

**WEBINAR & PANEL: Views from the NIGMS, including the Sepsis Research Priorities**

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June 8, 2020

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**NIGMS' Clinically-Oriented Research Areas**

**NIGMS supports research in selected areas:**

- Anesthesiology and Peri-operative Pain
- Clinical Pharmacology
- Injury and Critical Illness (includes Trauma and Burn)
- Wound Healing
- Sepsis – *Sepsis Research Priorities*

**NIGMS is one of several institutes funding in these areas**

- Also NHLBI, NIAID, NICHD, NINDS, NIAMS
- NIGMS: Affects multiple organ systems
- NIGMS: Involves host inflammatory and immune responses

Zuzana Justinova  
Martha Garcia  
Xiaoli Zhao  
Sarah Dunsmore

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**NIGMS-convened Sepsis Working Group**

**Alfred Ayala, Ph.D.**  
Rhode Island Hosp./Brown Univ.

**Craig Coopersmith, M.D.**  
Emory Critical Care Center

**Monica Kraft, M.D. (Co-Chair)**  
Univ. of Arizona College of Med.

**Vincent Liu, M.D., D.Sc.**  
Kaiser Perm. Div. of Research

**Nuala Meyer, M.D., M.S.**  
Univ. Penn., School of Medicine

**Guy Padbury, Ph.D.\***  
Merck Research Laboratories

**Polly Parsons, M.D.**  
Univ. of Vermont College of Med.

**Ron Przygodzki, M.D.\***  
Genomic Medicine Res. & Develop.  
Dept. of Veterans Affairs

**John Younger, M.D.\* (Co-Chair)**  
Akadeum Life Sciences  
(now at University City Science Center)

\*member, NAGMSC

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**Working Group Recommendations**

1. Significantly expand support of clinically-related research
2. Broaden collaborations with other institutes as partners
3. Limit independent support of large scale clinical trials
4. Work with NIH Center for Scientific Review
5. Coordinate activities at the highest levels at NIH

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Specific recommendations in pre-clinical, clinical and translational areas

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**NOT-GM-19-054: Priorities for Sepsis Research**

**Higher priority areas include:**

- Rapid identification, classification of sepsis patients
- Mechanistic studies with patient-derived materials
- Clinical data from EHRs, for predictive algorithms
- Biomarkers to evaluate future therapeutics/diagnostics
- Cutting-edge data science, AI, machine learning

**Lower priority areas:**

- Rodent models, except where uniquely well-justified
- Large scale clinical trials, which were viewed as premature

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**NOT-GM-19-057: RFI on Human Biospecimens**

**Asked for information:**

- Types of materials to collect/store
- Optimum patient populations
- Challenges with consent, confidentiality
- Emerging technologies to be applied
- Available existing repositories
- Lessons learned from other materials collections
- Analysis of existing collections is underway

*Still accepting feedback! Tell us your thoughts.*

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### Reports and Follow-up at NIGMS

**NIGMS' actions:**

- [NIGMS Reports](#) webpage
- [NIGMS Feedback Loop](#) (search for Sepsis)
- Visited CSR review groups
- Actively coordinating with other institutes
- Prioritizing through our funding decisions
- Advising PIs individually about next steps
- Remain "investigator-initiated" in orientation
- Very attentive to early stage investigators



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### Support for Research at NIGMS

**NIGMS welcomes new applications through peer review**

- Individual and team grants:
  - Mentored clinical scientist awards: [Career Development Awards](#) (K23/K08)
  - Flagship program: [Maximizing Investigators' Research Award](#) (R35; MIRA, ESI MIRA)
  - Small business: [Small Business Innovation Research](#) (R41/R42 & R43/44)
    - **New!** [NOT-GM-20-026](#), Sepsis Priorities for Diagnostics & Therapeutics for SBIR/STTRs
  - Team science: [Collaborative Program Grants for Multidisciplinary Teams](#) (RM1)
  - *Limitations to research that meets NIH definition of a clinical trial, at NIGMS*
- To learn of new opportunities:
  - Subscribe to [NIGMS Feedback Loop](#) and talk to your program director



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### COVID-19 Related Information

**NIH Office of Extramural Research on COVID-19**

- [COVID-19: Information for NIH Applicants and Recipients of NIH Funding](#)
- Late application policies, peer review policies
- Spending guidance, human subjects and animal research guidance
- Notices specific to COVID-19



**NIGMS competing revisions for COVID-19 (supplements) are very specific**

- [NOT-GM-20-025](#), Urgent Competitive Revisions for Research on Coronavirus Disease
  - Repurposing diagnostic tools to enable rapid detection of infection (SBIR/STTR)
  - Rapid development of potential therapeutic agents (SBIR/STTR)

Design of predictive computational models for the spread of COVID-19 (all grants)



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### Diversity in Scientific Research

**NIH and NIGMS support at multiple levels**

- **Understanding our own biases:**
  - [NIH Diversity Matters](#) webpage has facts and information
  - [NIGMS Resources](#) has strategies to recruit and retain trainees and fellows
- **Offering opportunities:**
  - [BUILD](#) (U54) focused on pipeline institutions, relationships, & mentoring ([NRMN](#))
  - **New!** [MOSAIC](#) (UE5 & K99/R00) focused on attracting and supporting minority faculty
- **Diversifying your laboratories:**
  - Admin. Supps. (most grants), [PA-18-906](#), *Promote Diversity in Health-Related Research*
  - Training Grants (T32s), [NOT-OD-20-031](#), *Notice of NIH's Interest in Diversity*

\*The diverse group almost always outperforms the group of the best by a substantial margin." – Scott E. Page

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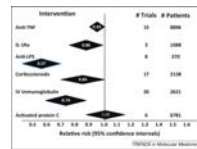
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### Limitations and Challenges Facing Sepsis Researchers


"Rodent models of sepsis found shockingly lacking"



"Execution of sepsis trials needs an overhaul"



Quotes from two NIGMS-funded sepsis researchers on the same page of the July 2012 issue of Nature Medicine

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### NIGMS Response to Sepsis Working Group Recommendations

**Goal: Invest in sepsis research in more targeted, strategic ways**

Greater emphasis on studies that:

- Provide mechanistic understanding of sepsis endotypes in patients
- Utilize patient-derived materials (bedside to bench)
- Use new approaches and models for sepsis research
  - machine learning, artificial intelligence, organoids, bioengineered devices

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**NIGMS Sepsis Research Priorities – NOT GM 19-054**

- Apply to all NIGMS funding opportunity announcements
  - Research grants
  - Training and career development awards
  - Small business opportunities
- Do not affect institute referral guidelines, study section assignment, or review criteria
- Providing new knowledge of biological mechanisms of clinical heterogeneity
- Enabling access to clinical data and biospecimens
- Partnering with other NIH institutes/federal agencies

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**NIGMS Sepsis Small Business Priorities - NOT GM 20-028**

- Diagnostic tools for pre-hospital and emergency department settings
- Predictive clinical algorithms, clinical decision support, electronic health record tools, biosensors, intelligent array systems
- Technologies that combine various types of data (analytical, clinical, molecular, -omic) for diagnosis and/or phenotyping of sepsis patients
- Biomarker panels to enable rapid diagnosis and/or optimization of treatment
- **Alternatives to or improved animal models for testing of sepsis therapeutics**
- Proof of concept evaluation of endotype-guided host-based therapies

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**NIGMS Sepsis Research Low Priority Area – Rodent Models**

- Study Section panels have been asked to specifically comment on:
  - "Justification for use of the animal model in relationship to human sepsis"
- Low priority for studies using rodent models of sepsis is applied by NIGMS staff as part of the funding recommendation process
  - Peer review comments
  - Rationale for proposed studies must be based on human data/observations
  - Trajectory of overall research program and level of support
  - Reverse translation, variety of models/approaches, loss of function/gain of function
  - Continued use of CLP, sampling of a variety of tissues/organs, rodent model clinical trials/ICUs
  - "Right models, right questions"

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### NIGMS Sepsis Research Low Priority Area – Clinical Trials

- NIGMS will only consider support of clinical trials that are designed to test strong mechanistic hypotheses and include appropriate patient stratification.
- NIGMS is unlikely to support large-scale clinical trials unless other NIH institutes/centers or federal agencies provide joint support to optimize trial efficiency, recruitment, and oversight.
- Some NIGMS clinical trial FOAs have restrictions on the types of clinical trials that are permitted. For example, clinical trials that are designed to test safety and efficacy of interventions (Phase I, Phase II, Phase III) for the purpose of future clinical treatment and/or regulatory approval are not permitted in the [NIGMS MIRA](#) and [Multidisciplinary Teams/Collaborative Research Programs](#).

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### Collaborative Program Grant for Multidisciplinary Teams (RM1)

- Must be in the Mission of NIGMS
- Must address a major research problem with significant impact on the NIGMS scientific portfolio
- Achievable in 5-10 years
  - May include clinical research, but may not include a clinical trial (current FOA);
  - May include technology development, but this should not be the major focus;
  - Will not support research resources
  - Is not a P01, P50, U54 or replacement of funds to continue previous programs
- Consult with NIGMS staff well in advance and before the institution commits to a particular application

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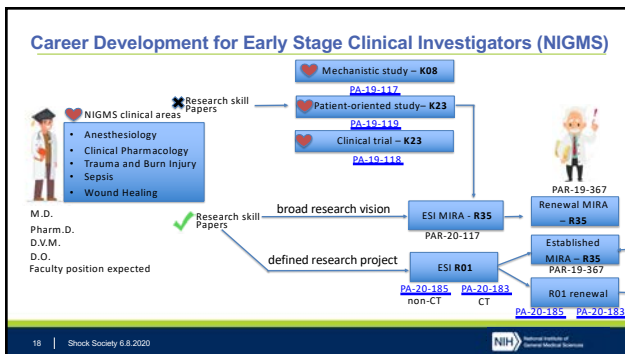
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### ESI MIRA – apply as soon as you are ready!

- **Flagship program of NIGMS**
- Higher success rate than ESI NIGMS R01 (36.8% vs. 23.6%, 2018)
- Higher success rate of R35 renewal than R01 (50.2% vs. 44.1%, 2018)
- Reduced burden in preparing application (6 pg. research strategy, no specific aims page)
- Most applications will be discussed in study section (~75%).
- Reduced burden in grant administration (flexible research direction when opportunities arise)

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### ESI MIRA – Key Points

- **Yearly** due date in **Oct.**, no resubmission but can submit as new application
- Support research **within NIGMS mission**: discuss with your PD if in doubt
- Apply **early!** ESI status, independent faculty appointment, no need for (substantial) preliminary data, not an “outstanding” investigator award
- Support the **main research program of the PI**: **51% of research efforts**
- Research program; may include multiple research directions/projects with or without a single unifying theme (distinct or complementary); need to address how to balance efforts and resources among these projects.

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### MIRA Proposal – Clinical Areas, Consortium, Equipment

- **CLINICAL STUDIES**: NIGMS supports **specific** clinical areas affecting multiple-organs (slide 1).
- **COLLABORATORS**: **yes**, but limited to essential collaborators (letter indicating why collaboration is not possible w/o the support from MIRA; **no** multiple consortiums (dilute contribution of the MIRA PI).
- **EQUIPMENT**: **yes**, well-justified in budget justification and evidence the need in the Research Strategy. MIRA awardee can also request equipment supplement later.
- **No** inflationary increases should be requested.

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**MIRA Proposal –  
Human Subjects and Clinical Trials**

- HUMAN SUBJECTS: **yes**, permitted in MIRA but there are **limitations on CTs**
- CLINICAL TRIALS(CTs): **yes**, if it is **mechanistic CT** and **an essential part** of the program (read PAR-20-117 and PAR-19-367 FOA and Q&A, consult PD)
- **NOT ALLOWED**: CT recruits patients from **multiple sites** or requests substantial financial support for **multiple collaborators**; CTs to **test safety and efficacy of interventions** (Phase I, II, III) for the purpose of future clinical treatment and/or regulatory approval

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**MIRA Review**

- Special Emphasis Panels organized by NIGMS
- Broad expertise and perspective
- No separate criterion scores
- Focus: **Sustainability** of the research program, **track-record** of the PI, and **impact** of PI on the scientific community
- **Research Strategy**: 6 pages, **significant scientific questions, sound experimental strategies**, no emphasize on novelty, no experimental details
- **Biosketch**: Evidences for **productivity, service** at national level (committee etc.), **mentoring** activity
- **Prior productivity**: Contributes more to the final score than regular R01 review. **Note**: there is a threshold of productivity expected to be competitive but no firm correlation of productivity with priority scores

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**Early Stage Investigator Resources**

- **NIGMS Feedback Loop**: highlights of important NIGMS policies and updates
- **NIGMS extramural webpage**: general information on FOAs, Q&A, contacts
- **K Kiosk**: learn about different types of NIH-wide career awards  
[grants.nih.gov/training/careerdevelopmentawards.htm](https://grants.nih.gov/training/careerdevelopmentawards.htm)
- **K Award sample proposal**: [accelerate.ucsf.edu/training/K-grant-writing](https://accelerate.ucsf.edu/training/K-grant-writing)
- **R01 sample proposal and summary statement**:  
[niaid.nih.gov/researchfunding/grant/pages/appsamples.aspx](https://niaid.nih.gov/researchfunding/grant/pages/appsamples.aspx)
- **Early Career Reviewer Program**: *ad hoc* reviewer opportunities offered by CSR, contact SRO of the relevant study section

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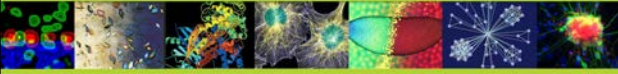


**Questions? Contact us:**

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