NIH Study Sections: What They Are and How They Function

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The Current Timelines
“What to expect and when to expect it”

Months

Submission to OER  
CSR gives SRG, I/C and PD assignment  
SRG review  
Council resubmission  
revised
The NIH Peer-Review Process

- Tracking your grant
- The SRG (study section)
  - Composition
  - Alternative means of review
  - Organization of the meeting
  - Review format
  - Scoring
The NIH Peer Review Process

- OER
  - CSR
    - most R grants
    - SBIRs
    - some PAs
    - some RFAs
  - I/C
    - PPGs
    - training (T & F) grants
    - K grants
    - some PAs and RFAs
Ro Grant Path Through CSR

CSR

↓

IRG

↓

SRG or Study Section

↓

Institute Council

↓

Institute Director
Grant Path Through I/C

I/C

SRG or Study Section

Institute Council

Institute Director
Mentored K Awards: Review Criteria

in order of priority

• Candidate
• Career development plan
• Research plan
• Mentor(s), consultant(s) and collaborator(s)
• Environment and institutional commitment to the candidate
Ro Grant Path Through CSR

CSR → IRG → SRG or Study Section → Institute Council → Institute Director
Restructured Research (R) Grant Applications as of 2/2010

- 5.1. Introduction (1 page max)
- 5.2. Specific Aims (1 page max)
- 5.3. Research Strategy (6 or 12 pages)
  - Significance
  - Investigator(s)
  - Innovation
  - Approach
    - Preliminary Studies/Progress Report
    - Experiments
  - Environment
Scientific Review Group (SRG)

• Membership
  – Reviewers (may include foreign reviewers)
  – Sometimes lay members

• Types of SRGs
  – “chartered”
    • Formal appointment process
    • Multiyear terms of service (usually 4-6)
  – Special Emphasis Panel (SEP)
    • Ad hoc membership
    • Usually meet on a single occasion
Scientific Review Officer (SRO)

- Works for the federal government
- Extramural scientist
- Identifies and recruits reviewers
- Manages conflict of interest
- Arranges and presides at SRG meeting
- Prepares and releases summary statements
What Happens to Your Application
Before Study Section

• ~10 weeks before:
  – SRO sends a roster of applications to reviewers to identify conflicts

• ~9 weeks before:
  – SRO sends email with all apps and assignments
  – ≥3 reviewers per application
  – Assignments based on expertise and C-of-I

• ~1 week before:
  – Reviewers post reviews and preliminary scores for all of the reviewers of the application to see
Usual Study Section

• Usual grant load per study section: 100
• Mean grant load per reviewer:
  • Permanent member mean load: 10-13
  • Mean grant load for temporary reviewers: 4
  • Mean grant load per reviewer: 8
• Mean number of reviewers per grant: 3.5
• Average number of reviewers at each study section meeting: $100 \times 3.5 \div 8 = 44$
  • 15 permanent
  • 29 temporary
Study Section Composition
[ratio of experienced:junior reviewers in JSA’s study section]
Alternate Styles of Review

- Study sections
- Teleconferences
- Video-enhanced discussions
- Asynchronous electronic review
- Editorial-style review
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<thead>
<tr>
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Significance: 2
Innovation: 2
Approach: 2
Environment: 2
Overall Score: 2

Significance: 1
Innovation: 1
Approach: 1
Environment: 1
Overall Score: 2

Significance: 1
Innovation: 2
Approach: 2
Environment: 1
Overall Score: 2

Significance: 1
Innovation: 2
Approach: 2
Environment: 1
Overall Score: 2

Significance: 8
Innovation: 8
Approach: 8
Environment: 8
Overall Score: 8

Significance: 7
Innovation: 7
Approach: 7
Environment: 7
Overall Score: 7

Significance: 3
Innovation: 3
Approach: 4
Environment: 4
Overall Score: 4

Significance: 4
Innovation: 4
Approach: 5
Environment: 5
Overall Score: 5

Significance: 4
Innovation: 4
Approach: 8
Environment: 8
Overall Score: 8

Significance: 3
Innovation: 4
Approach: 8
Environment: 8
Overall Score: 8

Significance: 4
Innovation: 4
Approach: 8
Environment: 5
Overall Score: 5
SRG or Study Section Meeting
Study Section Proceedings

- Call to order by study section chair
- Introductions of reviewers and NIH staff
- SRO delivers instructions for review
- Application review [7A-6P with working lunch]
  - Order: new invest R01; established invest R01; R21
  - Review only top 40% in each category
  - Start with grant having the highest preliminary score
  - Call for initial scores, discussion by all reviewers, call for final scores, all study section members vote
  - Discuss budget, human subject and animal use, resource sharing, overlap, etc.
- Bottom 60% “not discussed” unless requested
## OVERALL IMPACT

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## SCORED REVIEW CRITERIA

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Bullet Point Review Format

OVERALL IMPACT

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**Strengths**
- The most appealing experiments are those found in Specific A/m 2 (SAI) to determine if pharmacological amounts of vitamin D, 25D and 1,25D can prevent or rescue the EAE phenotype.

**Weaknesses**
- The Preliminary Studies section is virtually devoid of explanatory text for the presented figures; exactly how the reader is supposed to make use of this information as sound rationale for the presented experiments is unclear.
- The application suffers from a lack of explanation of abbreviations and jargon; examples include: MOGTCR, 2D2 mice, HUT102 cells, RQR, EL-4 cells, CD4+ CD25-T cells, FOXP3, aCD3, and aCD28.
- Preliminary data also lacks simple descriptive details like "n" and p values; there is not a summation of what the preliminary data purport to mean.
- The application appears to be "pasted" together; different parts display different fonts.
- Many of the outcomes in SAI experiments will be observational in nature and out of context with what is occurring within genomic DNA.
- Inclusion of experiments gauging the effects of dietary vitamin D deficiency on EAE expression would have strengthened the translational component of this work.

SCORED REVIEW CRITERIA

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**Strengths**
- The fairly recent discovery of IL-17 and a specialized subset of T cells that make IL-17 and an application to a study of the immunoregulation of the vitamin D hormone is of substantial significance.
- Uncovering a 1,25D-IL-17 regulatory mechanism that might limit progression of mouse models of MS would also be of great significance.

**Weaknesses**
- The fact that vitamin D insufficiency actually increases MS risks suggests that 1,25-D must be made locally as low 25D levels will be associated with secondary hyperparathyroidism and increased production of 1,25D made by the kidney.

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**Strengths**
- Mouse modeling of observations made "in vitro" is a major strength of Dr. Christakos.

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**Strengths**
- The hypotheses that 1,25D directed inhibition of IL-17 is immunosuppressive in MS is innovative.

**Weaknesses**
- 

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**Strengths**
- The general approach here is to: 1) identify regulatory elements and their transactors in the proximal 1L-17 promoter that mediate its decreased expression under the influence of 1,25D; and 2) manipulate upward dietary vitamin D and metabolite intake and administration to alter expression of the EAE-like MS syndrome in mice.

**Weaknesses**
- The applicant focuses solely in the proximal 1L-17 promoter, ignoring the possible presence and function of important distant 5, 3 and Intronic VDREs in and around the 1L-17 gene; relegating identification of such elements to "future studies" disregards the state-of-the-art VDR cis-trans relationship controlling gene expression.
- The applicant does not really test the effect of vitamin D insufficiency/deficiency on expression of the EAE phenotype.
- A simple schematic in the Background and Significance or Preliminary Results section summarizing the connection among different cells, cytokines, vitamin D metabolites, and disease activity would have been very helpful to the reader.
- In the crucial Figure 1, the disease suppressive effect of 1,25D requires doses of the hormone 10-fold greater than that which would be safe in humans; there is no indication as whether mice treated with such high doses developed hypercalciuria, hypercalcemia or died.
- In the applicant plans to study the effects of chromatin remodeling on expression of a transiently transfected, truncated promoter-reporter construct in an extra genomic context. Should not an endogenous gene in its naturally "chromatinized" environment be the focus of study?

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**Strengths**
- SAI and human cell experiments will take place in the Steinman Laboratory, these appear to be the most interesting experiments.

**Weaknesses**
- 

CRITIQUE 1:

Criterion Scores Table

Candidate: 1
Career Development Plan/Career Goals & Objectives: 1
Research Plan: 1
Mentor(s), Consultant(s), Collaborator(s): 1
Environment and Institutional Commitment to the Candidate: 1

Overall Impact:

Strengths
1. Dr. Liu is an outstanding candidate for this award.

2. Strong research productivity and letters of reference.

6. Career development program for this candidate appears to be excellent.

3. Research plan is clearly written, and it appears to be well within the candidate’s expertise and experience.

4. The area of study is highly significant, focusing on the role of vitamin D and innate immunity against *M. tuberculosis*.

Weaknesses
- No weaknesses are noted.

1. Candidate:

Strengths
- Dr. Liu is an outstanding candidate.

- The candidate has potential to become a successful independent investigator. This is supported by a strong publication record with papers in the *Journal of Immunology* and *Science* that are related to the area of the proposed work.

The candidate is an author on 18 research publications and six review articles. He is first-author on five of the research articles and one review article. Since 2007, 19 manuscripts were published or in press, and three are as a first-author in the *Journal of Immunology*. Thus, the candidate is productive, and his work is published in peer-reviewed, high-quality journals.

The reference letters are very good. The candidate’s letters are highly complimentary, and suggest the making of a strong independent scientist.
- Impact/priority score posted by SRO ≤ 3 days post study section completion
- Overall impact score calculation
  - Mean overall impact score x 10
  - Example: 2.7 x 10 = 27
The Current Timelines

“What to expect and when to expect it”

Months

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