KQED Forum with Michael Krasny
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Michael Krasny: From KQED in San Francisco I'm Michael Krasny, good morning and welcome to this morning's Forum program. University of California in San Francisco Chancellor, Sue Desmond-Hellmann, is hosting a brainstorming summit beginning this Thursday on the UCSF Mission Bay campus that will bring together top leaders in technology medicine and biopharma to discuss what has come to be known as precision medicine, a still evolving revolutionary approach to medical care characterized by a harnessing of data from the human genome and the molecular basis of disease. These in turn would be integrated on a personal and global level with environmental factors and, most controversially, patient electronic medical records. In this morning's opening Forum hour, I'm going to turn our attention and yours to precision medicine. Joining us by phone is Francis Collins, Director of the National Institute of Health, former Director of the National Human Genome Research Institute. Francis Collins, it's good to have you back with us at Forum, welcome.

Francis Collins: It's nice to be with you.

Michael Krasny: And we also want to welcome Margaret Hamburg who is Commissioner of the Food and Drug Administration and she is also with us by phone this morning. Welcome Margaret Hamburg.

Margaret Hamburg: Hello! Thank you very much. Delighted to participate.

Michael Krasny: Pleased to have you. And Susan Desmond-Hellmann is here in studio she's Chancellor of the University of California, San Francisco, former President of Product Development at Genentech, welcome.

Susan Desmond-Hellmann: Thank you.

Michael Krasny: Glad to have you back on Forum. Let's begin by maybe getting a sense of what is precision medicine and how does it differ from what used to be called personal medicine?

Susan Desmond-Hellmann: Well it, precision medicine, is really a vision of a new model of how we could transform the way patients are diagnosed and treated for disease and the goal of this new model is to make medical care predictive, preventative and precise and really the bottom line here is that we want to take advantage of this wealth of data we now have for patients. It may be genetic, it may be molecular or environmental but to use that data to better understand what causes diseases at the molecular level, precisely diagnosing patients and developing targeted therapeutics specific to sub-type. So we opted for the term precise and precision medicine because we didn't want to suggest that a unique treatment would be developed for each person, which personalized for some people does connotate but rather that each person would be treated for the particular underlying molecular driver of his or her disease and that many people would actually have the same drivers.

Michael Krasny: Can you give us an example?

Susan Desmond-Hellmann: Well, one of the examples that I'm most familiar with is breast cancer. In breast cancer, one of the types of breast cancer that can be the most serious happens in about one out of five women, and it's called Her-2 driven breast cancer. In fact, that's 20 percent of women with breast cancer. That's a lot of women, but the good news is that we can precisely target that one in five women, and just as importantly, the foreign five women who don't have that driver don't receive therapy targeted for that.

Michael Krasny: So a lot of work that has come out of Laura Esserman's, so right in your shops so to speak.

Susan Desmond-Hellmann: Absolutely, Laura Esserman is one of the thought leaders in this area, and I know you had her on last week, and I think this is a revolution and breast cancer, and one of the things it has been a driver of, for me in the precision medicine effort is having experienced this revolution in cancer, why can't we do something similar and quickly for diseases like diabetes, asthma, Alzheimer's disease so while we're furthest along in cancer, we have much further to go in many of these other disease areas.

Michael Krasny: Let me take you back, if I may, to the genesis of this--so we're talking really about an information commons really, aren't we? But it began back with an NAS report, National Academy of Science report 2011 that you and Charles Sawyers from Sloan-Kettering prepared and your co-chair, Francis Collins, who of course is on this panel this morning. The idea of the summit is to take this move forward.

Susan Desmond-Hellmann: Francis Collins was the customer for our National Research Council Report and Doctor Collins commissioned this report, and he should tell you why so I will leave that to him, but my friend Charles Sawyers who trained at UCSF, I should mention that, so we've been friends for a long time. And Charles and I were extremely pleased to co-chair this report with a wonderful committee in 2011 and what the report really wanted to do is to re-define disease. So why do we still call asthma one disease when in fact there are many different root causes?

Michael Krasny: Forgive me, but you are talking about a new taxonomy?

Susan Desmond-Hellmann: A new taxonomy? Now, a new taxonomy or classification system is a pretty bold undertaking. And yet we felt not only should such a bold undertaking happen, a new way to define disease, but in fact we should use this process of redefining disease to turn upside down how we think about delivering medicine to literally bring research to the bedside and to make a flexible system as new knowledge is created. And we started calling it amongst ourselves on the committee, a Google Map for Health, which is really thinking about your car's GPS or your car's guidance system when there's new road construction, you adapt in the same way. If we can redefine diseases based on root cause, when new knowledge comes, we can adapt.

Michael Krasny: Susan Desmond-Hellmann, again is the Chancellor of UC San Francisco. And Francis Collins is the Director of the National Institute of Health. Let's talk about your customer role here, Doctor Collins.

Francis Collins: Well, we are very pleased to be able to convene such a remarkable group of big thinkers, the Institute of Medicine did the convening but we at the NIH asked them to do a study on this whole question of a taxonomy of disease because, as we get deeper and deeper into molecular understanding of diseases, it's pretty clear that the way in which we have defined diagnoses over decades, or even centuries, don't reflect that. Cancer is maybe a most dramatic example. What we're learning about cancer is that the exact cell that develops this malignancy taps into a variety of different ways of growing when it shouldn't by activating oncogenes, or stopping the production of tumor suppressor proteins, but it doesn't matter a whole lot in terms of what you want to do for that whether this cancer arose in the colon or the breast or the prostate what matters is those molecular pathways. So our whole taxonomy, our classification, for cancer which tends to focus very heavily on the organ in which the tumor arose isn't helping us. In fact, it is getting in the way. And that can be said to go beyond cancer to other areas of medicine as well. So we wanted this group to think hard about how we could design a new taxonomy. And they went further with this then I actually expected by not just addressing that sort of end point of the problem, but how to get there, and coming up with this notion, the need for an information commons upon which you could then build a knowledge network. And ultimately, that would get you where you wanted to go in terms of precision diagnosis, precision treatment and better health outcomes.

Michael Krasny: And how does gene sequencing fit into this, especially since it is costly and not covered by insurance and really no guarantees of results? There haven't been really, if I may say so bluntly, not great gains in health outcomes.

Francis Collins: Well now, hang on a minute. I think that might have been influenced by people who expected the results of genomics to have immediate impact.

Michael Krasny: They were pretty high, I will agree with you there.

Francis Collins: Let's be clear here. It's been ten years since the completion of the Human Genome Project. The ability to do that kind of DNA and RNA analysis has absolutely revolutionized every approach that is being taken to human biology and human medicine, no question about it. Graduate students can't imagine how you ever did anything without having those genomics tools. And the costs have come down dramatically, so a complete human genome now can be derived for something in the neighborhood of six or seven thousand dollars. Compare that with the hundreds of millions ten years ago. How is this playing out in terms of clinical medicine? Well much of it is still not at the bedside, but we want to get there but certainly though in cancer, increasingly as part of research studies, and even beginning to spill out into clinical management, if you have cancer you want to have your particular tumor analyzed to find out what are the actual mutations that are driving that malignant behavior and therefore what would be the right choice of drugs for you. Sue already mentioned Herceptin as an example, but there is a long and getting longer all the time, list of this kind of targeted therapeutics based upon genomic analysis of cancers and then trying to do the match up with the best possible intervention instead of the one size fits all chemotherapy approach which is what we've traditionally done. So yeah, I would say it's not accurate to say that genomics has not transformed our approach to medicine it has not yet transformed the management of the average patient, but that's coming maybe five years from now. It's going to look very different.

Michael Krasny: What about the big question of privacy? I mean electronic medical records are available presumably where this whole project is concerned and obviously there is great concern about confidentiality.

Francis Collins: Well, there is, and maybe Sue wants to comment on that as well. That's certainly something that we at the NIH take with great seriousness, trying to balance the need to protect privacy and confidentiality but also not put barriers in the way of being able to do research that patients want us to do as well. Sometimes those barriers are most heavily objected to by patients who think that this is getting in the way of their ability to participate in a research study that might help them and other people too.

Michael Krasny: Chancellor Desmond-Hellmann?

Susan Desmond-Hellmann: Well, I do want to comment, and I would point out that just as Doctor Collins said that within an Institute of Medicine report, there was an Institute of Medicine report in 2009 and this was a report commenting on HIPAA and people hear about HIPAA, which stands for Health Insurance Portability and Accountability Act--everyone in medicine cares deeply about protecting patients' privacy--but what the IOM report pointed out is there are times when that very protection of patients impedes our ability to understand deeply what's wrong with patients, something that has consequences not just for themselves, but for society and their own families. So one of the follow-ons from participating in this project has been something that we've been trying to do to further engage patients. In fact, in concert with the summit that we're having, we are starting a public awareness campaign and we are calling it Me For You Org and this public awareness is in part to engage patients, patient advocates and their families to ask an important question about the balance between what everybody cares about which is their own privacy and confidentiality of their own data as compared to what is too infrequently discussed, which is "what are the consequences of perfect protection"? When I give the example, I like cycling and you know what this town is like for bicycle riders, there's a consequence to getting out on your bike. Well, I could stay at home and never get on my bike and I'd be perfectly safe from bike accidents. If we perfectly protect everything so that nobody could ever have access to any data, then we will literally stop innovation. So the question is, "how do we protect the data"? How do we provide security while doing something that's essential today in science, which is sharing.

Michael Krasny: You also want to galvanize the public, obviously, that's part of your intent here. You have to do something about low rates of participation in clinical trials, it's about what, five percent now?

Susan Desmond-Hellmann: It is estimated to be, for any given time, between three and five percent, a huge impediment to progress. And so I think that galvanizing the public to have them push us--and I would use the word push--push us for more sharing across investigators, across companies, across academic institutions to challenge the notion of "what are you protecting me from?" Because patients have often told that to me which I find delightful when patients challenge me, and really to ask about this, a certain call to arms, to use this data to the benefit of patients, their families and their communities.

Michael Krasny: Let me bring Commissioner Hamburg in, again who is Commissioner for the Food and Drug Administration, and we are talking about maybe redefinition of the FDA. Margaret Hamburg?

Margaret Hamburg: Well no, I think that the FDA is a critical partner as we try to advance the science that underlines precision medicine and the opportunities there and addressing the question of public confidence in this approach and the treatments that emerge. Our role is one really of helping to support the important scientific advances, to the right kinds of studies and development of evidence so that a good idea and the opportunities can actually translate into products and products that work and will make a difference in people's lives. And you know what? This really matters because we know that there are huge opportunities here in terms of the advances in genomics and other aspects of medicine and science to develop new treatments and cures and prevention so we know that there's tremendous variability in response for drugs that are commonly used. We know that there are huge opportunities to put in place new treatment strategies that really are making a difference. As Sue mentioned, the treatment of breast cancer--we see it in a number of areas--cancer in particular but other areas too, with remarkable breakthroughs based on understanding pharmacogenomics. And we know that we have to have some new approaches to really be able to get the information that we need to show what works and what doesn't. To identify those sub-populations of responders based on genetic traits. And so the FDA plays an absolutely critical role both in driving the science in the product development and in the review and approval and ongoing oversight of products that people ultimately are counting on.

Michael Krasny: I am impressed by what a shared vision this is, but I suppose, and I don't mean this in any way to be skeptical, but the scientific and regulatory structure needs to support the kind of growth you're talking about here.

Margaret Hamburg: Well, I think that's right. You know we really see this as an opportunity for academia, industry and government to work together to really harness the potential of science today and our role is to really develop some new strategies and approaches whether it's, you know, working in a collaborative way to identify, characterize, validate and then utilize genetic markers and biomarkers as we study these issues and develop new innovative clinical trial designs that let us, you know, really start to hone in on the sub-populations of responders and target therapies and do it in a way that doesn't take forever and that doesn't require huge numbers of people. You, I think, learned about the iSpy trial I suspect last week when you had Laura Esserman on your show. That kind of approach reflects I think a new flexibility on the part of the FDA as a regulator but new thinking across you know the scientific community about "how do we ask and answer critical scientific questions as we apply you know the opportunities of genomics"?

Michael Krasny: Are there going to be, in your judgment, any new and particularly innovative ways to expedite and to form studies? I mean we got all these newly discovered genes and proteins and pathways and that means new drug targets.

Margaret Hamburg: Well, I think it does and, you know, I suspect that Francis will want to speak to this issue as well, but the more we understand the underlying mechanism of disease, the more we can really identify those targets for drug development and frankly, the better the science is, the easier the task of the regulator to review and approve. And we have seen some amazing breakthrough products in recent years. Kalydeco is one that works on a small subset of patients with cystic fibrosis but it's really the first drug that treats not the symptoms of the disease, but the underlying cause, and reflects, you know, really

elegant science and works in a very targeted way. And the wonderful thing about Kalydeco is that in addition to being great science, the research was driven in many ways and fully supported by the patient community. The cystic fibrosis foundation actually helped to create an extensive patient registry and a clinical trial network so that when the drug was ready for study, the patients were ready and willing. The research went really quickly and the FDA review process actually went very quickly, a little more than three months because the data was so compelling, and the value of this drug is enormous.

Michael Krasny: If you've just joined us, we're talking about what really is tantamount to a call to arms for you the public and patients to get on board with was being called precision medicine and that came out of a 2011 National Academy of Sciences report which calls for the creation of a knowledge network of disease to help researchers and doctors share information and patient data more effectively. You can join us, in effect, I invite you to do that. We welcome your calls with questions and comments and the time to call now, our toll free number available 866-733-6786 which will work whether you're listening to us on radio internet or Sirius satellite. Your participation is invited again toll free number 866-733-6786 you can also email us forum@kqed.org or go right to our website KQED.org/forum and click on a segment or go to our Facebook page or tweet us, our Twitter handle is @kqedforum, but you are certainly welcome to participate. And Francis Collins, let me go back to your on this, we are talking about a lot of NIH work for drugs for rare and neglected diseases. You going to expand on the efforts to develop tissue banks that contain specimens with information linked to clinical outcomes?

Francis Collins: Well, let me tell you about something that's just been announced in the last week that I think is a major development in the topic we're discussing here today, and that is a new plan coming forward from the Patient-Centered Outcomes Research Institute (PCORI) this is a new organization, a nonprofit established by the Affordable Care Act and funded both through a congressional appropriations and a small tap on health care plans with a budget ,which by next year, will be in the neighborhood of half a billion dollars a year. They've just announced--and I am actually quite happy about this and have served on their board and had some hand in it--a plan to establish, over the next eighteen months, a national patient-centered clinical research network which would include something like twenty to thirty million patients with electronic health records, with appropriate attention to consent, privacy and confidentiality, all linked together in a way that allows you to do clinical research in the real world, essentially bringing research to the patients instead of asking them to come to the researchers. As another part of that, this network will also link up with what we're calling patient-powered research networks. These are organizations oftentimes focused on a particular disease like breast cancer or multiple sclerosis or multiple myeloma where patients are highly motivated. They want to be part of research, but it hasn't always been easy for them to get linked up. Putting that all together, this could be an engine for carrying out research studies that could be much faster and much cheaper than the way we currently do clinical research which requires a lot of setting up and tearing down of each individual study. Imagine, for instance, that you want to know "does it actually help outcomes to use genetic testing when you're prescribing a particular drug to choose the right dose of that drug for the individual, say a blood thinning drug like Warfarin?" And right now we're still a little unclear about that, but with this volume of individuals involved in such a network, you could imagine doing that quite quickly in a situation where you would learn results and be able to implement them in a matter of months instead of the years and years that it takes. So this is something to watch.

Michael Krasny: This is something exciting I must say. Sue Desmond-Hellmann right back to the summit, by the way, is the public invited to the summit?

Susan Desmond-Hellmann: This is a very small summit so it is not including the public.

Michael Krasny: Okay, but what do you hope will come out this? Some kind of initiative? An enterprise? What are we talking about?

Susan Desmond-Hellmann: Rather than listen to talks, which is typical of what one does at a meeting, we're spending much of the time brainstorming, really thinking about how can we accelerate--I mean you hear the enthusiasm I think from all of us--and so we're asking the question if we bring people from academia, industry, clinical patient groups, policy, regulators and our high tech around in northern

California, how come we accelerate this process? We are going to ask the question and have action items.

Michael Krasny: I'll ask the same question to our listeners because they are going to be joining us in the second half of the program and again you can do that toll free 866-733-6786 or email us forum@KQED.org or go to right to our website KQED.org/forum and click on the segment. Like to know your responses and of course any questions you have are welcome as well. You can go to our Facebook page or tweet us at our Twitter handle @KQEDForum. Chancellor Susan Desmond-Hellmann of UC San Francisco with us in the studio, Commissioner Margaret Hamburg, Commissioner of the Food and Drug Administration with us by phone and Francis Collins also with us by phone who is Director of the National Institute of Health. We'll hear from you when we return on Forum.

Michael Krasny: You're listening to Forum, I'm Michael Krasny and back in 2011, a couple years ago, a National Academy of Sciences report called for a creation of a knowledge network of disease to help researchers and doctors share information and patient data more effectively. And such a network would also allow scientists and clinicians to access data on the molecular makeup of diseases, vastly improving diagnosis and treatment. But the concept known as precision medicine is already raising ethical questions and concerns over patient privacy. We're talking to the heads of the National Institutes of Health, the Food and Drug Administration and the University of California San Francisco about precision medicine which is the subject of a two-day summit in San Francisco this week. With us, Francis Collins, the Director of the NIH, Commissioner Margaret Hamburg, Commissioner of the FDA and Susan Desmond-Hellmann, Chancellor of UCSF. We'll go right to your calls and emails here forth. I just have to ask you though Susan Desmond-Hellmann going back to the privacy issue just so people are clear on this because we did allude to it before, and I know many people are going to have serious questions. You are talking about some kind of federal agency to get involved in so what's actually the infrastructure that we are speaking of?

Susan Desmond-Hellmann: Well in the report--while we did not specify the particular federal agency that ought to be involved, but we called for policy makers and for patients and patient advocacy groups to get involved in this dialogue. Privacy is a critical issue and it needs to be seen in light of what's possible and the tradeoffs. We did think that policy has already started and the precision medicine effort should be added to the important work that is already being done.

Michael Krasny: Let's bring our listeners in. All of you have been patients at one time or will be patients in the future. We begin, Sean, with you, Good morning.

Sean: Good morning. I'm a patient with Crohn's Disease. I've had it for 14 years, and I started a network online called Crohnology, and it's a network of patients that track their health so they can contribute to research. I wanted to ask the guests how much they felt that apps on our smartphones--now that allow patients to record their symptoms--and record how the disease is affecting our body will contribute to this precision medicine research?

Michael Krasny: Good question. What do you envision, Francis Collins? With the apps?

Francis Collins: Oh it's a great question. We actually have an abbreviation for this kind of research called mHealth, as in mobile health, where you use cellphone technologies both for prevention and for management of chronic disease. There is an amazing proliferation of ideas out there. There's a summit that's held every December which started out with a few dozen people and now has thousands who come to show off their latest ideas. NIH is deeply interested in seeing how this goes but also anxious that we make sure that these apps--when they get applied do in fact improve outcomes--so there's an opportunity here and responsibility to do really good research and make sure that this is helping people and not just sort of being cool. And we think there's a lot of potential there for Crohn's Disease-- and I certainly get it because of the ability to be able to track symptoms--in response to various interventions for diabetes or hypertension where you can actually measure various body parameters and send them to your care provider over the internet in real time. A potential of much better medical management is there but we have to be sure that we're implementing it in a way where it actually works.

Michael Krasny: I want to thank Sean for the call and move right on to another caller and that's Craig. Good morning, Craig, you're on.

Craig: Good morning Michael, thanks. Great show. Listen I'm a big advocate for this kind of medicine and for evidence and science-based medicine and decision-making in general. But here's my concern. I'm hearing a lot of talk this morning from your guests particularly the NIH and the FDA officials who are really behaving as boosters for the industry. And while I'm sure there's a lot to celebrate here. It's a very exciting field, their job is different. And particularly the FDA's job. Their job is to protect the public and the nature of the drugs, on procedures and devices are safe and effective and I've heard nothing this morning about the role that the agency needs to play in being an advocate for the public to weed out bad drugs and to make sure we are protected. Because with all of the hype and all of the hoopla there will invariably be drugs and compounds that come forward that are not safe and not effective. And I want to hear more advocacy from the FDA and less booster-ism. There are plenty of drugs out there that the FDA knows that, for example, you mentioned Warfarin. There are plenty of drugs that are much less effective and much more costly that have been approved by the FDA as well as some that have been rejected. This is a profit making industry--there's billions of dollars at stake--and if the FDA is not vigilant we won't have the protection we need with the public.

Michael Krasny: Alright Craig, thank you for the call. Let me go to Commissioner Hamburg.

Margaret Hamburg: I absolutely agree with the caller and our mission is to promote and protect the health of the American people, and we take very seriously the fact that we have a responsibility to assess products for safety and efficacy. And to make a decision about whether the benefit to the patient in the actual ability to balance the benefits and the risk are fully assessed and this is a critical role that we play in precision medicine and of course beyond. I think that it's a huge challenge and in this arena because it is more complex and because there are a lot of people that are jumping to conclusions about, you know, miracle drugs and breakthroughs and making claims that aren't accurate. And that's why we have a very critical role to make sure that the genetic markers and the diagnostics actually do what they claim to do and to make sure that these therapies actually do what they are intended to do. So we take that role very seriously. I do want to mention the other side of it that by really delving more deeply into the science and really studying diseases and treatments with the benefits of more information about pharmacogenomics, there's also a safety role for patients because right now many of the drugs that are being given to patients may not be the right drug for that patient. And they may have side effects that are harmful and if we can begin to really drill down, as Sue Desmond-Hellmann said at the start of the show, to understand which sub-population within a broader diagnosis--like breast cancer--actually will benefit from a drug in which patients should not take that drug but take another drug, or which in some other cases patients might have unacceptable safety risks associated with drugs while ones won't, then we can really start to give individual patients or groups of patients the drugs that will most benefit them and will produce the least harm.

Michael Krasny: Susan Desmond-Hellmann, would you like a word in here?

Susan Desmond-Hellmann: Yeah, yeah. I think Craig raised a really important issue and Peggy just addressed one of the issues of what's the right medicine for the right patient at the right time. But take as an example breast cancer and prostate cancer--one of the things as we get a new taxonomy of disease and really understand a driver--there will be more patients with these diseases who avoid overtreatment. So the answer may be you need no treatment because you've got a slow indolent form of disease. So one of the things we took very seriously in writing this report is we talked about infrastructure of two types: an information commons that could be shared for research purposes and a very different validated knowledge network. In the U.S., that validation is the Food and Drug Administration approval that something is safe and effective. So we were careful to separate what is interesting, a theory, a possibility, information commons from what is proven and you can act on clinically. I think that's an important difference.

Michael Krasny: So something in my memory--that whole lexicon of the information super highway--I mean this is like that where you have to sift and winnow through that superhighway. Doctor Francis Collins, a question for you from a listener who says, “I’d like to know the opinion about the possibility of pharmacogenomics and if insurance providers will require a genome-wide analysis when approving drugs, especially the risky and expensive ones, while it might greatly improve the possibility of a positive outcome by refining the dosages and avoiding fatal scenarios, it would force people to reveal their genome.”

Francis Collins: That's a very sophisticated question. Pharmacogenomics is the science of trying to make better predictions about what the right dose of a particular drug should be for the individual or even, in some instances, whether that's the wrong drug for that person. As we've been able to show in a few examples like for instance the HIV drug, Abacavir, where about six or seven percent of the population will have a very serious hypersensitivity reaction to that drug, but we know exactly how to predict that and so that test is done before the drug is ever given. This is a great potential then for this kind of precision medicine. We all know that when you get a prescription even if the diagnosis was right--and it was the drug of choice--it doesn't always work and here's a chance to try to do a better job of getting a good outcome. It is the case that the ability to do DNA analysis is getting more and more inexpensive and so the potential of actually determining somebody's entire genome sequence instead of samplings bits and pieces here and there for specific purposes is starting to emerge as a cost effective approach. Because once you have that done, if it was done right, that's sort of your genome and you don't have to keep going back to it, and it's there electronically for your care provider to be able to use it in making a decision about writing a prescription . But there is this issue about how much else is going to be in such a data set and how much of that you want to know, and I think the general sense is that is private information and that is information which you should be able to make a decision about how much of it you want to look at and how much you don't. That really ought to be up to the individual. As long as we protect those kinds of principles, I think this is a very good set of developments. Again, an opportunity to practice more effective and more precise medicine.

Michael Krasny: You mentioned the sophistication of our listeners. Actually, trying to look at some emails here that would buttress that. Let me read a couple of them and then go into a couple questions that have come across the transom here by email. This is David’s, “As a practicing scientist, I am dismayed by the terrible state of genotype to phenotype data collection in humans. Academics live on publications so why not make it a precondition of publishing that any phenotype data be stored and linked to a single nuclear tied polymorphism database? One could do the same for the FDA approval in industries. The gene expression ‘omnibus’ which is implemented in the scheme for microarray results is a great resource and widely used.” A listener tweets, “let’s do comparisons between currently available stat (inaudible) frequently done by communities. It saves lives and money.” And a another writes, “are we coming to the conclusion that virtually all treatable disease has as its root cause the patient's DNA? Want to come in on that Francis Collins?

Francis Collins: Well, certainly not of the nature/nurture conversation which we’ve been having for decades, centuries-- it will continue--and both are involved. We have this power now with advances and genomics to be able to dissect out the nature part of this--at least the part that's reflected in inheritance in your DNA and also in mutations at a rise in DNA during a life particularly in the case of cancer. But that in no way means that the environmental influences are less important. A very interesting area where these all come together is what's called epigenomics where environmental influences may modify the way in which your genome is actually able to function.

Michael Krasny: This is a hot new field isn't it?

Francis Collins: It's a very hot new field and NIH is investing a lot in this area with, I think great and interesting results across the board from cancers to diabetes, rare diseases, common diseases but it is an exciting sort of molecular nexus of the gene environment interactions that we knew were important and now we have a better way to investigate them.

Michael Krasny: And question for you, if I may, Commissioner Hamburg. This is Barbara: “researchers, health care providers and health policy leaders talk a lot among themselves about the future of medicine or health care. How do we truly engage the consumer who sees the health care system as complicated, bureaucratic and unresponsive?”

Margaret Hamburg: So I think this is a question that is critically important. And one of the things that we see in our work at FDA where we are approving products for particular indications--is that just because we approve a drug and validate its use in the community--doesn't mean that it actually translates into use and even, you know, very important disease conditions like hypertension that has, you know, really very good treatment--and affordable treatments often go inadequately treated because of either failure to adopt new therapies or because of provider failure to provide the right drugs or patients not fully understanding how to effectively treat them et cetera. So that this is why we really need to work together as a community and health care providers and patients see a need to play a very active role. We’re actually trying at the FDA to bring the patient voice more into our regulatory process and actually are undertaking a big effort now--this relates to the question about Crohn’s Disease earlier--to actually use patient reported outcomes as part of the kind of tools that can be used in clinical trials in assessing the impact of drugs because we may not be using all of the right measures to assess the benefits of the drug. It's the patient's perceptions of the symptoms and the benefits of the drug that are also important to understand. It is also how patients are willing to accept risks and benefits of a given product. So it's a much more complicated system and where we're certainly trying to reach out more to the patient community in our work--and actually we just announced a new patient network to try to give patients a way to give us, you know, much more feedback and become much more engaged in what we do. But it's a very interesting moment in time that aligns of course with the goals and objectives of precision medicine.

Michael Krasny: Margaret Hamburg, again is Commissioner of the FDA. Let me go to more of your phone calls and we welcome D. Good morning, you're on the air.

D: Good morning, thank you. Speaking to the privacy issue, and I’m feeling strongly about that right now. I was a Kaiser nurse for over twenty years. I’ve been, throughout life, have had mental health issues. I have PTSD from my childhood and a variety of other things, but I have always trusted that when I went to speak to a therapist that it was completely private, completely confidential. And I have found out in the last year, without my knowledge, without my permission that that level of trust has been totally eroded and evaded. Every time I see any doctor in the medical department they have written at the top what my mental health status is and some of the doctors who have worked with me have said to me, D what is this? And I’ve gone back to mental health, trying to address it apparently between the doctors in the hospital, the medical people and the mental health people, there was a real battle and the medical people won because they felt they had a right to this.

Michael Krasny: I’m glad you raised that concern because a number of listeners have been raising concerns along similar lines. Let me just give another example Veronica who writes, “until the law guarantees everyone equal access to medical care no one should be required to share their health information. Medical information is regularly used to deny people medical care. My brother doesn't have health coverage. When he tried to pay out of pocket for a plan at Kaiser they gave it to him but excluded the condition he needed the health care for. Likewise, how can you ask everyone to share their information when not everyone can benefit because they can't pay for it? Altruism and generosity needs to go both ways. I will fight to protect the privacy of my health information until sharing it benefits not just the wealthy and privileged enough to afford real health care coverage.” Can I go to you on this Sue Desmond-Hellmann?

Susan Desmond-Hellmann: Yeah, I think that they--both the caller and the letter you just read--both articulate better than I can, how deeply personal your health information is and how much we don't want to share in the absence of benefit. So the way that I think about this is a social contract. A social contract means that I don't just give, I also receive and so as we have this dialogue I would say two things are most important. One is to be extremely clear about the benefits and because the risk is extremely clear and very frightening for many of us that we would risk having something either that just we feel private

about or could be embarrassing or we could be discriminated against. So the benefit has to be clear. It has to be justified for me, my family, society and the risks to be minimized. I also think though when we talk about this it's much too frequent that we talk about the adverse experiences, and we don't celebrate what's possible for the community and the caller or the writer also raised the issue of cost and access and I want to come back to cost and access because first UCSF is a public university, and we care deeply about this. As we talked about mHealth and mobile, one of our dreams is that in fact precision medicine could enable this kind of data sharing, this knowledge network that literally could get to low resource areas--to the underserved--because many of the impediments now are because you have to go to the mecca or research institute to get the kind of care we're talking about this morning. Whereas in fact there's a certain democratization, if we have the right decision support tools so that this could be available to many because of the generous social contract of people who did donate their information.

Michael Krasny: Well as at the risk of ... continuing with ... the negative side I'm interested in a listener tweet here and Doctor Hamburg let me go to you on this. This listener wants to know about a book by the Ben Goldacre called Bad Pharma: How Drug Companies Mislead Doctors and Harm Patients and this listener tweets, "it says the pharmaceutical industry finances most clinical trials and routinely withholds negative data."

Margaret Hamburg: Well it is, you know, certainly the case that the pharmaceutical industry supports many of the studies--the majority the studies--that are in support of product applications and you know that is, you know, the sort of of nature of our system. The FDA plays a critical role though in actually reviewing all of the data, and we do it unlike, you know, many other regulatory authorities down to the level of the patient in our data review. And, you know, we really do ask hard questions and we want to see the evidence about both the safety issues and the efficacy whether or not the drug works and, you know, the companies are expected to give us all of the relevant data, and they are also expected when we ask additional questions to provide more data. Sometimes that makes them very unhappy with us and sometimes unfortunately prolongs the time required to actually do the overall review, but we think it's absolutely essential to being able to do the kind of stuff. And quality and thorough and systematic analysis of whether the drug should be approved and moved into the marketplace. We also, I think it's important to tell the listener that in addition to reviewing the data that they provide, we also have a role in reviewing how the clinical trials are designed, making sure that the clinical trial designs both address, you know, key scientific questions but also are ethical and appropriate and undertaken in a way that supports both the right to the patient and the scientific needs.

Michael Krasny: Greg is our next caller. Greg, join us. Hi.

Greg: Hi, good morning. What a fun conversation, I feel like you all are the chorus from the same song sheet many, many of us are beginning to read from about participation in research. I lead a startup called Genomera that is doing participants driven or crowd sourced clinical trials. I'm also on on the board of an advocacy organization called Genetic Alliance which is also spurring a lot of translational research, and I want to ask your panel about themes we've been seeing in our work with participant-driven research. We're seeing in this era of participation that it is time also for a new ethic of expression in addition to protection. You know so much of the last thirty years of bioethics has been about protecting subjects in research for good reason but now we are excited that we finally have the tools that allow individuals, participants, patients as you call them, we like to call them people, to participate in research. And so the first thing I want to talk about is expression, the second one, related, is seeing a way to tap into this desire to participate and to express this by giving the individuals a very high degree of control, a very granular control about what is to be shared with whom and for what purpose, on a case by case basis rather than some kind of a blanket consent form. That's why I would love to hear the panel's thoughts.

Michael Krasny: Let me go to you first, if I may, Director Collins.

Francis Collins: It's a very appropriate and sophisticated question--and I'm aware of the work that Greg is talking about through three new groups like the Genetic Alliance-- I think that's extremely relevant and informative for the conversation we're having and for what's going to happen here at UCSF on Thursday and Friday. This notion of putting patients in a circumstance where they do have control, they are in the

driver's seat with various tools like a sort of portable consent, as one example, is a way I think to both preserve the individuals' desire to have a granular ability to decide what information is available and what's not and have that change from study to study depending on the study itself and the need for that information to be shared. That of course requires a rather sophisticated group of individuals serving as the patients, the people involved in this and groups like the Alliance and others are moving in that direction. We haven't mentioned Patients Like Me, another organization that's very involved in this space. The challenges are going to be, I think, are for those kinds of highly motivated groups to be able to share the benefits of this approach with a much broader swath of the population and get this whole ecosystem of patients and researchers--public and private--are working together in a way where everybody understands what role they can play and why this is such an amazing opportunity to make advances that are going to transform medicine.

Michael Krasny: Let me thank Greg for the call. Here's Beth who writes, "as a family nurse practitioner, I'm inspired and encouraged by this movement to improve health outcomes. As a diversity consultant for health care, what are the plans to reach out to minority populations whose trust in joining clinical trials is minimal at best. Have cultural health care consultants been invited to the upcoming summit?" Sue Desmond-Hellmann you touched on this before but maybe you can give this more illumination.

Susan Desmond-Hellmann: Let me just say two things. First of all, I really appreciate the question and and we're privileged at UCSF to have many of our faculty members with enormous expertise in care for the underserved in reaching out to populations who have not just been underserved, but have had bad experiences and there's a bad history about clinical trials with minorities. So first of all, we are tapping into that expertise here. And the second thing is, as I mentioned earlier, we are launching a public awareness campaign in concert with this summit that we're having Thursday and Friday and so if people want to go to UCSF.edu by Friday afternoon we are launching this public awareness campaign because we want the richness of all voices, not just the voices of those small number of people who will be at our OME Summit on Thursday and Friday. I think this is a critical issue and really, let's come back to the conversation this is about trust and even the presence or absence of trust with your caregiver, with researchers and at a place like UCSF where we have a medical center that has to come highest on our list is the public's trust in the process. So these are key issues that will get more discussion this week.

Michael Krasny: Well, I wish you the best of luck, and I hope you launch something that is as significant as the discussion we've had this morning.