Straight talk with…
Mahendra Rao

In October 2005, Mahendra Rao shocked the scientific community when he quit his job as head of the US National Institute on Aging's stem cell section and announced plans to go into industry. Rao felt that a ban at the time on federal funding for most human embryonic stem cell research hampered researchers in his division and prohibited him from doing the job he was hired to do. So he joined the research-tool giant Invitrogen (which later became Life Technologies) as vice president of regenerative medicine at the company's Maryland facility.

Six years on, times have changed in the field of stem cell biology: rules governing taxpayer-backed research involving embryonic stem (ES) cells have been relaxed in the US, and induced pluripotent stem (iPS) cells have come into the fray. Prompted by those changes, Rao opted to return to the US National Institutes of Health (NIH) in August to head the new Intramural Center for Regenerative Medicine. The $52 million center was launched in early 2010 by the agency to develop new therapies using stem cell approaches. With a heightened focus at the NIH on translational medicine, **Elie Dolgin** spoke to Rao to find out how he plans to turn stem cell discoveries into cell-based therapies.

Why did you want to return to the NIH?

I'm an academic at heart. So, when the policy changed and it became a lot more feasible to work with embryonic stem cells in academia—in particular within the NIH system—and when I heard that they were recruiting for a position where I could really make a difference to the community at large, it seemed to be an exciting opportunity. That's what really made me take the plunge.

Are you worried that the new center's efforts could be derailed given the recent litigation surrounding the NIH's stem cell policy?

I have to admit that was one of concerns when I took the job. The problem is that there's no way to predict the future. But there's a commitment from the NIH that this [new center] will be at least a five- to seven-year experiment. Maybe in two years' time policies will change or the Supreme Court will rule differently, but we will still have a path to get things done.

What sets the regenerative medicine center apart from other academic institutes dedicated to stem cell technologies?

Neither in size nor in scientific quality could one say that this center is any different from some of the other more established centers. However, there are two crucial differences. One, this is a government center, and the government's mandate is different than that at any other center. So, that's a really important distinction. The second thing is that the center doesn't function in isolation. It's what's around it that makes it very useful, and what's around it is a whole lot of infrastructure and investment that's gone in to building up a way to take things from the bench to the bedside. There are two really important pieces to that in the NIH Chemical Genomics Center and the NIH Clinical Center. Both of them are widely recognized, state-of-the-art, best-in-class type of centers.

Can you give me an example of how that infrastructure can help turn stem cell discoveries into therapies?

There are certain orphan disorders, for example, where we could generate the appropriate cell lines—iPS cell lines or lines where we perform a rescue with appropriate engineering techniques. We can either use those lines for screening in the Chemical Genomics Center, or we can use repaired lines that have been manufactured in a GMP [good manufacturing practice] environment—which is also available within the NIH—and then use the Clinical Center to perform the initial [human clinical] studies.

The new intramural center will be administered by the National Institute of Arthritis and Musculoskeletal and Skin Diseases. Is that where it will mostly operate?

I don't want to house everything in one institute. What I want to do is make sure we can seed the appropriate technology across the NIH and across sister organizations in the [Department of] Health and Human Services, including the Food and Drug Administration and the National Institute of Standards and Technology.

How will the center work with the new National Center for Advancing Translational Sciences once it's up and running?

It will be complementary. Initially, the National Center for Advancing Translational Sciences will be focused on small molecules to discover novel drugs, so we will be able to provide the primary cells that they may need for screening, we will be able to provide the right reporter systems and we will be able to help develop appropriate assays using stem cells.

Are you planning any other initiatives?

A pet peeve of mine is that there's a big lack of standards in the [stem cell] community. There are no off-the-shelf control experiments that you can use to really test whatever you're doing with your favorite cell line. Part of the reason for that is because there's been no central authority that has sufficient standing to take an unbiased leadership role. Companies can't do it; it has to be the government. My first effort is going to be to make sure there is some kind of standard [test] available, which is widely available, which doesn't have any sort of patent issues, which can be distributed easily, which is available at a relative low cost and which will be a control for people when they're comparing all these different lines that they're generating. This has become even more important, because the absolute number of iPS cell lines is way larger than the number of ES cell lines.