Moving your Science Forward: NIH K Awards and Other Tidbits

Clinical Trials Methodology Course
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1) Funding Opportunities
2) Some data
3) Setting yourself up for success

Major Relevant Funding Mechanisms

I. Individual Career Development Awards

K08/K23 (Mentored)

- For clinicians
- 75% effort required for most
- 50% effort required for neurosurgeons
- Up to 5 years protected time
- Salary and fringe (amount varies by IC)
- Research costs (amount varies by IC)

- All Ks are12 pages (plus various forms)
- Must be a US citizen or permanent resident for all Ks except the K99/R00

K99/R00: Transition to Independence

- Must have less than 4 yrs. postdoc. res. experience
- Must be in mentored (non-independent) position
- No citizenship requirement

  - 2 years K99 (mentored)
    - 75% effort required (50% for neurosurgeons)
    - salary (varies), usually $20,000 costs but varies

  - 3 years R00 (independent)
    - must have tenure track or equivalent position
    - 75% effort on research required
    - $249,000 total cost
    - Appropriate support (IC interpretation varies)

K02: NINDS flavor (pre R01)

- Clinician in independent position
- 5 years, min 75% protected time
- Salary, fringe, $50K per year research costs
- Not ready for R01 for a good, career-development reason
- Cannot draw additional salary from other federal sources
- Must get R01 by end of 3rd year to get last two years

Can consider a bridge between mentored K and R01

Later Career Development Option

K24 – Mid-career award

- Supports larger mentoring role plus research
- 5 years, 25 – 50% effort
- Salary, fringe, some supplemental support
- Total package depends on Institute

- NINDS does not support right now – many other institutes do

Digression: New NINDS Landis Award for Outstanding Mentorship

- Nomination by former and current mentees
- 3 cohorts, 1 per year
  - ➢ Junior (5-12 years from first tenure-track pos.)
  - ➢ Mid   (13-20 years from…)
  - ➢ Senior (21-100 years from…)
- 100K supplement to grant

You want to be one of these nominees!!
(Several clinician-scientists have been nominated and at least 2 have been selected for the award)

Loan Repayment Program (LRP)

Extramural, most institutes:
- Clinical Research
- Pediatric Research
- Primarily for clinician-scientists (varies)

Additional at some other institutes:
- Health Disparities Research
- Contraception and Infertility Research
- Clinical Research for Disadvantaged

Major Relevant Funding Mechanisms

II. Institutional Career Development Awards

NINDS K12 Awards (institutional)

- Two National Programs
- Support for scholars at any US institution
  - CNCDP
    - ► For Pediatric Neurologists
    - ► Junior Faculty, first years out of residency
    - ► Up to 3 years of support
  - NRCDP
    - ► For Neurosurgeons
    - ► Eligibility: 1st year Faculty only
    - ► Up to 2 years support, 5 years protected

Other Institute K12 Awards

- Based at individual institutions
  - ► e.g. Emergency Medicine (NHLBI)
    CTSA KL2s
- Some national programs
  - ► e.g. Pediatric Critical Care (NICHD)
    Pediatrics (NICHD)

There is one fundamental desired outcome of all K12s: Get to a major individual award (K, R)

T32 Awards for clinicians

At a number of institutions

- Some are exclusively for clinicians
- A couple are exclusively for clinical research
- Some support clinicians plus others
- Check out your institution (or another if you're planning to move)

Your goal on a T32: Get to a K.

Two examples demonstrate key approaches to success:

The NINDS R25 and the NINDS NRCDP

The NINDS R25 for Residents and Fellows

- Institutional Award – 22 institutions,
  31 residencies
- Neurology, Neurosurgery, Neuropathology,
  Neuroradiology, Emergency Medicine

- At least 6 months of 80% effort in residency
- Then two years of Fellowship
- Mandate: Get to a K award

- Thus far, 259 supported (169 neurologists)

The R25 Design

- Institutional Program – Oversight and accountability

- Initial support in residency, guaranteed fellowship

- Residents prepare research/transition plan (3 pg) in advance of support, mentor must also create detailed plan

- Programs have oversight committees to oversee both resident/fellows and mentors

- You <u>must</u> submit a K application by the 18th month of fellowship support to get the final 6 months

The NRCDP – for neurosurgeons

- Two years of NINDS support
- Five years of protected time committed by Chair
- To be competitive, need in advance:
    - High quality research proposal
    - High quality mentoring plan
    - Real commitment to success by Chair
    - Strong oversight
    - Profound understanding of your plan (learned via interviews)

Influence of R25 on K08/K23 Success Rates (2012-18)

	Following R25 support		
	Applicants	Application success rate	Applicant success rate
Ped Neuro	7	50%	71%
Adult Neuro	34	47%	68%
Neurosurgeon	9	45%	56%
	No Prior R25 or K12 support		
	Applicants	Application success rate	Applicant success rate
Ped Neuro	37	29%	38%
Adult Neuro	181	27%	39%
Neurosurgeon	44	20%	30%

Influence of R25 on Time (months) from Residency to K (2012-18)

	K08		
	All	MD	MD/PhD
R25 supported	31 ± 3 (26)	32 ± 6 (8)	31 ± 3 (18)
No prior R25	52 ± 5 (43)	61 ± 7 (18)	45 ± 3 (25)
	K23		
	All	MD	MD/PhD
R25 supported	44 ± 7 (7)	51 ± 7 (5)	27 (2)
No prior R25	71 ± 4 (55)	75 ± 4 (44)	52 ± 6 (11)

NRCDP K12
Subsequent NIH Funding

First 13 scholars (2012-2016)	
Applied for Any NIH Award	100% (13/13)
Awarded K, R, or U Grant	77% (10/13)
Applied for K08 or K23	62% (8/13)
K success rate	50% (4/8)
R01 or equiv (award/app)	75% (6/8)
Received major funding	At least 11 (85%)

Some Lessons from R25/K12 Programs

- Plan your project early and well
- Understand a good mentorship situation
- Identify TRULY appropriate mentors
- Set up a good mentorship situation
- Focus on where you're trying to get to
- Keep refining your project as you go
- Make sure you have good institutional support
- Do something important!

NINDS K Review Policy

For K applicant with prior, high quality research accomplishments (e.g. high quality pre-residency papers):

1. A lack of research papers in residency and 18 months post-residency should NOT count against the applicant
2. A lack of publications specifically in the K application research area for should NOT count against the applicant

In other words, don't make applicants wait to publish post-residency in order to compete for a K

Major Relevant Funding Mechanisms

III. Research Awards

R01 (bread and butter)

- 5 years, $250,000 or more
- Apply anytime
- Multiple P.I. grants possible

Once independent, you should apply as soon as you can put together a competitive application

You can apply <u>any time</u> after getting your K

Other choices

- **New Innovator Award (DP2)**

  Highly innovative, exceptionally creative; potential for high impact, no prelim. data required ; $300K per year, up to 5 years (clinicians do well)

- **Program Project (P01)**

  3 or more subprojects, $1,000,000 max

- **Exploratory Research Grant (R21)**

  2 years, $275,000 total, non-renewable

- **Small Grant (R03)**

  2 year max, $50,000/yr max, non-renewable

Some Policies, Facts and Data

NIH, and especially NINDS, policies and practices continue to facilitate the success of early stage investigators

Definitions

New Investigator (NI) is somebody who has not had an R01 or equivalent NIH grant

Early Stage Investigator (ESI) is somebody who is within 10 years of terminal degree or clinical training

ESI/NI Benefit at NINDS

	%tile funded or considered for funding		
	Established		NI/ESI
2007	9		>25
2008	10		>25
2009	11		20 / 30
2010	13		20 / 30
2011	14		20 / 30
2012-2017	14-15-12		ESI–Plus 10
2018-19	15-16		ESI-Plus 10

Effect of ESI/NI Benefit on Time to R01 (NINDS)

	Time to First R01	
	From Start of K Award	
	2003-2007	**2008-2011**
K08	6.3 ± 0.4 (46)	4.9 ± 0.2 (34)
K23	6.5 ± 0.5 (22)	4.5 ± 0.3 (22)

Some Success Rates

Keep in mind, whenever you see application success rates, these underestimate real success

Applicant success rate is higher!

NIH-wide Career (K) Awards
Application Success Rate

	2018	2014	2010	2009	2008	2003
K08	40%	40%	44%	47%	44%	47%
K23	38%	38%	38%	44%	38%	42%
K24	52%	49%	61%	47%	51%	45%
K99	26%	22%	25%	29%	23%	N/A

NINDS K Award <u>Applicant</u> Success Rate (2012-2018)

	MD/PhD	MD
K08	48%	43%
K23	40%	37%

How many K awards are made on the first submission?

	K08		K23	
FY 2013-2018	-01	Amended	-01	Amended
Awards Made	61%	39%	42%	58%

2018 R01 <u>Application</u> Success Rates

New			Renewal	
NINDS	21%		NINDS	41%
NIMH	18%		NIMH	37%
NIDA	16%		NIDA	32%
NIDCD	24%		NIDCD	46%
NIA	21%		NIA	38%
NIGMS	23%		NIGMS	50%

NINDS 2018 payline: 15th %tile

Transition of K08/K23 to R01/DP2/U01
(K end dates 2005-2018)

Specialty	# K awardees	% applied for "R"	% of Ks that got at least one "R"	Applicant Success Rate
Pediatric neurologists	45	84%	60%	71%
Adult neurologists	234	81%	50%	62%
Pediatrics (includes critical care and neonatologists)	37	84%	54%	65%
Neurosurgeons	42	86%	60%	69%

NINDS K to R transition

For K awards terminating 2003-2011

For both K08s and K23s, 75% obtained competitive, post-K independent funding

2012 analysis

NINDS Clinician K careers

For K awards terminating 2003-2008

<u>Currently in Academic Position</u>
K08s: 86%   K23s: 88%

<u>Published between 2010-May 2012</u>
K08s: 88%   K23s: 85%

<u>In Academic Position and Published…</u>
K08s: 95%   K23s: 96%

2012 analysis

NINDS K99/R00s

- 165 K99s since 2007

- 113 to an R00 thus far

- 78% R01 applicant success rate

- 85% of completed R00s have R01 or DP2 (67/79)

Some things you need to know to succeed

National Institutes of Health

- **27 Institutes and Centers**
- **Each Institute has its own mission**
- **Each Institute has its own budget**
- **Each Institute has its own activities**
- **Each Institute has its own ways of doing things**

When you're planning to submit a grant, check with program directors from different institutes to determine their interest in your science.

www.ninds.nih.gov
Training and career award link at left

Electronic submission is unforgiving

1. You must be on time and get it right

2. Your institution submits it, but it's your application – be early and check on it

Your application is reviewed at study section by:

- Experts
- Non-experts
- People who are reading lots of grants
- People who want to be excited by your science
- People who will be irritated by a sloppy application

Submit a high quality application!

Have people review your application critically
WELL BEFORE submission

All parts of an application need to be excellent

- Specific aims
- Significance
- Innovation (this doesn't just mean technical)
- High quality preliminary data
- Experimental approach
- Scientific premise, rigor…
- Training Plan (if applicable)
- Discussion of potential problems and solutions
- How you will interpret your data and where you will go with it
- Your track record

Clinical Trials and K applications

- Can <u>YOU</u> do it?
- Do you have the resources to do it?
- The most common approach is to do a "piggy-back" study in an on-going trial
  - Is your plan reasonable?
  - Is your study important?
- You WON'T be funded to just jump in and work on an already planned project

Clinical Trials and K applications

- You need to have a project that you own and that has "legs"
  - Can you move it beyond the K?
  - Will you get the appropriate training?

- You need to be in an appropriate environment for your work

Make sure you get outstanding and appropriate mentoring – do not underestimate its importance - (and be a good mentee!)

This is the number one problem in clinician-scientist training

You need to manage your mentors and see them often (at least weekly!) - and be prepared

Schedule appointments and have an agenda
And don't wait for problems

- Protect your protected time

- It's critical that you publish…

- Focus on high quality publications

- Mind the important (and difficult)
  balancing act:
      publications vs preliminary data

- Devote enough time to crafting your grant –
  the bar is high, as it should be

You need to consider and address everything

- The rigor of the pre-clinical data
- Recruitment feasibility
- Power analysis / data analysis
- Impact on the clinic
- Obstacles to success and what you'll do
- Time needed for the study
- Appropriate controls
- Administrative needs and challenges
- …

At the end of the day…

Will you have a definitive answer to the specific question you are asking?
(and is it important that you answered it?)

If a foreseeable event can go wrong and screw up your project, you haven't planned it well enough!

Get hypercritical advice from people who know how to get an NIH grant – preferably the kind you're seeking

(give your grant to people who will constructively hate it, tell you what's wrong with it, and give you real advice on how to fix it)

Getting Started on Multi-center Trials after a mentored K

- If you have done outstanding research
- If you have done clinical research
- If you have done some pilot single site interventional projects
- But you have little or no experience at doing a multi-center trial
- Two options at NINDS:
  - Apply for R01 with highly experienced trialist who is relevant to the project
  - Apply for NINDS K02 to gain experience

Write clearly, coherently, logically

Do not be sloppy

DO NOT BE BORING

DO NOT TAKE REJECTION PERSONALLY!

And don't get frustrated.

And don't blame reviewers.

PERSIST!

Fix the problems

- You get unlimited submissions now

- But it isn't a lottery!

- Understand what will be required for success. What is the summary statement saying?

- Get advice from your mentor, program director and others with funding success

Fix the problems

- Don't get trapped by the new expedited review process for ESI/NI

- Don't assume you should come back in quickly and don't succumb to pressure to come back in quickly

Respond appropriately to reviewer comments

If you have questions:

Email or Call
(Email is better for first contact)

Program Director - questions related to science

Training Director (e.g. me) - for questions related to mechanisms, application preparation, direction, problems, etc.

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