

- 1- Welcome, and thank you for coming! I am really honored to be the new scientific director for the intramural research program of the National Institute of Mental Health. We work in a truly great institution, a privileged place where we are free to pursue our ideas with unparalleled resources, and we have an incredible group of researchers and clinicians in our ranks!
- 2- I am here to share with you some of the ideas, dreams, really, that I have for this wonderful institution, ideas and dreams that I hope to form and fine tune with your help. I will continue to make one of my priorities to see you individually and to discuss with you our great and exciting future. Your unique insights, your knowledge of this place will be critical in shaping and adjusting the ideas that I am about to share with you. I must say that I look at our immediate, short and long-term future with a great deal of optimism, hope and anticipation!
- 3- The ideas that I would like to discuss with you today fall into two categories. The first has to do with the nuts and bolts of the inner working of the institution, including much-needed changes in accounting and administration. Fortunately, we have a dedicated administrative support staff that will be invaluable as we reform the way we disburse, track and follow expenses. A few years back the IRP grew considerably and our administrative structures have not yet had time to catch up with this growth. Efficiency is especially critical now, when budgets are no longer growing and belts are being tightened... Concerning the tightening of belts, although we are far more insulated from financial cuts than our colleagues in the extramural community, I know that the cuts in recent years were significant. The good news is that at this point I am hopeful that we will not need deeper cuts (but at this time, only Congress and White House knows...). Usually, cuts in resources lead to a loss of flexibility in research, and it is my sincere hope that we can partially compensate for that with a series of fairly straight forward changes that will increase your ability to make choices with your research resources. Tom Insel started a series of reforms that essentially will allow PIs in our program an unprecedented amount of discretion on how they allocate their resources. Over the next year, we plan to phase in these changes, again with your help and feedback. Nevertheless, I understand that even seemingly very positive changes (shifting control over science budgets to the people that do the science) can have unintended consequences on complex organizations, such as the IRP, and therefore, I will make sure to consult with you and to get your impute before and during any changes are introduced or implemented in the IRP. We have a special place and I will work hard to protect what makes it unique and successful.

- 4- The second category of ideas that I would like to discuss has to do with scientific programmatic decisions, the nature and quality of our interactions and the overall distribution of resources in our community. These issues touch the core of our identity as an institution and I thought this would be an appropriate time to share with you some of the thoughts and ideas that I have been considering in the last few months. I realize the critical role that the Scientific Director's office has in our community and it is important that we work together in shaping the exciting future of our great institution. Let me start with some general principles of operation:
- 5- First, no significant changes will be put in place without consulting with you, getting your input and feedback. The SD's office serves a community of enormously talented individuals and I plan to harness that talent to set and adjust our course. It's true that occasionally I may have to make some difficult decisions, some that may even be unpopular, but one thing I can promise you: Nothing critical will be decided without first seeking your opinion. You will be part of the process, because again, the results of the process are meant to serve, help our community! I realize that despite all of my good intentions, that decisions often have complex ramifications and that talking with you is one way to identify well intentioned but misguided policy. I am here to help and I understand that one of the best ways to do that is to listen intently. Besides consulting with you, when appropriate, I also intend to involve members of the board of scientific councilors (BSC) and others in the extramural community. The BSC in particular have been an important source of insight with respect to the individual research of our investigators, and now I would like to involve them more in programmatic issues. They are an excellent group of smart people with a real commitment and interest in the IRP and I believe it is a good idea to seek their advice when considering important matters. Actually, I am about to have a meeting with them and a few others in January to discuss the most important issues that we are facing at the moment.
- 6- Second, It is essential to listen attentively before making a decision, but it is just as critical to be decisive once the information is in.
- 7- Third, I will make every effort to insure that decisions from the SD's office are always transparent. It is important to me that you know what's going on and that you have insight not only concerning what is decided and why, but also on how it was decided. Why? First, it is the right thing to do, but most importantly, because I believe that if the process is transparent, you will be contribute to it. On the other hand, if you don't understand the process, it will be more difficult for you to help. Again, I understand that good intentions do not equal effectiveness, and I know

that I will need your help to get it right. I would like to extend this transparency to every aspect of our program, including allocation of new resources, budgets, etc. I suspect that many of you would rather not be bothered with this type of thing, but I want to make sure that factors that affect our community, budgets, policy and anything else with an impact on our future, are open and transparent so that the community can participate in shaping its own future. Again, I may be forced at times to make difficult, even unpopular decisions, but I will try not to hide them within our administrative labyrinths.

- 8- Fourth, synergy is another important concept that I will keep in mind as we discuss the future of the IRP. We need to expand, to change, to develop emerging areas of interest and opportunity, to be responsive to the ever-changing needs of mental health and the challenges of research in this difficult but extremely exciting area. However, we can never forget synergy: this means that we need to be mindful of our areas of strength and build from there and make sure that our growth is coordinated so that once again we can explore latent and emergent synergies in our program. This is another reason why I think it is important that we create incentives to explore alternative collaborative arrangements that may take us to unfamiliar, but incredibly exciting new areas.
- 9- Fifth, leadership requires guiding principles and ideas, but it requires just as often humility, the ability to recognize that the complexity of the world does not always fit simplistic internal representations of that reality, and that to be effective one needs to fine tune those ideas, no matter how invested we are in them.
- 10- I have been talking about “our” community as if there was a real separation between the NIMH IRP and other neuroscientists in our larger NIH community. As you know, there are a number of exciting collaborations with members of other institutes and I see in our future a trans-institute neuroscience community that explores synergies beyond the administrative boundaries of each institute. Tom Insel and Story Landis worked hard for this, and I will continue to work closely with Alan Koretsky and others in our intramural community to devise ways to encourage the already exciting collaborative infrastructure between Neuroscientists at NIH.
- 11- Additionally, I also think that it is extremely important to support on going programs designed to connect intramural researchers with their extramural colleagues. Science is best without walls and I hope to work hard to enable and facilitate the links between our program and others in the intramural and extramural community.

- 12- Let me now shift my comments more directly to science: Let me start by saying that as we prepare to grow again, and grow we must, the most important thing is that quality of science is placed above everything else. Strangely, it is not rare to see programmatic pressures drive institutions to make scientific choices that they would not otherwise make, and to settle for choices that are less than ideal because they are simply good programmatic fits. Often one hears arguments that include “this is the best that the field has to offer” almost as apologies for sub-standard science done under the guise of compelling programmatic themes. I am convinced that if ever there was a rationale to make such compromises, it is no longer useful to do so. Good science is good science, and I never came across a situation where it is wise to place quality second to other considerations, no matter how important they may seem at the time.
- 13- I want to emphasize the importance that I place on research directed to understand and develop treatments for mental health problems such as autism, schizophrenia, depression, bipolar, PTSD, ADHD, cognitive deficits, etc. We have a mandate from congress to work on these problems because they are an enormous burden to our country, and I am absolutely committed to this cause. Those of you that know my work would not be surprised to hear that I believe that the interface between basic, translational and clinical neuroscience is terribly exciting, and I was delighted to find out that many of you work exactly at this interface. Besides all of the obvious benefits of working on problems of the importance and gravity of depression, learning disabilities, schizophrenia, etc., this exciting interface forces researchers to be integrative and nimble, to develop non-traditional perspectives and explanations to fundamental research problems of brain function and dysfunction. I think for the first time in the history of neuroscience, we have the tools and intellectual framework to start to make real progress within the exciting interface between basic, translational and clinical neuroscience. Our institution can provide much needed leadership at the vanguard of this movement since we are free from the obvious conventional constraints that limit the research choices of our colleagues elsewhere.
- 14- Besides placing good science first, being excited about the interface between basic, translational and clinical science, I also recognize the enormous power of diversity. We need to fight hard to preserve the diversity of our program, and we should not let programmatic imperatives decrease the wonderful diversity that has made the IRP great. It is important to recognize that at this point we still do not know where the real solutions for our challenges in mental health will come from. Will they come from genetic studies, cognitive neuroscience, Drosophila studies,

mouse models? Really, at this point we do not know, and we should keep this in mind as we make choices for the future of our program. That is another reason why quality should always be paramount as we plan our exciting, but wonderfully uncertain future. We cannot forget that at this point in mental health research we are explorers first and foremost. The time to call in large teams of methodic farmers, colonizers of this amazing problem space, is not here yet. At this point we need scouts, risk takers, intrepid souls with the courage and perseverance to try new ideas and strategies.

- 15- And this leads me to another very important point: Labels like exploratory, ambitious, risky, untried approach, uncertain outcome, etc, are pejorative in RO1 study sessions but should be laudatory in BSC reviews... I say, they should, although I am not sure that they have always been... I am committed to work hard with the BSC to make sure that the important periodic reviews of our individual research programs reflect the nature and goals of our special community, and are not a watered down version of study session rules. I think that it is absolutely critical that our approach to research continues to be distinct from the extramural community: we are supposed to try new things, push the boundaries of the credible and the possible, take risks, and yes, fail. Yes, we are supposed to fail. If we do not fail it's because we are not pushing the envelope of science, we are not going beyond the current paradigms. There is a lot of great science to be done within current paradigms, but we should probably not go out of our way to do it here in the intramural program. Consequently, the BSC review process should take into consideration the tenuous nature of science at this unique but exciting interface.
- 16- I think that our science is best when we can describe it as a scouting exercise, a relatively small, nimble and opportunistic operation that can change on a dime, readdress priorities, reorient its goals, redirect its energies. This was one of the key recommendations of the distinguished blue ribbon panel that advise us in 1998, and I still think it applies to us today. The larger the size of individual research units, the harder it is to capture and preserve this nimbleness, this reactivity, this ability to respond and change quickly. Again, I am not proposing anything that is either radical or even new: I am simply articulating for the nth time an argument that over the last 20 years has led the intramural research programs at NIH towards smaller and more responsive individual research groups. Reasonable sized research groups are also important for another reason very close to my heart, which I would like to discuss next.

- 17- I believe it is critical that we devise the conditions necessary to nurture and help grow our junior research laboratories and that our more junior faculty feel that they are full members of our community with the same say, impute and voice as the more senior investigators. We also have to make sure that they have access to the resources they need to fulfill their full potential. Reasonable sized research groups insure that the resources are available for this critical growth and expansion. But let me pause for a second so that I can try to make this point clear: I am not talking about helping the growth of junior labs just because they are junior. No. Instead, I am proposing that we have a resource allocation system that is nimble and responsive enough to recognize merit and appropriately stimulate the growth of all of our labs. This is critical not only for the future of the IRP, but also for the future of mental health research.
- 18- I really hope that one of the essential functions of the IRP will be to serve as an incubator for extraordinary junior labs working in mental health research, a place where the best minds can find a uniquely nurturing environment where they can quickly get started and hit the ground running, a place where they can spend the most creative years of their lives while their labs expand and perhaps enter more mainstream pursuits elsewhere.
- 19- Science needs a mixture of cultures, and despite the great undeniable success of the RO1 mechanism, I think that the balance has tipped too much towards the side of research that shies away from risk, that conforms to existing paradigms and that is perceived as safe, sure bets, worthwhile explorations in familiar ground. NIH extramural research is enormously successful, but science needs a mixture of research cultures. The IRP provides a much needed balance that you and I need to protect. One way to do this is to make sure that the most creative, iconoclastic and unconventional minds find a place among us so that their voices are heard at the most productive but also perhaps, the most fragile time of their careers.
- 20- I believe that we all recognize the value of less well-defined, unconventional, risky research, but unfortunately, there are not many places for this type of science. Some established extramural investigators with multiple grants often shelter their more risky research within more conventional projects. However, because of their smaller programs, junior investigators rarely have this luxury in the extramural world! I hope our IRP will become known as a place where the best and the brightest come to do their most innovative research on mental health, a place where outstanding scientists can grow, before their ideas become more established, before these ideas are able to effectively compete in the RO1

Darwinian pool. Again, this is not a disparaging note on the extramural review program, an enormously successful experiment on the sociology of science, one that has benefited my personal science enormously. Instead, what I am saying is that we need a variety of ecosystems to take advantage of different talents and address specific challenges... The growth and success of our outstanding junior investigators is just one of several challenges that we need to address. Another unique challenge that faces mental health research is the need for close collaborations amongst a diverse group of researchers with a wide spectrum of expertise. I will discuss this challenge next.

- 21- We need to continue to provide incentives for collaborations between investigators in the IRP. This need for tightening the collaborative networks among IRP investigators was a key idea behind the creation of MAP and CGAP a few years back, and I propose to follow the spirit of these initiatives and continue this worthwhile effort. I would like to add incentives and flexibility to programs that stimulate collaborations between investigators in the IRP. I am especially interested in fostering the growth of new collaborative ideas amongst investigators in our general neuroscience community, including those within the NIMH IRP.
- 22- I also would like to provide a robust mechanism to fund new ideas, even those that may sound a little crazy initially. Jim Watson once told me that it is critical that we work on ideas before they are fully articulated, before we can easily defend them to others. By the time we can do that, it is already too late. I want to make sure we develop a mechanism that funds these not quite ready ideas, the stuff we are excited about but need to fine tune, mold, adjust, create.
- 23- With that in mind, every 4 months I will send out a general e-mail to NIMH investigators requesting new research ideas that will place a premium on novelty, unconventionality and yes, collaboration. I hope to make the application process as easy, simple and straightforward as possible. The goals are to have an open, transparent process that will require a small initial investment from you, and that would hopefully provide you with the resources to pursue your best new ideas! Again, I hope we will work together to iron out the details in this new program.
- 24- Some of you may ask, why have a more formal process, however simple, why not continue what we have now, with individuals contacting the SD's office requesting resources as needed. The rationale is simple: I would like to put in place a process that is predictable enough that faculty will be able to plan for it, fair and balanced so that all faculty have equal access to it (so as to avoid the squeaky wheels get greased phenomenon) and one that involves the community.

Again, I want to emphasize that this process will not be like a study session. I do not want to reproduce extramural programs in our intramural community. Instead, I plan to put in place a system to help me understand the science and impact of your innovative ideas. Currently, besides core facilities, the IRP spends more than 12 million in programmatic activities, that means monies that are meant for synergies between groups. I plan to use the SD's office share of these programmatic resources to provide incentives for new, collaborative research ideas.

25- It is important to look at these funds as stimuli for our ability to connect with others and reinvent our research programs and not as endowments or legacies. Again, this is by no means a new idea and it is at the very heart of the wise programmatic intentions that Steve Hyman, Bob Desimone and Tom Insel used to guide our programmatic decisions in the past. At this point it may be appropriate for our community to assess once again where we are and to plan together where we need to be in the next 10 years.

26- In this respect, I am in the process of planning a series of small intimate workshops built around the strengths in our IRP research. These workshops will allow small groups of our faculty to meet with a select list of outside experts to help charter our future. Much of this process needs to be fine tuned with you, but at this point I imagine we will have 4 workshops. In the near future I will be asking you to help me put together the themes, participant lists and formats of these meetings. These workshops could be modeled after the famous workshops run out of Cold Spring Harbor laboratory in Bambury. I happened to organize a few of them over the years and I know that this type of informal, small gathering is just the kind of event that could help us forge together a vision for our future. At the end of these workshops, we will invite some of the outside participants to form a blue ribbon panel that will then come up with a report concerning our strengths and weaknesses, the areas that we have done well, those that need more of our attention, etc.

27- In this respect, I am very excited about the creation of our newest branch, the molecular and cellular cognition branch, a small group of laboratories, including my own, that I believe will capitalize on our common interest in cognitive mechanisms including those associated with psychiatric disorders. This is part of the hiring package that I negotiated with Tom Insel, and I am looking forward to discussing this new branch with you.

- 28- I would like to emphasize that the growth that I envision should be tightly connected to our current areas of strength. The whole process that will guide our growth should be mindful of synergy, of potential interactions with current, better-established, areas. For example, take our proposed growth in molecular and cellular cognition: I believe it will be a good complement to current areas of strength in system levels approaches to cognitive function, our programs studying cognition in schizophrenia, plasticity mechanisms in depression, etc.
- 29- Before I end, I would like to share with you why I am here: I must confess that I never thought I would be the head administrator of one of the world's largest institutes with over 1200 people and a budget of nearly 160 million dollars! I always thought of myself as first and foremost a scientist, imagined continuing to work in my lab for the rest of my life, and I never thought very highly of administration as a profession: in my mind administration was part of the group of professions that I was glad other people had!
- 30- Additionally, my lab is doing very well: we have a number of new and exciting projects and even in these tough times we had funding for them. For example, in addition to a couple of RO1s that we had for a number of years, our lab had just been awarded a 10 year NIH Merit grant, we had funds from the Army, two center grants from private sources, etc. Money is never enough but we were doing OK.
- 31- This is probably the most active and successful period of my scientific career: for example, we recently had a key role in opening up a new area of memory research, the study of the molecular and cellular mechanisms underlying remote memory: we identified the first pharmacological and genetic manipulations that affect specifically remote memory, unraveled evidence for a role of specific cortical circuits in this critical but poorly understood phase of memory, developed a genetic screen that was able to identify several new remote memory mutants, etc... Additionally, as some of you know from my job seminar, based on our molecular, cellular and behavioral studies of learning deficits associated with Neurofibromatosis type I, we found a treatment that is effective in mice and are currently testing it in patients in clinical trials around the world. This is very exciting because it is the first integrated attempt to understand and treat learning disabilities, a large cluster of disorders that affects one in 20 people worldwide. So, since funding and science were great, and I never thought of myself as an administrator, why am I here?
- 32- First, you have Tom to blame! Although working with Tom was one of the key incentives that persuaded me to take this job, it was the incredible exciting

challenge of heading this great institution that slowly seduced me to accept this position! Simply put, this is the very best mental health research institute in the world, and we have a better chance than any one else to understand and solve the mental health problems that have become one of the most serious health burdens that our country faces. I do not have to tell this audience how critical and serious these problems are, or neither do I have to tell you that there is a lot of work yet to be done. To me this is the principal and most exciting challenge of modern science, and I saw an amazing opportunity to try to make a real difference here!

- 33- If we, with all of the talent, funding, clinical and basic science resources, cannot tackle this problem, who can, who will? We are not bound by grant review cycles, by shortages in funding (REAL shortages in funding), by teaching and onerous administrative duties, by the lack of physical resources, clinical infrastructure, access to patients, we have great colleagues, the best and most successful research community in the world, and we are essentially free from most of the research, clinical limitations and uncertainties that plague our colleagues out there. We are the research elite, we have more resources and freedom than anyone else and what is more, I believe that we may be on the verge of actually making inroads into the many mental health problems that have vexed science for so long!
- 34- I'm convinced that in the next 20 years neuroscientists will make the seminal discoveries that will do for mental health what the discovery of oncogenes did for cancer. Most importantly, I saw an opportunity to be here and have a role in leading this institution through these exciting times. I know that this sounds a bit grandiose, but the history of science has special periods, turning points, defining moments, after which clear changes take place that affect science and society alike. I am convinced that we are about to witness one of those moments and I know that together we can lead this institution into playing a critical and central role in the exciting changes ahead! It is clear that we are a tremendously privileged group, but with great privilege, comes great responsibility... I am confident that the future will show that we were deserving of such responsibility, and I hope to help you make it so.
- 35- Before you go, let me finish with an important tribute: I am not sure whether all of you had the opportunity to thank Su and Tom for their service to our intramural community. So, please join me in thanking these two great people!