How to Be More Competitive in the NIH Peer Review Process for Grants

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Trends in NIH Peer Review of Clinical Research Project Grants

- Overall success rate of *clinical research* projects lower than for *basic* research projects
  - ~28% for basic research projects
  - ~22% for "mechanism of disease" clinical studies
  - ~20% for projects including clinical trials
- Difference in success rates not due to:
  - Higher budgets for clinical research
  - Review panel assignment
  - Number or % of clinical applications in review meeting
  - Number or % of clinical scientists on review panel
- Clinical projects harder to design well
- Clinicians may "give up" rather than revise

There is no amount of grantsmanship that will turn a bad idea into a good one……..

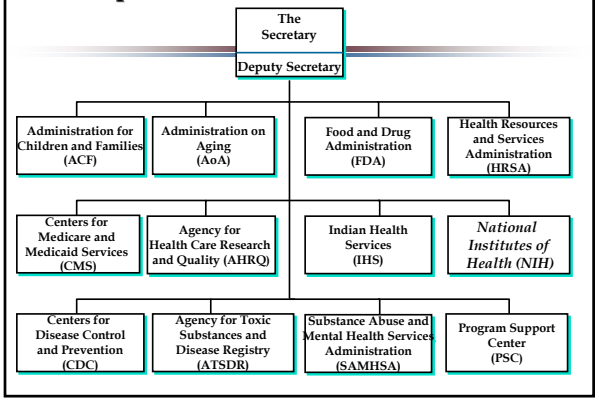
But there are many ways to disguise a good idea.

Dr. William Raub
Past Deputy Director, NIH

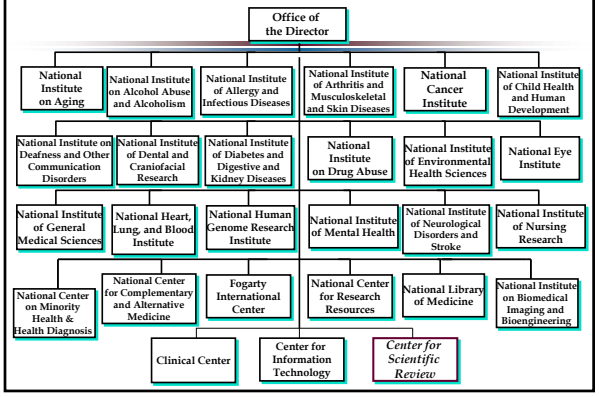
Topics for Today

- Overview of NIH Peer Review Process
- Review criteria for research project grants
- Career Development award mechanisms
- Recent changes in the NIH grants process
  - Electronic Submission
  - Multiple PIs
  - Shortening the review cycle for new investigators
- NIH Roadmap Initiatives
- Hints for preparing a stronger application

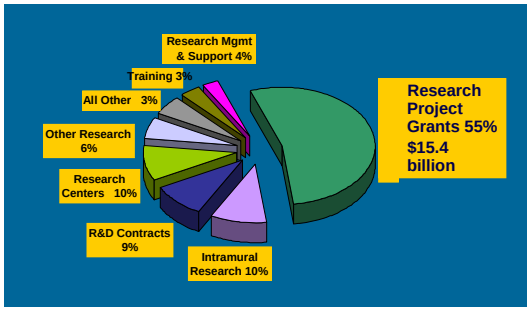
U. S. Department of Health and Human Services



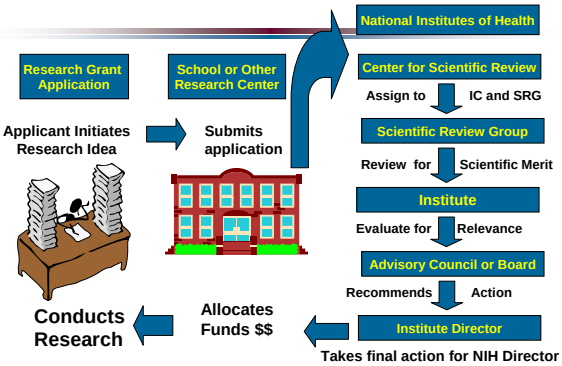
National Institutes of Health



FY 2006 NIH Budget
$28.58 Billion



NIH SUBMISSION AND AWARD PROCESS



NIH Dual Review System for Grant Applications

First Level of Review

Scientific Review Group (SRG)

- Scientific merit review
- Rate/score applications and recommend appropriate budget and duration of award
- Does NOT make any funding decisions

Second Level of Review

Advisory Council/Board

- Assesses quality of SRG review of grant applications
- Makes recommendation to Institute staff on funding
- Evaluates program priorities and relevance
- Advises on policy

NIH Grant Receipt, Review, and Award Schedule – 3 Overlapping Cycles/Yr

Jan-May May-Sept Sept-Jan	Receipt Dates
May-July Sept-Nov Jan-Mar	Review Meetings
Sept-Oct Jan-Feb May-June	Advisory Councils/Boards
Dec 1 Apr 1 July 1	Earliest Possible Start Date

NEW Application Receipt Dates as of January 2007

- **R01** 5th of Feb, June, October
- **All K series** 12th of Feb, June, October
- **R03, R21** 16th of Feb, June, October
  - K/R series renewals and revised/amended due one month later (March, July, November)
- **All P series** 25th of Jan, May, Sept
- **All F series** 8th of April, August, Dec

(see http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-001.html for complete list)

NIH Staff Involved in the Extramural Grants Process

- **Scientific Review Officer (SRO) (PhD or MD)**
  - In Center for Scientific Review and in Scientific Review Office of each NIH Institute/Center (I/C)
  - Organizes and manages scientific review groups (peer review committees)
  - Prepares summary statements documenting the review
  - Liaison between applicants and reviewers
- **Program Officer/Director (PhD or MD)**
  - In NIH Institutes/Centers
  - Manages a portfolio of awarded grants/contracts
  - Monitors scientific progress made on grants/contracts
- **Grants/Contracts Management Officer**
  - In NIH Institutes/Centers
  - Fiscal stewardship of portfolio of awarded grants/contracts
  - Negotiates fiscal aspects of awards
  - Monitors financial progress made on grants/contracts

NIH Solicitations for Applications

- *NIH Guide for Grants and Contracts* announces new or ongoing interest of one or more NIH Institutes/Centers (I/Cs) in supporting research, training, resources in a field
- **Program Announcement (PA)**
  - Addresses a relatively broad field/category of research
  - Usually no set-aside I/C budget
  - Usually submit on regular receipt dates
  - Usually regular review criteria for type of applications
- **Request for Applications (RFA)**
  - Addresses a well defined area of research
  - Set-aside I/C budget for RFA applications
  - Submit on special, one time only receipt date
  - Often special eligibility and/or review criteria
  - Often special application format and/or submission instructions

NIH Center for Scientific Review (CSR)

- Central receipt point for all grant applications for NIH and other DHHS components
- Assigns applications NIH Institute/Center as potential funding component
- Manages ~200 Scientific Review Groups ("Study Sections")
- You may request study section and/or multiple Institute/Center assignment in cover letter submitted with application
  - Institute/Centers share interest areas, so multiple assignments common

CSR Division of Receipt and Referral Assigns Applications

- Topic/research area
- Past review history (if any) of application
- Type of Application –
  - CSR Study Sections
    - Research project grants (R01, R03, R21)
    - Small business innovation research
    - Pre/Postdoctoral Fellowship (F) applications
  - Institute review offices
    - Career development (K series) and Training
    - Complex and special types of grants
    - Multi-site clinical trials
    - Responses to RFAs, specialized PAs, RFPs
    - Other "mission-targeted" applications

What Happens In A Study Section Meeting?

- Study Section Composition
  - Usually 15 - 25 members primarily from academia
  - Senior investigators in a broad range of related fields
  - Ad hoc reviewers for special expertise
- As many as 60 - 100 applications reviewed at each study section meeting
  - Generally 3 assigned reviewers per application
  - Meetings last 1 – 2 days
- SRO provides orientation re: policy/process
  - Introduction of persons present
  - Conflict of interest/confidentiality
  - Roles of persons present
  - Policy, process, review criteria

What Happens In A Study Section Meeting?

- Streamlining (unscoring) of applications in "lower half"
- Application by application discussion
  - Persons with conflicts of interest excused
  - Assigned reviewers give preliminary scores
  - Discussion of application's scientific and technical merit; comments re: each review criterion
  - Assigned reviewers first, then other panel members
  - Range of scores recommended by assigned reviewers
  - All panel members (except those in conflict) score privately
  - Assignment of codes for human subjects protection, gender, minority, and children
  - Budget recommendations

Review Criteria for Research Project Grants

- **Significance**: Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge **or clinical practice** be advanced? What will be the effect of these studies on the concepts, methods, technologies, **treatments, services or preventive interventions** that drive this field?
- **Approach**: Are the conceptual **or clinical framework**, design, methods, and analyses adequately developed, well-integrated, well-reasoned and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics? Are plans to coordinate among multiple PIs adequate?
- **Innovation:** Is the project original and innovative? For example: Does the project challenge existing paradigms **or clinical practice,** address an innovative hypothesis **or critical barrier to progress in the field?** Does the project develop or employ novel concepts, approaches, methodologies, tools or technologies for this area?

Review Criteria for Research Project Grants

- **Investigator:** Are the investigator(s) appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator(s) and other researchers? Does the investigative team bring complementary and integrated expertise to the project (if applicable)?
- **Environment:** Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed studies benefit from unique features of the scientific environment **or subject populations**, or employ useful collaborative arrangements? Is there evidence of institutional support?

Review Criteria: Other Considerations

- Human Subjects Protection
- Data and Safety Monitoring Plan
  - Required for ALL clinical trials
- Plans for Inclusion of Women, Minorities and Children in Clinical Research
- Animal Welfare Protection
- Any RFA-specific criteria, if applicable
- Appropriateness of the Budget

Initial Review Group Options

- **Not Scored (UN)**
  - Application not in top half of all applications
- **Not Recommended for Further Consideration (NRFC)**
  - Lacks significant and substantial merit or serious ethical problems in Human Subject or Animal use
- **Deferred**
  - Review Committee needs more information to decide on the scientific merit of the application
- **Scientific Merit Rating (Priority Score) Assigned**
  - 1.0 (best) to 5.0 (worst)
  - Target a mean score of 3.0 for all applications

Priority Score

- For each scored application, a single global score is assigned by each review committee member not in conflict
- The score is to reflect the ***overall impact that the project could have on the field***.
- The emphasis on each review criterion may vary from one application to another, depending on the nature of the application and its relative strengths. An application does not need to be strong in all criteria to receive a high priority score.

The Summary Statement Documents Results of the Review

- SRO prepares summary statement when review is completed
- The summary statement contains:
  - Priority Score and Percentile Ranking
  - Codes for Human Subjects protection, gender, minority, children
  - Resume and Summary of Discussion
  - Essentially unedited critiques of assigned reviewers
  - Budget recommendations
  - Administrative Notes
- Forwarded to the Program staff in NIH Institute/Center, where a funding decision is made
- Advisory Councils/Boards see summary statement
- PI can retrieve priority score, percentile ranking and summary statement through the NIH eRA Commons

Career Development Awards

(**See NIH "K" Kiosk at** http://grants.nih.gov/training/careerdevelopmentawards.htm)

- **K01- Mentored Research Scientist Development Award**
  - Usually for Ph.D.'s, for basic research
- **K02 - Independent Scientist Award**
  - Additional time/effort support for new researcher with R01
- **K05 - Senior Scientist Award**
- **K07 - Academic Career Award**
- **K08 - Mentored Clinical Scientist Development Award**
  - For clinicians to get basic/laboratory research training
- **K12 - Mentored Clinical Scientist Program Award**
- **K22 - Patient-Oriented Research (POR) Transition Awards**
- **K23 - Mentored Clinical Scientist Development - POR**
- **K24 - Mid-Career Patient-Oriented Research Award**
- **K99/R00 - Pathway to Independence (PI) Award**
  - **Announced January 27, 2006**
  - **For postdocs with no more than 5 yr of training**
  - **1 - 2 yr mentored phase followed by 3 yr independent phase**

Review Criteria for Career Development Awards

- Qualifications of candidate
- Qualifications of mentor (if applicable)
- Appropriateness of career development plan for candidate's career stage
- Quality of the career development plan
- Quality of the research plan
- Quality of training/institutional environment

What Determines Which Applications are Awarded?

- **Scientific merit**, as indicated by priority score and/or percentile ranking
  - Each NIH Institute/Center sets its own "paylines"
  - Paylines vary for different types of grants
  - Usually more liberal payline for applications from "new investigators" (R01* applications)
- **Programmatic considerations** of the awarding NIH Institute/Center
  - Balance of models, geographic sites, approaches, etc in portfolio
- **Availability of funds**
  - Funds for "competing" grant awards limited; most of budget already committed to continuing grants and programs
  - Doubling of NIH budget FY 1998 – 2003
  - Essentially "flat" budget in FY 05 - 08 means tighter paylines

NIH Loan Repayment Program
Special Opportunity for Clinical Researchers

- Designed to attract health professionals into research
  - Clinical
  - Pediatric
  - Health disparities
  - Contraception and fertility
- Also program for researchers from disadvantaged backgrounds
- Repays up to $35,000 per year of qualified educational debt (student loans) in exchange for 2 – 3 yr commitment to research
- Must be US citizen
- One receipt date per year, special application form
- See http://lrp.nih.gov/about/extramural/index.htm

Important Recent Changes in the NIH Grants Process

Electronic Application Submission

- NIH is in the process of converting to SF424 (Research and Related [R&R]) forms and electronic submission through Grants.gov
  - Forms generated by Grants.gov for cover page, administrative information, budget
  - PDF attachments for biosketches, research plan, other narrative sections, and literature cited
- Single component research project grants ("R" series) and resource grants have already transitioned
- Transition of Career Development ("K"), Fellowship, Training and complex applications currently on hold
- **See http://era.nih.gov/ElectronicReceipt/ for timeline, FAQs, training materials, tips, contacts**

Multiple Systems Working Together

- **Grants.gov** – the Federal government's on-line portal to find and apply for all Federal grant funding
  - Used by all 26 Federal grant-making agencies
- **eRA Commons** – the NIH electronic Research Administration (eRA) system for receiving and transmitting application and award information
  - Used by NIH and other DHHS components
- Each system has its own registration process
  - Institutions register in Grants.gov
  - Institutions register institution and their PIs in eRA Commons

Applying Through Grants.Gov Is a Very Different Model for NIH

- Applications **must** be in response to an open Funding Opportunity Announcement (FOA) in Grants.gov
  - NIH "Parent FOAs" = "umbrella" FOAs for "investigator initiated" applications – see http://grants.nih.gov/grants/guide/parent_announcements.htm
  - NIH Guide for Grants and Contracts provides link to correct FOA for each NIH PA and RFA
  - Download the specific application package with forms and instructions for the specific FOA from within Grants.gov.
  - Always download "fresh" to ensure latest version of forms
- Applications submitted only by authorized institutional officials
- Grants.gov and eRA Commons electronically validate forms and attachments – applications with "errors" rejected

Parent FOAs for Common NIH Investigator Initiated Applications

FOA Title	Announcement Number	NIH Activity Code
Research Project Grant	PA-07-070	R01
Small Research Grant	PA-06-180	R03
Exploratory/Developmental Research Grant	PA-06-181	R21
Academic Research Enhancement Award	PA-06-042	R15
Small Business Innovative Research Grant	PA-06-120	R43/R44
Small Business Technology Transfer Grant	PA-06-121	R41/R42

Note: Some NIH Institute/Centers do not accept applications under the R21 and R03 Parent FOAs

Changes in Terminology related to Grant Applications

- **Resubmission** = Revised/Amended
- **Renewal** = Competing Renewal or Competing Continuation
- **Revision** = Request for Supplemental funds for ongoing awarded grant
- **Corrected** = Fixing errors noted in Grants.gov or eRA validation process

Multiple Principal Investigators (PIs)

- More than one PI may be designated for projects that require a "team science" approach
- Multiple PI option will be implemented for grants (except Ks and Fs) as they transition to SF424 and electronic submission
  - Available for R01s since February, 2007
- Must designate "Contact" PI for communications with NIH
- Application must include a new section describing the "Leadership Plan"
- **http://grants.nih.gov/grants/multi_pi/index.htm**

New Limits on Inclusion of Publications in Appendix Materials

- **Published Papers:** Include **only** a publication list with links to the publicly available on-line journal or the NIH PubMed Central ID #
- **Manuscripts accepted for publication and "in press":** Submit as a PDF attachment for electronic submissions or in hard copy for paper applications.
- **Manuscripts published without an on-line journal link:** Submit as a PDF attachment for electronic submissions or in hard copy for paper applications.
- See NIH Guide for details – http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-018.html
- Refer to instruction guides and specific Funding Opportunity Announcements for allowable # of publications

Shortened Review Cycle for New Investigators

- Reduce time to next review for New Investigators with unfundable R01 research project grant applications
- Shortened Review Cycle - Saves about 4 months
  - Review meetings held earlier & summary statements completed sooner
  - Special receipt date allows about a month to revise and resubmit for the very next review cycle
- Appropriate for projects with easily addressable problems
  - PI must decide if weaknesses cited in Summary Statement are amenable to "quick fix"
- See: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-083.html

CSR Peer Review Pilots

- Shorten and/or restructure the NIH Grant Application
  - Reduce length of Research Plan
  - Specific sections to address all review criteria
- Refine review criteria to emphasize significance or innovation
- Alternative review formats – video or online
- "Editorial Board" style review
- Electronic Referral
  - Test fingerprinting and artificial intelligence software to assign applications

NIH Roadmap

- Purpose: To identify major opportunities and gaps in biomedical research that no single Institute at NIH could tackle alone but that the NIH as a whole must address, to make the biggest impact on the progress of medical research
- Idea and Prioritization Process involves input from many sectors
  - NIH staff and Intramural scientists
  - NIH funded investigators
  - Other investigators
  - Patient Advocates
  - General public
- Activities
  - Initiatives
  - Pilot Studies
  - Coordination Areas
  - Strategic Planning Areas
- Website: http://nihroadmap.nih.gov/

NIH Roadmap Initiatives

- New Pathways To Discovery
  - 2008 Initiatives: Microbiome and Epigenetics
  - To be phased in: Protein Capture Tools and Phenotyping Tools
- Research Teams Of The Future
- *Re-engineering The Clinical Research Enterprise*
  - Clinical Research Networks
  - Clinical Research Policy Analysis and Coordination
  - Clinical Research Workforce Training
  - Clinical Outcomes Assessment
  - Translational Research

Other NIH Road Map Activities

- Pilot Study – Genetic Connectivity Map
- Coordination Groups
  - Regenerative Medicine
  - Pharmacogenomics
  - Bioinformatics
- Strategic Planning Activities
  - Training/Careers
  - Health Disparities
  - Science of Science Administration

Enhancing Peer Review at NIH

- Begun in June 2007
- Goal: Optimize efficiency and effectiveness of the NIH grants process as science becomes more complex
- Wide ranging examination of all aspects of the NIH grants and peer review process
  - Internal: NIH Steering Committee Working Group
  - External: Advisory Committee to the NIH Director Working Group
    - Public comments, regional meetings, meetings with professional societies and advocacy groups
- Recommendations expected Winter/Spring 2008
- May lead to pilots re: types of grants, length/format for grant applications, review criteria, review formats

Tips for Better Grantsmanship

"Psychology" of the Review Process

- **Reviewers are:**
  - Over committed, over worked and tired
  - Inherently skeptical and critical
  - "Informed strangers"
- **A happy reviewer is likely to be more positive, so make their job easier:**
  - Flow diagrams, charts, figures
  - Well organized, clearly written application
- **Avoid things that irritate reviewers:**
  - Not following instructions: ie, exceeding the page limits, font too small, putting information in the wrong section, omitting or mislabeling references/figures
  - Spelling, grammar, and math errors, etc.

Preparing to Write a Grant Application

- **Critically Assess Yourself**
  - Do you have the necessary expertise, resources, personnel, and preliminary data to be competitive?
- **Assess the Competition**
  - Who are the important contributors to the field? (remember, they might end up being your reviewers)
  - What have they accomplished?
  - Search the literature and the NIH CRISP database of funded grants in the field (http://crisp.cit.nih.gov/)
- **Assess the Potential for Your Idea**
  - What has already been done/reported/funded in your area? What are the "gaps"?
  - How can you take what's been done a step farther?

Choosing Your Research Project

- **What Makes an Research Project Outstanding?**
  - Addresses an important problem clearly
  - Potential to lead to seminal new observations or new ways of thinking
  - Lays the foundation for further research in the field
  - Addresses a difficult problem in a way that seems simple in retrospect, making reviewers wonder why they didn't think of the idea themselves
  - All aspects of the project are clearly linked

Preparing the Research Plan

- Include 2 - 4 closely related specific aims
- Explicitly state the rationale for the proposed studies
  - Never assume the reviewers will “know what you mean”
- Use flow diagrams for overview, and for complex experiments and protocols
- Include well-designed, easy to follow tables and figures
- Address priorities if patients, reagents or resources will be limited
- Include data analysis and interpretation plans and methods
- Involve the statistician EARLY in project design

Key Features of Successful Applications

- **Hypothesis**
  - A meaningful hypothesis AND a means of testing it
  - A sound rationale for the hypothesis
- **Preliminary Data**
  - Documents feasibility of the proposed project
  - Shows training for research proposed & ability to interpret results
  - Include alternative interpretations and address limitations of methods
- **Well Organized Research Plan**
  - Aims focused - and related to each other and the hypothesis
  - Rationale for methods proposed, with alternatives addressed
  - Research flow and priorities clearly indicated
  - Sufficient experimental detail to show you understand methods
  - Emphasize MECHANISM - avoid “descriptive data gathering”

In God We Trust….

All Others Must Bring Data.

Key Features of Successful Applications, con't

- **Biosketches**
  - Indicate your qualifications to carry out the work proposed
  - Don't "pad" with lots of "in preparation" manuscripts
  - Add a senior collaborator, if needed, to provide expertise you lack
- **Literature Cited/Bibliography**
  - Be thorough, but critical, in citing previous work in the field
- **Description (Project Summary in SF 424 applications)**
  - Most read part of the application
  - Basis for referral to study section and funding Institute/Center
  - Write it last, after the Research Plan is finished
  - State problem, specific aims, types of methods to be used
- **Letters of Collaboration**
  - Should be strong and definitively state what will be provided

Most Common Reasons for Unscored or Not Recommended for Further Consideration

- **Rationale for hypothesis or methods not sound or not supported by preliminary data**
- **Diffuse/unfocused or superficial research plan**
- **Aims don't address hypothesis**
- **Flaws in experimental approaches**
- **Models not relevant to human situation**
- **Unrealistically large amount of work proposed**
- **Work not new or original - Lack of appreciation of published relevant work**
- **Lack of experience in essential methods**
- **Insufficient experimental detail**
- **Serious risks to human subjects or use of animals**

Make Sure Your Application is Complete and Correct as Submitted

- **START EARLY** – both registering in Grants.gov and eRA Commons AND planning the science
- Read instructions thoroughly and follow them carefully
  - Especially important for electronic applications
  - Avoid validation errors in Grants.gov and eRA Commons
- Allow time for frank feedback from a senior investigator with review experience
- NIH processed > 75,000 grant applications in FY07
  - NIH cannot "change pages" after submission
  - Poor grammar, missing information, confused figure legends, etc will be very apparent to reviewers
- Contact the SRO if you need to send corrected information after submission

NIH Program and Review Staff Can Help

- **Know the NIH program officer(s) in your field**
  - Check programs in several NIH Institutes and Centers
  - Information about upcoming initiatives, opportunities, “gap” areas
  - Information about potential collaborators, NIH resources
  - Explain NIH policies, procedures, award mechanisms, eligibility requirements
  - Advice in revising unfundable applications
- **Know the Peer Review System and your SRO**
  - Review criteria and receipt/review schedules
  - Explain NIH policies, procedures, award mechanisms, eligibility requirements
  - Problems with referral or review
  - Use the NIH and other websites to get latest information, forms, policies

Selected Web Sites of Interest

- **National Institutes of Health** (http://www.nih.gov)
  - NIH Office of Extramural Research homepage, with links to the NIH Guide, grants policy information, and resources for new investigators: http://grants1.nih.gov/grants/oer.htm
  - Overview of NIH Extramural Research, with links to tools and FAQs: http://grants1.nih.gov/grants/welcome.htm#introduction
  - Career Development Awards Information http://grants.nih.gov/training/careerdevelopmentawards.htm
  - NIH Electronic receipt http://era.nih.gov/ElectronicReceipt/
- **NIH Center for Scientific Review** (http://www.csr.nih.gov)
  - Has links to Resources for Applicants, standing Study Section rosters, policy information, review procedures and review criteria, video of mock study section, and advice for investigators submitting clinical research applications
- **Grants.gov** (http://www.grants.gov)