastructure and framework for initiating and operating a bigger center like KOMP. The launching of GEEC-Nebraska would be the first step in this direction, and will position the university to attract an NIH designated mouse genetics center like KOMP. **In addition, having an NIH designated center within the UN system will stimulate innovative research, contribute to the education and knowledge-sharing missions of the university and importantly it will also increase the skilled workforce and significantly contribute to the overall economic growth in Nebraska; the typical number of full time employees in the existing KOMP centers is 10-fold or more.**

This proposal builds upon a number of MGECF core accomplishments made during the past half decade and extends the research to a larger number of investigators both inside and outside the University.

- MGECF laboratory has published a series of high impact papers on traditional transgenic technologies as well as the latest advanced technologies including the CRISPR-Cas (clustered regularly interspaced short palindromic repeats) system. Some of the MGECF papers are regarded as landmark papers in the field and several have been cited more than 50 times. Please see **Appendix A** for a list of 25 important papers from MGECF.
- Innovations made at the University of Nebraska Medical Center's (UNMC) MGECF, such as Efficient Additions with *ss*DNA *i*nserts-CRISPR *(Easi*-CRISPR) and Genome editing by Oviductal Nucleic Acids Delivery (*i*-GONAD) methods, have been regarded as scientific breakthroughs *that have redefined transgenic technologies practiced for the last 30 years".*
- *Easi*-CRISPR and *i*-GONAD methods have now been adopted at over a hundred laboratories/core facilities worldwide.
- The inventions have earned the UNMC core director over 80 invitations for keynote talks and presentations, meetings and workshop organizations, and the prestigious position of serving as chair for sessions at international conferences (17 invitations in 12 countries).
- These scientific contributions have been instrumental in the awarding of NIH grants to UNMC researchers totaling 25M dollars and are responsible for the director receiving the **Outstanding Investigator Award from the National Human Genome Research Institute (NHGRI).** This award allows the recipient complete flexibility to explore any research idea in the area of genomic technologies. See **Appendix B** for list of extramural funding received as a direct result of the technologies and/or mouse models developed at MGECF.
- **MGE Core's scientific accomplishments** have made several local, national and international news headlines **(See Appendix C).**
- **Attracted numerous collaborations, worldwide**. The UNMC MGECF work has attracted collaborations with diverse areas from neuroscience, immunology, developmental biology, virology and oncology. The director has demonstrated exceptional abilities in building and maintaining a large number of fruitful collaborations locally, nationally, and globally (see section H for list of external collaborations).
- **UNMC director received** one-of-a-kind NIH grant for developing CRISPR mouse genome engineering technologies and for advancing mouse genetics https://www.genome.gov/news/news-release/NHGRI-announces-six-inaugural-genomic-innovator-awards.
- **Developed breakthrough technologies:** PITT[1], i-PITT[2], CRISPR-First;PITT-next[3], GONAD[4,5], i-GONAD[6] & Easi-CRISPR[7,8]. The research community regards MGECF contributions as *"breakthroughs that have redefined the previously Nobel Prize awarded transgenic technologies practiced for the last four decades"*[9].

Important landmark papers relevant to MGECF's contribution on mouse genome engineering technologies

1 Ohtsuka M, Miura H, Sato M, Kimura M, Inoko H, Gurumurthy CB. PITT: pronuclear injection-based targeted transgenesis, a reliable transgene expression method in mice. *Exp Anim Jpn Assoc Lab Anim Sci* 2012;**61**:489–502.

2 Ohtsuka M, Miura H, Mochida K, Hirose M, Hasegawa A, Ogura A, *et al.* One-step generation of multiple transgenic mouse lines using an improved Pronuclear Injection-based Targeted Transgenesis (i-PITT). *BMC Genomics* 2015;**16**:274. https://doi.org/10.1186/s12864-015-1432-5.

3 Quadros RM, Harms DW, Ohtsuka M, Gurumurthy CB. Insertion of sequences at the original provirus integration site of mouse ROSA26 locus using the CRISPR/Cas9 system. *FEBS Open Bio* 2015;**5**:191–7. https://doi.org/10.1016/j.fob.2015.03.003.

4 Takahashi G, Gurumurthy CB, Wada K, Miura H, Sato M, Ohtsuka M. GONAD: Genome-editing via Oviductal Nucleic Acids Delivery system: a novel microinjection independent genome engineering method in mice. *Sci Rep* 2015;**5**:11406. https://doi.org/10.1038/srep11406.

5 Gurumurthy CB, Takahashi G, Wada K, Miura H, Sato M, Ohtsuka M. GONAD: A Novel CRISPR/Cas9 Genome Editing Method that Does Not Require Ex Vivo Handling of Embryos: GONAD: A Novel CRISPR/Cas9 Genome Editing Method. In: Haines JL, Korf BR, Morton CC, Seidman CE, Seidman JG, Smith DR, editors. *Curr. Protoc. Hum. Genet.* Hoboken, NJ, USA: John Wiley & Sons, Inc.; 2016. p. 15.8.1-15.8.12.

6 Ohtsuka M, Sato M, Miura H, Takabayashi S, Matsuyama M, Koyano T, *et al.* i-GONAD: a robust method for in situ germline genome engineering using CRISPR nucleases. *Genome Biol* 2018;**19**:25. https://doi.org/10.1186/s13059-018-1400-x.

7 Quadros RM, Miura H, Harms DW, Akatsuka H, Sato T, Aida T, *et al.* Easi-CRISPR: a robust method for one-step generation of mice carrying conditional and insertion alleles using long ssDNA donors and CRISPR ribonucleoproteins. *Genome Biol* 2017;**18**:92. https://doi.org/10.1186/s13059-017-1220-4.
8 Miura H, Quadros RM, Gurumurthy CB, Ohtsuka M. Easi-CRISPR for creating knock-in and conditional knockout mouse models using long ssDNA donors. *Nat Protoc* 2017;**13**:195.
9 Burgio G. Redefining mouse transgenesis with CRISPR/Cas9 genome editing technology. *Genome Biol* 2018;**19**:27. https://doi.org/10.1186/s13059-018-1409-1.

The overarching goal of the center will be to attract NIH funding to create a Nebraska Mouse Resource and Research Center (NMRRC). The NIH has a funding mechanism to support several centers called Mutant Mouse Resource and Research Center (NMRRC). The launching of a regional MMRRC center in Nebraska (NMRRC), will position UNMC to attract multi-million dollar program project grants from the NIH and it will increase the workforce and economic growth in Nebraska (described in the later sections).

The Center will have three objectives:

- ***Research:*** *The proposed center will develop novel technologies for animal genome engineering.*
- ***Service:*** *The center will offer services to internal and external researchers working on numerous human diseases and develop animal models suitable for their research.*
- ***Education:*** *The center will organize CRISPR and mouse genome editing workshops for new technologies. The director of the mouse genome engineering core has received over 80 invitations to deliver keynote talks, seminars and workshops worldwide. With the initiation of the center at UNMC, we will organize workshops at UNMC. The center will offer opportunities for teaching and training students, technicians and post-doctoral fellows including summer training programs for post-secondary students.*

The ultimate goal of these three objectives is to position UNMC to attract multi-million dollar program project grants from the NIH (see below) within 5-10 years.

B. Centrality to UNMC Role and Mission

The proposed center directly fulfills the UNMC missions of research innovation, services, and education as follows. **The** UNMC MGECF has excelled in research innovation *(several high impact methods and technologies have been developed at UNMC that are now followed as standard methods at hundreds of laboratories worldwide)*. The core has served numerous internal university researchers in addition to external research clients and has had significant impacts on their research projects. Our education and knowledge dissemination presentations are in high demand. The *MGECF team has conducted highly popular workshops and offered seminars and lectures at conferences in several countries*. These activities have earned worldwide recognition for UNMC in the field of Genome Editing. The trajectory of these efforts—research innovation, education and services—will continue to climb and will be performed at an even higher level through the initiation of the GEEC-Nebraska Center. The work done by the center will raise the stature of the University with the ultimate goal for an NIH Designated Center to be established at UNMC in the next 5-10 years (see section I "**Anticipated Outcomes, Significance, and Specific Measures of Success**").

C. Relationship of the proposal to the NU Five-Year Strategy

Broad themes of the NU Five-Year Strategy are:

- *student access and success,*
- *excellence in teaching and research,*
- *diversity and inclusion,*
- *partnerships, and*
- *fiscal effectiveness.*
- *Workforce development*

The goals of the GEEC-Nebraska align very well with these NU Five-Year Strategy themes as follows:

Student access and success: One of the objectives of GEEC-Nebraska is to provide education that will serve students at all levels. Specifically, the knowledge and the technologies developed at the center will be made available to the learning community through courses, lectures, seminars, and hands-on workshops.

Excellence in teaching and research: Genome editing technology is a very hot field. UNMC MGECF has made significant contributions to genome editing research already and the core director has received dozens of invitations for lectures and seminars all over the world. With the initiation of the GEEC-Nebraska center, we anticipate expanding the teaching of genome editing technologies and related applications and better serving the learning communities within and outside the state.

Diversity and inclusion: We anticipate recruiting additional workforce that includes faculty members and technicians. We thrive on fostering an Inclusive Culture and Environment while serving the community and expanding the GEEC-Nebraska team. The director of MGECF strongly believes in and practices diversity and inclusion. Dr. Gurumurthy was invited and is enrolled in an NIH mentoring and training program called Culture Change (C-Change) for leadership and diversity training; a one-year course that will be completed Fall 2021.

Partnerships: As evident in the list of collaborating institutes (see section H), UNMC MGECF has successfully partnered with research teams at dozens of institutes and universities external to the UN system. The initiation of GEEC-Nebraska is expected to greatly enhance the partnerships and collaborations that MGECF has established over the years.

Fiscal effectiveness: MGECF has developed highly efficient gene editing technologies (such as Easi-CRISPR and GONAD), which have reduced the costs of generating disease models by about one-third based on reducing the length of time from the one to two years that it used to take to make a model with the previous technologies. Easi-CRISPR technology can now produce a usable mouse model in approximately four to six months. With our demonstrated success in developing cost effective and efficient technologies and with additional newly trained workforce additions, we will be able to deliver the best (technologies and services and education) to the community.

Workforce development: Currently the staff at UNMC MGECF is the director and two technicians (three FTEs) and a part time administrator. This core offers end-to-end services (including designing, construct generation, microinjection, genotyping up to germ line transmission, and breeding) while most cores offer mainly microinjection services. Excluding phenotyping and our mouse repository services, MGECF core already operates similar to a mini-KOMP center. In the next three to four years, we aim to demonstrate to the NIH that: (a) we have infrastructure and capabilities on par with the existing KOMP centers, and; (b) that our unique technical capabilities will be particularly useful for the KOMP operations. Our specific plans to achieve KOMP status would be: (i) to recruit a few more technical personnel to the core which will allow us to develop new techniques and provide more services, (ii) this will increase our critical mass and provide the technical personnel necessary to compete for a center grant, and; (iii) to develop high throughput technologies and tools appropriate for plugging-in to the on-going operations of KOMP (through the use of the currently funded R35 grant to Dr. Gurumurthy).

D. Consistency with the Comprehensive Statewide Plan for Post-Secondary Education

GEEC-Nebraska will contribute to five specific areas of Nebraska's statewide goals listed in four (of the seven) chapters: https://ccpe.nebraska.gov/sites/ccpe.nebraska.gov/files/CompPlan.pdf

Postsecondary education for Nebraska's future (Chapter 1) and meeting the educational needs of students (Chapter 2): There is local, regional, national, and international interest in CRISPR-based technologies. Dr. Gurumurthy has received numerous inquiries from high school students, schoolteachers, industry and the general public, all wanting to learn more about CRISPR and to visit the lab to learn how it is done. Under the

education component of GEEC-Nebraska, this need will be served (see below). The director has given talks at Omaha high schools, public libraries, and to colleges (Kearney) and at science cafes. This will be expanded, and plans are already underway to organize workshops every 18 months to two years that will integrate multiple campuses including and beyond UNMC. The director brings extensive experience in teaching GE technology. Dr. Gurumurthy has received and accepted multiple invitations to deliver talks and to organize conferences and workshops all over the world, including Greece, Belgium, Australia, UK, Czech Republic, and India. We plan to partner with teaching faculties from UNL, UNK and UNO, where undergraduate teaching is a major focus. Some of the participating teaching faculty have been involved in highly successful learning programs such as the Institutional Development Award Program Networks of Biomedical Research Excellence (INBRE) (Kimberly A. Carlson, Ph.D., Professor & Assistant Chair, Biology Department, UNK – Geneticist) and uBEATS, STEM e-learning program which is a UNMC-UNO partnership under the leadership of Dr. Paul Davis [faculty advisor to the Molecular and Biomedical Biology (MBB) and B.S. degree program at UNO] and Dr. Dele Davies (Senior Vice Chancellor for Academic Affairs at UNMC).

Meeting the needs of the state: workforce development, research and technology transfer, serving citizens, using technology to meet state needs (Chapter 3). As mentioned above (section A "Purpose and context of the center"), launching of GEEC-Nebraska is expected to ultimately attract an NIH designated center like KOMP leading to the opportunity to increase the workforce of the Genome Editing center by 10 fold or more. Under this new designation as a center (GEEC-Nebraska), MGECF will continue to do cutting edge research and technology development as well as present through workshops and provide additional teaching activities. The Center will transfer those technologies and disseminate knowledge to the learning community.

Meeting needs through exemplary institutions (Chapter 4): Through continued success of the GEEC-Nebraska Center and with the support of an NIH funded center like KOMP, we envision a strong probability that such an investment could lead to the launch of an institute (for example Genome Editing Institute), which would be targeted to develop in a decade or so.

Meeting educational needs through partnerships and collaboration (Chapter 5): The center expects to partner with the major institutions locally (Creighton University, Boys Town National Research Hospital) and the other campuses of the University of Nebraska system in addition to dozens of external institutes (see list in section H)

E. Evidence of Need and Demand

Laboratory mice constitute over 70% of all types of animal models used in biomedical research. Genetic engineering technologies, that became highly feasible in the mouse system during the past 3 decades, have made mouse models the most preferred genetic model system. When cost and feasibility are taken into account, the mouse becomes the animal model of choice for many researchers.

UNMC MGECF has developed hundreds of models for UNMC researchers in the past decade allowing them to publish dozens of papers and earn grant awards of over $25M in the past five to six years (see **Appendix B** for list of grants).

UNMC MGECF is also regarded as a role model core facility, attracting a large number of external collaborators to use its services. Unlike transgenic mouse core facilities at other institutes, UNMC MGECF offers end-to-end services including designing, construct generation, microinjection, genotyping, breeding to segregate mosaic mice, re-genotyping the offspring in the next (F1) generation, generating figures and writing of the technical sections for grants/manuscripts and consultation and knowledge-sharing with the PI's team on their model/s. Due to these unique and exceptional services, UNMC MGECF has attracted several external clients. A list of a few examples of our external client base includes the NIH, Harvard University, Stanford University, University of Miami, University of Utah, University of Minnesota, University of North Dakota, University of California San Francisco, University of California San Diego, and University of California Davis.

The UNMC MGECF director has demonstrated exceptional collaborative skills and published several papers in high profile journals through those collaborations. In a recent example, the UNMC MGECF director led a consortium of 17 institutes around the world (from seven countries), publishing a comprehensive research study, with 112 authors, designed to understand the reproducibility of various CRISPR based methods of generating mouse models.

By establishing a center, we will provide the opportunity to undertake similar activities at a much higher level, serving two to four times the number of research teams and investigators, which will further the breakthrough research success we have achieved to date. As stated in section A, *performing these activities as part of a designated center at the University with multi-disciplinary teams of expertise utilizing its services and overseeing its services will ultimately position UNMC to attract the support needed to become a*n NIH designated Center. In turn this will bring more recognition and financial support along with workforce development and economic growth to Nebraska.

F. Organizational Structure and Administration

Director: *Channabasavaiah Gurumurthy (provides overall leadership and direction to the center).*

The Center members will include several key faculty (listed below) who have been using genetically engineered mouse models for basic and translational research for several decades and who are from multiple disciplines ranging from pharmacology to cancer research to neuroscience. These faculty will serve as key users and advisers of the new center. The availability of this local expertise and faculty-pool will also serve as a critical factor in demonstrating (to extramural funding agencies in the future) the outstanding environment and expertise available at UNMC when applying for major center grants such as KOMP.

Within the Pharmacology and Experimental Neuroscience Department
Howard Gendelman, Pharmacology and Experimental Neuroscience
Larisa Poluektova, Pharmacology and Experimental Neuroscience
Santhi Gorantla, Pharmacology and Experimental Neuroscience
Xinglong Wang, Pharmacology and Experimental Neuroscience

Outside the Pharmacology and Experimental Neuroscience Department
Surinder Batra, Biochemistry and Molecular Biology
Mark Carlson, Surgery
Zeljka Korade, Pediatrics
Merry Lindsey, Physiology
Karoly Mirnics, Munroe-Meyer Institute
Wallace Thoreson, Ophthalmology

Outside the UNMC campus

Investigator	Campus	Area of expertise: Research and/or Education
Bruce Chase	*UNO*	*Education-Genetics, Developmental Biology Advanced Genetics*
Kimberly Clarkson	*UNK*	*Research and Education- Biology and undergraduate teaching and STEM education and outreach research and Intracellular pathogens*
Thomas Clemente	*UNL*	*Plant Transformation Core Research Facility*
Paul Davis	*UNO*	*Research and Education, Toxoplasma research laboratory, undergraduate teaching, STEM education, K8 teaching and outreach*
Jeff French	*UNO*	*Research-Behavioral neuroscience- Marmoset model*
Clayton Keling	*UNL*	*Research- cattle genomics*
Brandon Luedtke	*UNK*	*Research and Education- Molecular Biology and undergraduate research and teaching and STEM education and outreach*

Jay Reddy	*UNL*	*Research- Mouse models and Veterinary Immunology*
Donald Reynolds	*UNL*	*Research-Poultry Veterinarian*
William Tapprich	*UNO*	*Research and Education- Molecular Biology and undergraduate research and teaching and STEM education and outreach*
Paul Twigg	*UNK*	*Research and education- plant molecular biology and STEM education, K8 teaching and outreach*
Brett White	*UNL*	*Research- Transgenic pig model core*

Advisory board
Howard Gendelman
Surinder Batra
Karoly Mirnics
Larisa Poluektova
Bradley Britigan

External advisory board will be formed once the center is officially launched.

G. Partnerships with Business

UNMC Mouse Genome Engineering core services have attracted multiple collaborations across the country and internationally (please see section H for the list of external collaborators that UNMC MGECF has attracted during the past 4 years). Some collaborations have led to several research grants from NIH popularly known as R21 and R01 grants with collaborators outside of UNMC (R21 with University of Colorado in which Dr. Gurumurthy is a contact PI and R01 with University of Utah; recently funded). More collaborations are underway.

The technologies and innovations made at UNMC MGE have attracted collaborations with industries and startup companies. Two patents and one provisional patent have been submitted. One technology (Easi-CRISPR) is licensed to Taconic. Easi-CRISPR is one of the leading model generation companies in the world. Tailored Therapeutics, a startup company is establishing a research collaboration with UNMC to leverage the potential of Easi-CRISPR in CAR-T therapy for cancer. Similar to this, we anticipate multiple collaborations from industries in the future.

H. Collaborations with Higher Education Institutions External to the University

UNMC MGECF has also been regarded as the role model core facility attracting a large number of external collaborators to use its services. Below is a list of external investigators and their institutes collaborating with MGECF on Mouse Genetics Projects.

	External to UN system Investigator	Institute
Within state of Nebraska	Dominic Cosgrove	Boys Town National Research Hospital
	Barb Morley	Boys Town National Research Hospital
	Yesha Lundberg	Boys Town National Research Hospital
	Shanshank Dravid	Creighton University
	Laura Hansen	Creighton University
	David He	Creighton University
	Weston, Michael	Creighton University
	Kirk Beisel	Creighton University
Outside state of Nebraska	Suzanne Mansour	University of Utah
	Jarrod Barnes	University of Alabama
	Ying-Xian Pan	Rockefeller University
	Tekin Mustafa	University of Miami
	Vadim Gladyshev	Brigham and Women's Hospital
	Michael Green	MD Anderson Cancer Center
	Christopher Gregg	University of Utah
	Prashant Mali	University of California San Diego
	Kent Lloyd	University of California Davis
	Cynthia Morton	Brigham and Women's Hospital
	Jyotika Sharma	University of North Dakota
	Brian North	Creighton University
	Sunil Sudarshan	University of Alabama
	Doris Wu	NIH
	Cynthia Morton	Harvard University
	Doris Wu	NIH
	Paul Bray	University of Utah
	Luca Brunelli	University of Utah
	Xue Zhong Liu	University of Miami
International	Francois Lallemend	Karolinska Institute Sweden
	Guy Richardson	University of Sussex, UK
	Claus Nerlov	Oxford University, UK

Even though the institutes/universities of all these external investigators (except Creighton and BTNRH) have transgenic mouse cores, they choose to work with UNMC because of the scientific excellence and the unique array of services and consultation offered at the UNMC MGE core

Establishing a center will provide the opportunity to undertake similar and additional activities that will take this success to the next level, earning accolades and further recognition for the UN system.

I. Constituencies to be Served

The center anticipates serving about 40 to 50 investigators annually, both internal and external to UNMC.

Below is the list of 47 UN system investigators and 32 external investigators that used the services of the Mouse Genome Engineering Core Facility services during the past three years (2017-2020)

Internal to UN system

Investigator	Institute
Karoly Mirnics	UNMC
Kishore Bhakat	UNMC
Merry Lindsey	UNMC
Steve Bonasera	UNMC/VA
Larisa Poluektova	UNMC
Santhi Gorantla	UNMC
Wallace Thoreson	UNMC
Sung-Ho Huh	UNMC
Aiming Peng	UNMC
Kyle Hewitt	UNMC
Tieshi Li	UNMC
Surinder Batra	UNMC
Hamid Band	UNMC
Vimla Band	UNMC
Donald Becker	UNL
Abdalla Meher	UNMC
Jyothi Arikkath	UNMC
Kishore Bidasee	UNMC
Kaustubh Datta	UNMC
Punitha Dhawan	UNMC/VA
Amar Singh	UNMC/VA
Jixin Dong	UNMC
Dunaevsky Anna	UNMC
Howard Gendelman	UNMC
Richard Gumina	UNMC
Kyle Hewitt	UNMC
Michael Hollingsworth	UNMC
Kate Hyde	UNMC
Peter Kador	UNMC
Adam Karpf	UNMC
Woo-Yang Kim	UNMC
Robert Lewis	UNMC
Paras Mishra	UNMC
Ram Mahato	UNMC
Ali Naushad	UNMC
Babu Padanilam	UNMC
William Rizzo	UNMC
Nora Sarvetnick	UNMC
Pankaj Singh	UNMC
Joyce Solheim	UNMC

Anna Spagnoli	UNMC
Keer Sun	UNMC
Xinghui Sun	UNL
Sarah Thayer	UNMC
Kay-Uwe Wagner	UNMC
Nicholas Woods	UNMC
Janos Zempleni	UNL

In addition to internal investigators, a large number of external investigators from institutes throughout USA and international (listed in section H) will be served.

Anticipated Outcomes, Significance, and Specific Measures of Success

As described in the section 'Purpose and Context for the Center' above, mouse models have made tremendous contributions to our understanding of human physiology and for development of therapies for human and animal diseases. During the past few years, UNMC's mouse genome engineering core has created a couple hundred mouse models for investigators working in various research fields such as cancer, neuroscience, immunology, HIV, hearing, eye diseases, COVID19 research and many fields of basic science research. The center anticipates developing a greater number of mouse (and other animal) models, expanding collaborations, publishing impactful papers, disseminating knowledge and protocols through courses and workshops and attracting additional extramural funding.

Number of mouse models: *Currently MGECF generates about 15-20 mouse models per year for investigators. In years one and two, the center will aim to attract additional users and to increase model development to 20-25 models per year. By years four and five, the center plans to develop an average of 30 to 50 models per year.*
Number of users: *Currently MGECF serves about 35-45 investigators per year. In years one and two, the center will increase the user base to 50-55 users. By year five, we will increase this number to over 75 users per year.*
Publications: *MGECF has consistently published high impact papers in the genetic engineering field. Some papers published by the UNMC MGECF are regarded as landmark papers in the field (related to Easi-CRISPR and GONAD technologies). The center will continue to be a leader in genetic engineering. Historically, MGECF users publish 10-20 papers per year as a direct result of the research findings they were able to achieve using services received through the core. The center anticipates this number to increase and by year five we expect at least 50 core citations per year.*
Education/dissemination of knowledge: *The center will organize workshops and courses for students and technicians within and outside of UNMC*
Attracting extramural funding: One of the major goals of the center will be to prepare UNMC to attract a multi-million dollar KOMP center grant from NIH, which is described in detail below.
Background: In 2006, the NIH started a large-scale program called Knockout Mouse Project (KOMP) to create knockout mouse models for every gene. Several global organizations then joined efforts to form International Knockout Mouse Consortium (IKMC). The IKMC's goal was to complete nearly 90% of genes in the first two-phases (of a five-year plan); however, only about 25% of the genes were completed by 2013, the year when CRISPR slowed the project's workflow. The focus was diverted by the developing CRISPR methods. None of the efforts to create conditional knockout mice were successful until 2017. **That was when UNMC's *Easi*-CRISPR method drew the world's attention.** Now, *Easi*-CRISPR has not only been adopted by hundreds of laboratories worldwide but it has also helped steer activities at the KOMP centers. For instance, the KOMP centers had gone back to creating old fashioned knockout mice rather than conditional knockouts (cKO) using the $85M ($28.3M each) funds they received in KOMP2 phase because technologies to create cKO models were not available.

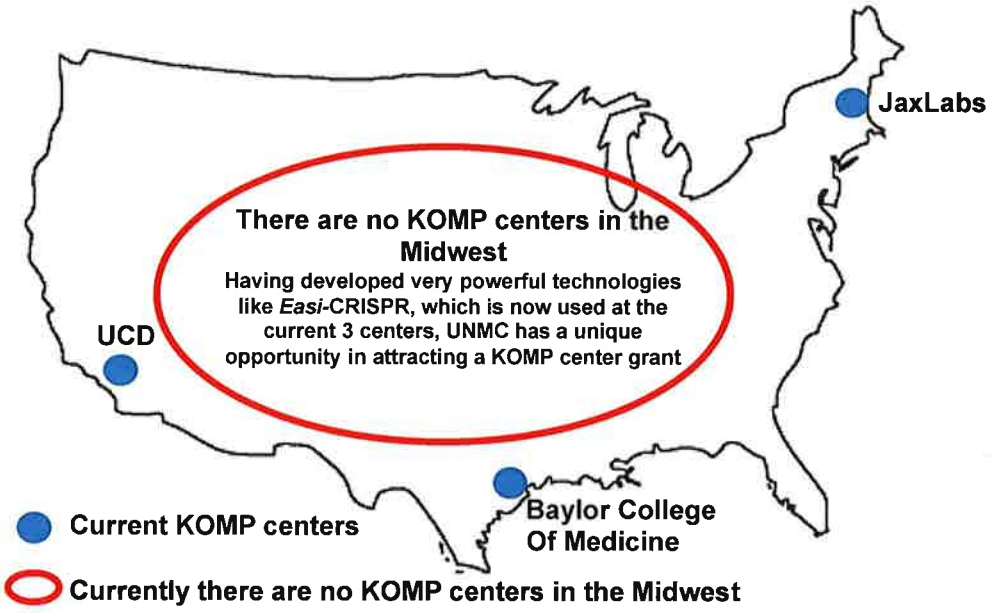
NIH has awarded its KOMP funds (>$250M so far) to only three centers in the nation thus far (Jackson Labs in Maine, University of California Davis, and Baylor College of Medicine in Texas) which were all established over 10 years ago. Now, UNMC has made a significant impact in this field and we've drawn the attention of prominent NIH KOMP program officials (from NHGRI and Commons fund). Therefore, phase III funding could be

available to begin a KOMP center at UNMC to fill the noticeable gap in coverage for the Midwest region. The center plans to prepare our *organization and facility* to ultimately attract KOMP/IMPC program-project funding in the next 5-10 years.

Recently, IMPC released its strategic plan for the next 10 years (2021-2030). It proposes a strong commitment from the global funding agencies to support the development and use of mouse models for understanding and developing therapies against human diseases. https://www.mousephenotype.org/wp-content/uploads/2019/05/IMPC_Strategy_2021-30.pdf. IMPC lists six major goals for the next decade. The first three utilize CRISPR based technologies, particularly the ones developed at UNMC:

- **IMPC Goal One:** The IMPC will generate 8,000 new null alleles to complete the null resource. All mouse strains will continue to be made available and accessible through open access repositories to the global biomedical research community
- **IMPC Goal Two:** By 2025, the IMPC aims to be generating ~1,000 human coding disease-variant strains per year.
- **IMPC Goal Three:** By 2025, the IMPC aims to be generating around 500 targeted deletions of conserved noncoding elements (CNEs) per year.

Below is the current geographic distribution of KOMP/IMPC centers in the USA



Several funding opportunities will be available in the next 10 years through IMPC strategic plans. Anticipated funding amount received at each center would be about $25-$30M

There are no KOMP centers in the Midwest: **having developed very powerful technologies like *Easi*-CRISPR, which is now used as the method of choice at the current three centers, UNMC has a unique opportunity to attract a KOMP center grant**

The center will aim to attract IMPC funding in the next 5–10-year period with support from the GEEC-Nebraska center. Currently the staff at UNMC MGE core is the director, two technicians (three FTEs) and a part time administrator. The core offers end-to-end services (including designing, construct generation, microinjection, genotyping up to germ line transmission breeding) while most cores offer mainly microinjection services. Excluding phenotyping and mouse repository services, our core is already like a mini-KOMP center. In the next three to four years, we aim to demonstrate to the NIH that: (a) we have infrastructure and capabilities *on par* with the existing KOMP centers, and (b) our unique technical capabilities will be particularly useful for the KOMP operations. Our specific plans to achieve this would be: (i) to recruit a couple more technical personnel to the

core to help develop and provide more services, (ii) which will increase the critical mass of technical personnel necessary for competing for a center grant, and (iii) to develop high throughput technologies and tools appropriate for plugging-in to the on-going operations of KOMP. Through the initiation of "GEEC-Nebraska" and expanding the core services and activities, UNMC can be highly competitive in their application for the Phase III KOMP funding.

Beyond 5-10 years: With the initiation of GEEC-Nebraska, we would like to undertake research in technologies much bigger than CRISPR. We would like to take our success in developing impactful technologies to the next level. A new fascinating technology on the horizon is Genome Project-Write (GP-W). GP-W is a highly ambitious project where the whole genomes are written new, from scratch. In contrast to CRISPR technology that can "edit" the existing genomes, GP-W "writes" new genomes. The GP-Write project was recently conceived and launched by several prominent genomics technology-developers, led by Dr. George Church at Harvard University. Their ambition is to write the first human genome by 2025. GP-W is still in it's infancy; many technologies are yet to be developed to accomplish its goals and fulfill it's potential. Currently, the GP-W project is organizing the efforts of hundreds of scientists around the world in developing technologies. Dr. Church regards Dr. Gurumurthy as one of the leading experts in technology development and we plan to be involved with GP-M (M= mouse) in this large scale consortium.

A. Potential for the Center to contribute to Society and Economic Development

As stated in the above sections, GEEC-Nebraska will contribute to society and economic development in a number of ways. *First,* by performing world-class research and innovations, it will develop technologies that will advance scientific fields for multiple research groups (locally, nationally and globally) that are working from the basic research and into translational research areas. *Second,* it will contribute to the education and knowledge dissemination in teaching, training and technology transfer to students and researchers (technicians and post-doctoral trainees). *Third,* GEEC-Nebraska is expected to attract major grants to UNMC, such as KOMP, in the next 5-10 year period. *Fourth,* the center will provide opportunity to increase workforce (of the current core) to 10 fold or more. *Fifth,* the center will create several hundreds more of custom mouse models useful for scientists working in various fields of research such as cancer, immunology, HIV, hearing, eye diseases, Covid19 and many areas of basic research fields.

Beyond, mouse model generation and impacting several disciplines of basic and translational research, in the long run, establishing GEEC-Nebraska will most likely have a strong impact on local industries and the local economy. For example, CRISPR gene editing technology has been adapted to many areas of biology including agriculture and medicine, particularly for developing disease resistant crops or for combating infectious agents like viruses that infect livestock and humans. Here we provide a few examples of areas that could potentially benefit long-term from the scientific advances made by the GEEC- Nebraska. The first example is Costco's site in Fremont, Nebraska to raise over 125 million chickens/yr. which is expected to generate business of $1.2B. Deadly viruses like avian influenza can cause catastrophes to such businesses. Previous work done in Dr. Donald Reynolds laboratory at UNL, and by others, in understanding susceptibility differences of avian influenza in chickens versus ducks has shed some light on viral (hemagglutinin) and thrombocyte (cellular-receptor) genes. Further dissecting those molecular mechanisms was not easily possible earlier due to a lack of technologies. Now Easi-CRISPR can be a tool to undertake such studies that can help keep millions of birds healthy, and more importantly to become prepared for the worst—to protect the people of Nebraska, and the world, from public health consequences (because of the cross species infectability of influenza with other species including humans). Some examples of CRISPR developed livestock are cattle with no horns, which helps to avoid dehorning of the newborn calves, and super muscly pigs to produce lean meat. While such works used either the cumbersome traditional methods or the first-generation CRISPR technologies, where gene pieces were simply snipped out, newer technologies such as Easi-CRISPR (that have the capability to precisely insert new gene sequences), can open up an even broader range of possibilities to create designer crops and livestock species. Such accomplishments will undoubtedly change the world and will allow us to be able to feed the expected world population of 8.5B by 2030. Further, some scientists have already developed plants that can

metabolize carbon dioxide two or three times as fast as they otherwise would. Such plants can help solve the climate change issue of greenhouse gas emissions.

B. Adequacy of Resources:

1. Faculty/Staff

   The key faculty needed for implementing the proposed program constitutes five members (Drs. Gurumurthy, Poluektova, Gorantla, Wang and Gendelman), all from the Pharmacology and Experimental Neuroscience. The primary staff of the mouse genome engineering core constitutes two highly skilled technicians Mr. Donald Harms and Mr. Rolen Quadros.

2. Physical Facilities and Equipment

   No additional facilities or equipment needed.

3. Budget Projections *[see attached budget tables].*

Appendix A: List of 25 important papers from MGECF (* Corresponding author)

1. **Gurumurthy CB***, Quadros RM, Richardson GP, Poluektova LY, Mansour SL, Ohtsuka M. Genetically modified mouse models to help fight COVID-19. Nat Protoc. 2020 Dec;15(12):3777-3787. doi: 10.1038/s41596-020-00403-2. Epub 2020 Oct 26. PMID: 33106680; PMCID: PMC7704938.
2. Wu H, Petitpré C, Fontanet P, Sharma A, Bellardita C, Quadros RM, Jannig PR, Wang Y, Heimel JA, Cheung KKY, Wanderoy S, Xuan Y, Meletis K, Ruas J, **Gurumurthy CB**, Kiehn O, Hadjab S, Lallemend F. Distinct subtypes of proprioceptive dorsal root ganglion neurons regulate adaptive proprioception in mice. ***Nat Commun***. 2021 Feb 15;12(1):1026. doi: 10.1038/s41467-021-21173-9. PMID: 33589589.
3. Urness LD, Wang X, Li C, Quadros RM, Harms DW, **Gurumurthy CB**, Mansour SL. Slc26a9P2ACre : a new CRE driver to regulate gene expression in the otic placode lineage and other FGFR2b-dependent epithelia. Development. 2020 Jul 8;147(13):dev191015. doi: 10.1242/dev.191015. PMID: 32541002; PMCID: PMC7358128.
4. Gomez-Ospina N, Scharenberg SG, Mostrel N, Bak RO, Mantri S, Quadros RM, **Gurumurthy CB**, Lee C, Bao G, Suarez CJ, Khan S, Sawamoto K, Tomatsu S, Raj N, Attardi LD, Aurelian L, Porteus MH. Human genome-edited hematopoietic stem cells phenotypically correct Mucopolysaccharidosis type I. ***Nat Commun.*** 2019 Sep 6;10(1):4045. doi: 10.1038/s41467-019-11962-8. PMID: 31492863
5. **Gurumurthy CB***, O'Brien AR, Quadros RM, Adams J Jr, Alcaide P, Ayabe S, Ballard J, Batra SK, Beauchamp MC, Becker KA, Bernas G, Brough D, Carrillo-Salinas F, Chan W, Chen H, Dawson R, DeMambro V, D'Hont J, Dibb KM, Eudy JD, Gan L, Gao J, Gonzales A, Guntur AR, Guo H, Harms DW, Harrington A, Hentges KE, Humphreys N, Imai S, Ishii H, Iwama M, Jonasch E, Karolak M, Keavney B, Khin NC, Konno M, Kotani Y, Kunihiro Y, Lakshmanan I, Larochelle C, Lawrence CB, Li L, Lindner V, Liu XD, Lopez-Castejon G, Loudon A, Lowe J, Jerome-Majewska LA, Matsusaka T, Miura H, Miyasaka Y, Morpurgo B, Motyl K, Nabeshima YI, Nakade K, Nakashiba T, Nakashima K, Obata Y, Ogiwara S, Ouellet M, Oxburgh L, Piltz S, Pinz I, Ponnusamy MP, Ray D, Redder RJ, Rosen CJ, Ross N, Ruhe MT, Ryzhova L, Salvador AM, Alam SS, Sedlacek R, Sharma K, Smith C, Staes K, Starrs L, Sugiyama F, Takahashi S, Tanaka T, Trafford AW, Uno Y, Vanhoutte L, Vanrockeghem F, Willis BJ, Wright CS, Yamauchi Y, Yi X, Yoshimi K, Zhang X, Zhang Y, Ohtsuka M, Das S, Garry DJ, Hochepied T, Thomas P, Parker-Thornburg J, Adamson AD, Yoshiki A, Schmouth JF, Golovko A, Thompson WR, Lloyd KCK, Wood JA, Cowan M, Mashimo T, Mizuno S, Zhu H, Kasparek P, Liaw L, Miano JM, Burgio G*. Reproducibility of CRISPR-Cas9 methods for generation of conditional mouse alleles: a multi-center evaluation, ***Genome Biol.*** 2019 Aug 26;20(1):171. doi: 10.1186/s13059-019-1776-2. PMCID: PMC6709553
6. **Gurumurthy CB*,** Masahiro Sato, Ayaka Nakamura, Masafumi Inui, Natsuko Kawano, Md Atiqul Islam, Sanae Ogiwara, Shuji Takabayashi, Makoto Matsuyama, Shinichi Nakagawa, Hiromi Miura, Masato Ohtsuka*; Creating CRISPR-based germline genome engineered mice without ex vivo handling of zygotes by i-GONAD, ***Nature Protoc.*** 2019, doi.10.1038/s41596-019-0187-x, PMID: 31341289
7. Grassmeyer JJ, Cahill AL, Hays CL, Barta C, Quadros RM, **Gurumurthy CB**, Thoreson WB. Ca(2+) sensor synaptotagmin-1 mediates exocytosis in mammalian photoreceptors. ***Elife.*** 2019 Jun 7;8. pii: e45946. doi: 10.7554/eLife.45946. PMCID: PMC6588344.
8. **Gurumurthy CB**, Lloyd KCK. Generating mouse models for biomedical research: technological advances. ***Dis Model Mech.*** 2019 Jan 8;12(1). doi: 10.1242/dmm.029462. Review. PubMed PMID: 30626588.
9. Dagur RS, Branch-Woods A, Mathews S, Joshi PS, Quadros RM, Harms DW, Cheng Y, Miles SM, Pirruccello SJ, **Gurumurthy CB,** Gorantla S, Poluektova LY. Human-like NSG mouse glycoproteins sialylation pattern changes the phenotype of human lymphocytes and sensitivity to HIV-1 infection. ***BMC Immunol.*** 2019 Jan 7;20(1):2. PMC6322283.
10. Koczok K, **Gurumurthy CB**, Balogh I, Korade Z, Mirnics K. Subcellular localization of sterol biosynthesis enzymes. ***J Mol Histol.*** 2018 Dec 8. doi:10.1007/s10735-018-9807-y, PMID: 30535733.
11. Roth TL, Puig-Saus C, Yu R, Shifrut E, Carnevale J, Li PJ, Hiatt J, Saco J, Krystofinski P, Li H, Tobin V, Nguyen DN, Lee MR, Putnam AL, Ferris AL, Chen JW, Schickel JN, Pellerin L, Carmody D, Alkorta-Aranburu G, Del Gaudio D, Matsumoto H, Morell M, Mao Y, Cho M, Quadros RM, **Gurumurthy CB**, Smith B, Haugwitz M, Hughes SH, Weissman JS, Schumann K, Esensten JH, May AP, Ashworth A, Kupfer GM, Greeley SAW, Bacchetta R, Meffre E, Roncarolo MG, Romberg N, Herold KC, Ribas A, Leonetti MD, Marson A. Reprogramming human T cell function and specificity with non-viral genome targeting. ***Nature***. 2018 Jul 11. doi: 10.1038/s41586-018-0326-5. PMID: 29995861.

12. McMillan JM*, Cobb DA, Lin Z, Banoub MG, Dagur RS, Branch Woods AA, Wang W, Makarov E, Kocher T, Joshi PS, Quadros RM, Harms DW, Cohen SM, Gendelman HE, **Gurumurthy CB***, Gorantla S, Poluektova LY*. Antiretroviral drug metabolism in humanized PXR-CAR-CYP3A-NOG mice. ***J Pharmacol Exp Ther***. 2018 Feb 23. pii: jpet.117.247288. doi: 10.1124/jpet.117.247288. [Epub ahead of print] PMID: 29476044.
13. Miura H, Quadros RM, **Gurumurthy CB***, Ohtsuka M*. Easi-CRISPR for creating knock-in and conditional knockout mouse models using long ssDNA donors. ***Nat Protoc.*** 2018 Jan;13(1):195-215. doi: 10.1038/nprot.2017.153. PMID: 29266098.
14. Jung EM, Moffat JJ, Liu J, Dravid SM, **Gurumurthy CB**, Kim WY. Arid1b haploinsufficiency disrupts cortical interneuron development and mouse behavior. ***Nat Neurosci.*** 2017 Dec;20(12):1694-1707. doi: 10.1038/s41593-017-0013-0. PMCID: PMC5726525.
15. Quadros RM, Miura H, Harms DW, Akatsuka H, Sato T, Aida T, Redder R, Richardson GP, Inagaki Y, Sakai D, Buckley SM, Seshacharyulu P, Batra SK, Behlke MA, Zeiner SA, Jacobi AM, Izu Y, Thoreson WB, Urness LD, Mansour SL, Ohtsuka M, **Gurumurthy CB***. Easi-CRISPR: a robust method for one-step generation of mice carrying conditional and insertion alleles using long ssDNA donors and CRISPR ribonucleoproteins. ***Genome Biol*** 2017;18: https://doi.org/10.1186/s13059-017-1220-4
16. Jacobi AM, Rettig GR, Turk R, Collingwood MA, Zeiner SA, Quadros RM, Harms DW, Bonthuis PJ, Gregg C, Ohtsuka M, **Gurumurthy CB***, Behlke MA*. Simplified CRISPR tools for fficient genome editing and streamlined protocols for their delivery into mammalian cells and mouse zygotes. ***Methods.*** 2017 May 15;121-122:16-28. doi: 10.1016/j.ymeth.2017.03.021. PubMed PMID: 28351759.
17. Schilit SL, Ohtsuka M, Quadros RM, **Gurumurthy CB***. Pronuclear Injection-Based Targeted Transgenesis. ***Curr Protoc Hum Genet***. 2016 Oct 11;91:15.10.1-15.10.28. PMID: 27727435
18. **Gurumurthy CB*,** Grati M, Ohtsuka M, Schilit SL, Quadros RM, Liu XZ. CRISPR: a versatile tool for both forward and reverse genetics research. ***Human Genetics***. 2016; 135 (9) : 971-976, PMCID PMC5002245.
19. Huang K, Zhang J, O'Neill KL, **Gurumurthy CB**, Quadros RM, Luo X. Cleavage by Caspase 8 and Mitochondrial Membrane Association Activate Bid during TRAIL-induced Apoptosis. ***J Biol Chem.*** 2016 Apr 6. pii: jbc.M115.71105.1PMID: 27053107.
20. **Gurumurthy CB*,** Takahashi G, Wada K, Miura H, Sato M, Ohtsuka M. GONAD: A Novel CRISPR/Cas9 Genome Editing Method that Does Not Require Ex Vivo Handling of Embryos. ***Curr Protoc Hum Genet***. 2016 (88):15.8.1-15.8.12. PMID: 26724720
21. Quadros R, Poluektova L, **Gurumurthy CB***: Simple and Reliable Genotyping Protocol for Mouse Prkdc^{SCID} Mutation. ***J Immunol Methods.*** Volume 431, April 2016, Pages 60–62. PMID: 26851521.
22. Mir RA, Bele A, Mirza S, Srivastava S, Olou A, Ammons SA, Kim JH, **Gurumurthy CB**, Qiu F, Band H, Band V. A novel interaction of ECD protein with R2TP complex component RUVBL1 is required for the functional role of ECD in cell cycle progression. ***Mol Cell Biol***. 2015 Dec 28. pii: MCB.00594-15. [Epub ahead of print] PMID: 26711270
23. **Gurumurthy CB***, Joshi PS, Kurz SG, Ohtsuka M, Quadros RM, Harms DW, Lloyd KC. Validation of simple sequence length polymorphism regions of commonly used mouse strains for marker assisted speed congenics screening. ***Int J Genomics***: 2015, 735845.
24. Quadros RM, Harms DW, Ohtsuka M, **Gurumurthy CB***. Insertion of sequences at the original provirus integration site of mouse ROSA26 locus using the CRISPR/Cas9 system. ***FEBS Open Bio***. 2015, 5: 191-197.
25. Harms DW, Quadros RM, Seruggia D, Ohtsuka M, Takahashi G, Montoliu L, **Gurumurthy CB*.** Mouse Genome Editing Using the CRISPR/Cas System. ***Curr Protoc Hum Genet.*** 2014, Editor. Board Jonathan Haines Al 83, 15.7.1–15.7.27.

Appendix B for list of extramural funding received as a direct result of the technologies and/or mouse models developed at MGECF.

Grant	Period	Direct cost	Indirect cost	MGECF contribution in the grant proposal that impacted the funding decision
R24OD018546 Larisa P	07/2014-06-2018	$1,943,073	$981,252	Established so called speed congenics method which was the key strength of the proposal to earn this award (Dr. Poluektova can provide more information)
P30GM110768 Shelley S	09/2014-08/2019	$3,690,000	$1,080,800	Mouse Core section received the best scores (1s & 2s) among 5 other cores, and was crucial for this grant to be funded
R01NS091220 Woo Y Kim	03/2015-02/2020	$1,665,950	$541,748	Designed & developed mouse models, which served as crucial tools for the Nature Neuroscience paper and for this funding
R01GM118437 Xu Luo	09/2017-08/2021	~ $1,100,000	~ $570,000	Designed and developed CRISPR reagents for a number of Apoptosis gene-knockouts in cells
R01CA210637 Ponnusamy M	06/2017-05/2022	~$1,200,000	~$620,000	Designed and developed mouse models, which served as crucial tools for the Easi-CRISPR paper and for this funding
R01CA222907 Mark Carlson	04/2018-03/2021	~ $1,150,000	~$600,000	Contributed to CRISPR genome editing strategies proposed
P01CA217798 S Batra Surinder	06/2018-05/2023	~$5,200,000	~$2,800,000	Designed and developed Muc16 conditional knockout model, one of the most difficult genes for which the existing transgenic technologies would not work.
R35HG010719 Gurumurthy	09/2019-08/2024	~$1,500,000	~$750,000	Development of Modular CRISPR Genome Editing Technologies and Tools
21GM129559 Gurumurthy	07/2019-06/2022	~$275,000	~$140,000	Engineering Long ssDNA for Genome Editing Applications
21AI143394 Poluektova/Gurumurthy	04/2019-03/2022	~$425,000	~$220,000	Development of humanized transgenic mice for HBV/HIV co-infection studies
Total financial benefits to UNMC		**$18.3M**	**$8.4M**	

Appendix C: Local, National and International news headlines about MGECF scientific contributions

- http://www.omaha.com/livewellnebraska/molecular-scissors-used-in-gene-editing-receive-an-upgrade-courtesy/article_2ebb9930-07ec-5ad6-8b93-fc87e0059fe9.html
- https://www.omahamagazine.com/2020/01/02/300961/using-cut-and-paste-to-edit-out-human-disease
- http://blog.addgene.org/easi-crispr-generating-knock-in-and-conditional-mouse-models
- https://www.technologynetworks.com/genomics/articles/easi-crispr-technology-could-revolutionize-animal-testing-299680
- https://www.unmc.edu/news.cfm?match=24317
- https://www.genengnews.com/gen-articles/genome-editing-explores-new-depths/5924
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UNMC
BREAKTHROUGHS FOR LIFE
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Surinder K. Batra, MSc., Ph.D.
Stokes-Shackelford Professor and Chairman
Department of Biochemistry and Molecular Biology, College of Medicine

May 14, 2021

Re: Letter of support for Genome Editing and Education Center-Nebraska (GEEC-Nebraska)

Dear Members of the NU Board of Regents:

As the chair of the Department of Biochemistry and Molecular Biology at UNMC, College of Medicine, I am writing this letter to support the Genome Editing and Education Center-Nebraska (GEEC-Nebraska) proposal submitted by Dr. Gurumurthy. As we all know, CRISPR genome editing, which received a Nobel prize last year, is a revolutionary technology that has impacted multiple fields of biology including medicine and agriculture. It is a right time now for research and education institutes like UNMC to invest in the CRISPR technology.

Dr. Gurumurthy, while serving as the director of UNMC's mouse genome engineering core facility has made significant contributions in the field of CRISPR genome editing. Of note, he developed technologies like Easi-CRISPR, which has solved one of the major problems of the first version of CRISPR that could not be used for generating widely usable mouse models.

A large number of research projects in my laboratory use genetically engineered mouse models. Unfortunately, the majority of the genes that my laboratory is interested in are quite complex containing highly repetitive sequences. They are not easy for generating models like conditional knockout and inducible transgenic mice. In fact, we had tried collaborating with other well-known service laboratories including NIH funded KOMP centers for generating the models without success. A few years ago when the CRISPR technology was very new, Dr. Gurumurthy, director of UNMC's mouse genome engineering core facility, had some elegant ideas of technology development and he was looking for collaborators (that are willing to use his innovative ideas for generating mouse models).
He pitched some of those ideas with me for collaboration. His collaboration with my team, combined with his innovative technology development ideas (like Easi-CRISPR) led to several high impact publications. Dr. Gurumurthy and I have published 5 papers together (3 from his laboratory and 2 from mine) which have been already cited highly. His technologies and the mouse models he developed have also helped us in getting NIH grants. Specifically, two of the models he developed were key reagents for receiving one of our program projects and two R01s.

About 2 years ago, Dr. Gurumurthy discussed with me his big idea grant submitted to NU. I was very impressed with the idea because of its high potential of impacting large number of researchers at UN system including students. I am very glad to hear that UNMC is interested in initiating a Center in the theme of genome editing.

I would be delighted to be part of the center serving as an advisory committee member and I strongly support launching of the Center. Please do not hesitate to contact me if you need further information in support of the center application.

Sincerely,

Surinder K. Batra, Ph.D.
Professor & Chair,
Department of Biochemistry and Molecular Biology,
Dr. Alfred and Linda Hartmann Chair of Biochemistry and Molecular Biology
Associate Director for Translational Research, Fred & Pamela Buffett Cancer Center, Eppley Institute for Research in Cancer

Enclosures

cj/SKB

UNIVERSITY OF Nebraska Medical Center

NEBRASKA'S HEALTH SCIENCE CENTER
A Partnership with Nebraska Medicine

DEPARTMENT OF PHARMACOLOGY AND
EXPERIMENTAL NEUROSCIENCE

May 8, 2021

Re: Letter of support for the Genome Editing and Education Center-Nebraska (GEEC-Nebraska)

Dear Board and Regents of the University of Nebraska,

Greetings! I write this letter with the greatest of enthusiasm in support of the establishment of the GEEC-Nebraska Center. I have seen the growth, implementation, development and impact of this research first-hand. Indeed, the work moving forward has already seen dozens of new human disease models, propelled research efforts amongst many faculties and have led to new support for many research investigators in our state of Nebraska and globally. To our own University ends we have made the first humanized mouse model of Alzheimer's disease, helped secure innovative models for the neurological manifestations of HIV/AIDS, developed novel cancer therapies and propelled efforts to find a final cure for a spectrum of inflammatory, infectious and degenerative disease. Other examples include those of Drs Surinder Batra and Donald Reynolds whose pioneering work has led to a greater understanding of the causes and remedies of cancer and viral diseases were supported directly through these works. For the latter, the susceptibility differences of avian influenza in chickens were made possible through studies of the viral (hemagglutinin) and thrombocyte (cellular receptor) genes and aided by this research and its activities. Further dissecting those molecular mechanisms of human diseases was moved forward through the proposed center's technologies. Easi-CRISPR was one tool now used to generate the science to deal directly with a myriad of current and future potential public health needs and the proposed remedies. I myself see this Center as the future of our biomedical research efforts for the state, the country and the world. Please do not hesitate to contact me if further questions do arise in a favorable judgment in moving this important and timely proposal forward.

Sincerely yours,

Howard E. Gendelman

Howard E. Gendelman, M.D.
Margaret R. Larson Professor of Internal Medicine and Infectious Diseases
Professor and Chairman, Department of Pharmacology and Experimental Neuroscience

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University of Nebraska Lincoln

INSTITUTE OF AGRICULTURE AND NATURAL RESOURCES
SCHOOL OF VETERINARY MEDICINE AND BIOMEDICAL SCIENCES

May 11, 2021

To whom it may concern

With great enthusiasm, I am writing this letter to support Dr. Gurumurthy Channabasavaih (Guru)' efforts to establish the Genome Editing and Education Center-Nebraska. At the outset, I know Guru for over 10 years and I have received unmeasurable support on various aspects of his genomic technological platforms, which really gave a new direction to our research. To exemplify a few of these, Guru was instrumental in generating the T cell receptor transgenic mice for the first time to one heart protein, and his collaboration has led me to secure NIH grants, which otherwise was not possible.

Guru brought to my attention about the big idea grant in 2019 and as I was excited to learn about his vision to develop a center described above, a few of my colleagues joined me to participate in this grant submission. Although, not funded, Guru's conviction stayed strong and I simply hope that his efforts will pay all of us as Nebraska residents and the research community. I say this with an element of emotion that if all of us as one Nebraska University unit cannot establish a cutting-edge center described above, who else can take such an initiative, is my thinking. Hope that we will not be too late in competing with others in the region or across the country.

I am a strong believer that our actions must speak better than words, and establishing a center is not a joke. Fundamentally, everything must be right, and the most important element is the need to have a committed individual on board to initiate the process. In that direction, I cannot think of any other better individual than Guru. He has a good breadth of expertise in life sciences, most importantly, molecular biology. This includes, cutting edge technologies such as CRISPR genome editing (Easi-CRISPR), i-GONAD, and CRISPR-First: PITT-next. In fact, he is a cofounder of Easi-CRISPR technology that has earned him a remarkable success, and reputation in the research community. I am very pleased to note such an advancement has been made in our own sister concern institute. I begin to wonder, how many people are out there to have 'all-in one' category i.e., DVM education, PhD in virology; postdoc training in the mouse genetics and expertise in the cutting-edge technologies, and an MBA degree. I am sure that all of these qualities synergistically help him to establish the proposed centre quite successfully.

Speaking about my own research about the utility of the centre, we focus on the determination of immune mechanisms of non-ischemic heart diseases and their prevention. One such condition is dilated cardiomyopathy (DCM) and ~50% of those affected undergo heart transplantations due to the lack of effective chemotherapeutic options. The estimated cost of caring for DCM patients is more than $7 billion annually

in the U.S alone. Serendipitously, a discovery was made that deficiency of taurine, an essential amino acid, can lead to the development of DCM in dogs and cats. However, recent investigations suggest that taurine deficiency can lead to pathological changes that can affect various organs such as, heart, eye, pancreas, liver, kidney and brain, in addition to modulating immune functions. However, it has been a challenge to mechanistically delineate the functionalities of taurine in these tissues involving a complex mixture of cells, since all express receptors for taurine. Thus, we propose to use CRISPR technology to conditionally knockout the taurine-receptor organ-specifically, such that receptor expression (on and off) can be controlled that can serve as an excellent platform to dissect taurine's biology in human and animal health and disease. Likewise, we propose to use CRISPR-based tools to engineer some of the vaccine candidates that we have recently identified in the prevention of both heart and pancreatic diseases by developing edible vaccines in the plants.

In summary, I am glad to have an opportunity to share my thoughts as to the vision of the proposed centre under the leadership of Guru both in the context of my own research and also other stakeholders of NE. Personally, Guru is a passionate individual and he makes extraordinary commitments, and very selflessly extend his helping hand when needed. I wish him all the very best in his attempts to establish this centre within our own state of Nebraska.

Please do not hesitate to contact me, if you need any additional information for your evaluations.

Sincerely,

Jay Reddy, MVSc., PhD
Professor
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Web: http://jayreddy.unl.edu

University of Nebraska Medical Center

May 9, 2021

Re: Letter of support for the Genome Editing and Education Center-Nebraska (GEEC-Nebraska)

Dear Members of the NU Board of Regents:

It is my great pleasure as dean of the UNMC College of Medicine to provide my highest level of endorsement for the establishment of the Genome Editing and Education Center-Nebraska (GEEC-Nebraska), which will function under the direction of Dr. Channabasavaiah Gurumurthy, Professor of Pharmacology and Experimental Neuroscience. Genetically engineered animal models of human disease have become a mainstay of research into pathogenesis, prevention, and treatment of these diseases. One of the most highly impactful advances in biomedical research in the last several decades has been the development of clustered regularly interspaced short palindromic repeats (CRISPR)-based genome editing technologies. This technology allows targeted and rapid editing of genes at both a cellular and whole animal level. Indeed, CRISPR is being explored as a treatment of human genetic diseases such as beta thalassemia and sickle cell anemia. This technology has already begun to revolutionize medicine.

This new center will result from a transformation of UNMC's Mouse Genome Engineering Core Facility (MGECF) into an Academic Multidisciplinary Research Center. It will utilize the and build of the unique accomplishments that director and other members of the proposed center have already achieved. Most notable has been the development of novel technology that enhances the ability to utilize CRISPR, including Efficient Additions with *ss*DNA *i*nserts-CRISPR *(Easi*-CRISPR) and Genome editing by Oviductal Nucleic Acids Delivery (*i*-GONAD) methods. These approaches are both major breakthroughs transgenic technologies. These UNMC approaches *are* now being utilized by over one hundred laboratories across the globe.

The research to date at UNMC has already resulted in $25M in grant funding, including the highly prestigious outstanding investigator award from the NHGRI to the director of the proposed center, Dr. Gurumurthy. As detailed in the application, numerous current and potential users and members of the center, both within and outside UNMC, have already been identified. Thus, there is no question that the timing is right for the establishment of the center to further and support the use of CRISPR technology and development of animal models of disease at UNMC.

In summary, CRISPR technology is one of the most impactful advances in biomedicine in decades. We are fortunate at UNMC to have faculty and staff who have demonstrated their abilities to lead the field in the sue of CRISPR technology. It is timely and important for the advance of gene-based science at UNMC that the center proposed move forward. Therefore, this application has my full support and I will work with its leadership to assure its success.

Sincerely,

Bradley Britigan

Bradley E, Britigan, M.D.
Stokes-Shackleford Professor and Dean

985520 Nebraska Medical Center / Omaha, NE 68198-5520
402-559-4204 / FAX 402-559-9798

University of Nebraska Kearney

COLLEGE OF ARTS AND SCIENCES
Department of Biology

May 6, 2021

Channabasavaiah Gurumurthy, MVSC, PhD, Exec. MBA
Director, Mouse Genome Engineering Core Facility
Durham Research Center II 1030/8187
985930 Nebraska Medical Center
Omaha, NE 68198-5930

RE: Genome Editing and Education Center-Nebraska

Dear Dr. Gurumurthy:

Greetings! It is my pleasure to write this letter of support for the Genome Editing and Education Center-Nebraska. The Genome Editing and Education Center-Nebraska has a very well-devised plan for success, which I endorse and support. One of the goals in creating this Center is to further develop the infrastructure, services, resources, educational opportunities, and community relationships for not only the University of Nebraska System, but the state as a whole. I can attest that my campus will benefit from such a Center. At the University of Nebraska at Kearney (UNK), teaching and education are paramount. We utilize the research setting as a teaching and mentoring tool for students, as well as our own research interests. I have a strong connection with UNMC, especially in terms of education and training and for this Center, I would be happy to serve as a UNK campus liaison or in any capacity you see fit. I am so excited, as are a number of faculty and students at UNK, especially after the talk you gave to us recently. It was such an honor and pleasure for us to have you as our 7th Distinguished Speaker for Doug Lund DNA Day. Who would have thought 7 years after meeting Dr. Mario Capecchi at this same event that you would give a talk that rivaled the Nobel prize laureate! The technology you have developed is fantastic. In fact, I would like to use EASI-CRISPR in both my work with fruit flies and the immune genes underlying aging, as well as in the cell culture work to study the RNA virus we found in *Drosophila melanogaster,* Nora virus. In addition, there are a number of faculty in the Biology department who are interested in using EASI-CRISPR for questions dealing with microbes, such as *Staphylococcus aureus*, Rickettsia, mouse models for allergy, mouse models for diabetes, and a whole host of other questions.

In terms of educational experiences, we would like to have you come and lecture to in Genetics course, Molecular Biology course, Bioethics course, as well as give a seminar for our Molecular Biology class that is offered each semester. Because this technology is at the forefront of research, I, as an officer of our award winning local chapter of Sigma Xi – The Scientific Research Honorary, would like to invite you to give a talk to the lay public on this topic. These talks will help to engage faculty, students, and the lay public in the technology and the Center, as well as the collaboration between UNK and UNMC.

Another goal that can be addressed at UNK through the Center is to expand professional development activities to cultivate a cadre of successful investigators who are prepared to develop and implement innovative tools and approaches to address biomedical issues pertinent to all areas. In addition, we have amply demonstrated at UNK the ability to create an environment that fosters innovative multidisciplinary (EPSCOR), multisite and cross-entity (e.g., public-private) partnerships, IDeA (national CTR, COBRE, INBRE, ICPCTN, SEPA) and other national (e.g., CTSAs) collaborations. I have been a member of the NE-INBRE program since 2003 and serve as the Institutional Coordinator for UNK for that program, as well as being the Campus coordinator and Steering committee member for the UNMC Great Plains Center in Translational Research (GP-CTR). I commend you for your efforts to create a Center that will further establish areas of collaboration across the NU system.

In closing, on behalf of the UNK campus, we wholeheartedly support your application to create the Genome Editing and Education Center-Nebraska. We have created cross campus and cross region collaborations that are invaluable. In addition, the educational opportunities that you are willing to provide us and our students are invaluable. As stated previously, I will gladly serve in any capacity you deem necessary to aid in fostering a connection between the Center, UNK, NE-INBRE and the GP-CTR. I am highly supportive of the creation of the Genome Editing and Education Center-Nebraska. If I can be of any help in any way, please do on hesitate to contact me.

Sincerely,

Kim Carlson

Kim Carlson
Professor & Assistant Chair
Biology Department
University of Nebraska at Kearney
Kearney, NE 68849
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308-865-1554

May 13, 2021

Nebraska University Board of Regents
University of Nebraska–Lincoln
Lincoln, NE 68583-0907

Re: Letter of support for the Genome Editing and Education Center-Nebraska (GEEC-Nebraska)

Dear Members of the NU Board of Regents:

It is my great pleasure to provide a letter of support for the establishment of the Genome Editing and Education Center-Nebraska (GEEC-Nebraska). I currently serve as the Stokes-Shackleford Professor and Chair of the Department of Cellular and Integrative Physiology and Director of the Center for Heart and Vascular Research at the University of Nebraska Medical Center.

I first came to know about the outstanding contributions made by UNMC in the CRISPR field, when I was interviewing at UNMC in 2018 and met with Dr. Gurumurthy. I also follow the literature and conversations on Twitter regarding CRISPR technology and can see that it has revolutionized biomedical research. It has impacted translational research as a gene therapy tool in less than 6 years from its invention, which is truly remarkable. Dr. Channabasavaiah Gurumurthy, Director of GEEC-Nebraska, has made significant contributions to CRISPR technology. It is clear this is a passion for him. The improvements he has made, such as Easi-CRISPR and GONAD technologies, have drawn worldwide attention to UNMC in a very positive way. Dr. Gurumurthy has published in over two dozen high-impact papers in just the past several years on technology development and mouse models generated. He has also earned UNMC over $25M and has attracted dozens of collaborators nationally and internationally.

As an advisory committee member and a user of mouse models, the CRISPR technology mouse models, and technologies like CRISPR are highly valuable and now almost indispensable for a multitude of research projects. When Dr. Gurumurthy mentioned his big idea grant that was submitted to NU in early 2019, I was already impressed with his work and its potenatial benefits to the UN research community. I am now thrilled to hear that UNMC is interested in investing in this area by launching a Center. A designated center for genome editing, and converting it from the existing mouse genome engineering core would help us to conduct the best research possible.

In summary, I strongly support the launching of a center in the area of enome editing. Dr. Gurumurthy possesses the attributes and expertise in establishing the Genome Editing and Education Center-Nebraska (GEEC-Nebraska). Let me know if I can provide any additional information.

Sincerely,

Merry L. Lindsey, Ph.D.
Chair and Stokes-Shackleford Professor,
Department of Cellular and Integrative Physiology
Director, Center for Heart and Vascular Research
MLL:cb

University of Nebraska Medical Center

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May 12, 2021

Subject: Letter of support for the proposal of Genome Editing and Education Center-Nebraska (GEEC-Nebraska)

Dear Members of the NU Board of Regents:

It is my pleasure to provide this letter of support for the establishment of the Genome Editing and Education Center-Nebraska (GEEC-Nebraska) which is being organized by my long-term collaborator, Dr. C.B. Gurumurthy.

Dr. Gurumurthy has developed some impactful CRISPR technologies while a faculty member at UNMC, such as Easi-CRISPR and GONAD. These technologies have been widely popular and have drawn worldwide attention to our university. In general, CRISPR has revolutionized biomedical research, changing the whole field of gene therapy in the 6 years since its initial description.

Dr. Gurumurthy also is Director of the UNMC Mouse Genome Engineering Core Facility. The research collaborations and services available through this Core Facility are exceptional and have contributed to the success of dozens of researchers at UNMC and elsewhere.

I have known and worked with Dr. Gurumurthy for over five years now. Together we have been developing several novel transgenic swine for use in pancreatic cancer and breast cancer research (Dr. Gurumurthy's expertise is applicable to numerous species, not just mice). We have also prepared and submitted multiple federal grants together, and have several manuscripts in preparation. Dr. Gurumurthy currently is a Co-Investigator on our NCI R01 award to develop a porcine model of pancreatic cancer.

When Dr. Gurumurthy mentioned his Big Idea proposal on a gene editing center to NU in early 2019, I was already impressed with this concept and the potentially enormous benefits to the NU research community. I am thrilled to hear that UNMC is interested in initiating the Genome Editing and Education Center. This should enable Dr. Gurumurthy's team to deliver the best possible service to NU investigators.

It is my privilege to be associated with this Center, both as an end user and as an advisory committee member. I strongly support the establishment of GEEC. I am happy to provide further information in support of the Center's application as needed.

Mark A. Carlson, MD, FACS
Professor, Department of Surgery
Director, Center for Advanced Surgical Technology (CAST)
University of Nebraska Medical Center
Office: 402-995-5371; Mobile: 402-650-4219
Assistant: Sarah Dawson (sarah.dawson@unmc.edu; 402-559-4581)

University of Nebraska Omaha

COLLEGE OF ARTS AND SCIENCES
Department of Biology

21 May 2021

Dear Dr. C.B. Gurumurthy:

I am writing in support of the concept you've described as the Genome Editing and Education Center-Nebraska (GEEC-NE).

As a tenured faculty member in the UNO Department of Biology, I believe this Center would be a beneficial resource to our nearly 1000 Biology students. As the faculty academic coordinator for the Molecular and Biomedical Biology (MBB) B.S. degree program, I could envision that GEEC-NE could support MBB students through the development of hands-on learning modules which could be incorporated into the senior-level Molecular Genetics course.

Further, UNO Biology faculty and students could work together to generate e-learning modules for grades 7-12 across the state, in conjunction with the already established uBEATS STEM e-learning program. Partnering with the strong STEM outreach leadership experience of UNO, GEEC-NE could leverage such training modules beyond the state through the STEM TRAIL center and lead the nation in learning more about and encouraging discussion on gene editing.

I'm happy to continue to work with you as this Center is further developed.

Sincerely,

Paul H. Davis, Ph.D.
Associate Professor of Biology
University of Nebraska at Omaha
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TABLE 1: PROJECTED EXPENSES - NEW ORGANIZATIONAL UNIT
UNMC Genome Editing and Education Center - Nebraska

	(FY2020-21) Year 1		(FY2021-22) Year 2		(FY2022-23) Year 3		(FY2023-24) Year 4		(FY2024-25) Year 5		Total
Personnel	FTE	Cost	FTE	Cost	FTE	Cost	FTE	Cost	FTE	Cost	**Cost**
Faculty	0.10	$20,000	0.50	$100,000	0.50	$100,000	0.50	$100,000	0.50	$100,000	$420,000
Non-teaching Staff: Professional	0.20	$10,000	1.00	$50,000	1.00	$50,000	1.00	$50,000	1.00	$50,000	$210,000
Core Administration	0.01	$1,000	0.05	$5,000	0.05	$5,000	0.05	$5,000	0.05	$5,000	$21,000
Non-teaching Staff: Support											
Subtotal	0.31	$31,000	1.55	$155,000	1.55	$155,000	1.55	$155,000	1.55	$155,000	$651,000
Operating											
General Operating		$60,000		$70,000		$80,000		$90,000		$100,000	$400,000
Equipment											$0
New or renovated space	One module close to DRC II, room 1014 is requested.										$0
Library/Information Resources											$0
Other											$0
Subtotal		$60,000		$70,000		$80,000		$90,000		$100,000	$400,000
Total Expenses		$91,000		$225,000		$235,000		$245,000		$255,000	$1,051,000

TABLE 2: PROJECTED REVENUES - NEW ORGANIZATIONAL UNIT
UNMC Genome Editing and Education Center - Nebraska

	(FY2020-21) Year 1	(FY2021-22) Year 2	(FY2022-23) Year 3	(FY2023-24) Year 4	(FY2024-25) Year 5	Total
Existing Funds[1]						
Extramural grants	$40,000	$50,000	$50,000	$50,000	$50,000	$240,000
UNMC internal support	$40,000	$50,000	$50,000	$50,000	$50,000	$240,000
Required New Public Funds						$0
1. State Funds						$0
2. Local Funds						$0
Tuition and Fees						$0
Other Funding						
1 Revenue from core services	$11,000	$105,000	$105,000	$105,000	$105,000	$431,000
2 Extramural grants	$0	$20,000	$30,000	$40,000	$50,000	$140,000
Total Revenue	$91,000	$225,000	$235,000	$245,000	$255,000	$1,051,000

[1] The funds are from Dr. Gurumurthy's R35 NIH grant (34-5160-2132-001) and from institutional start ups for his research. Dr. Gurumurthy has been provided $550,000 over 2 years ($275,000 from the Vice Chancellor for Research Office and $275,000 from the Dean of the College of Medicine).