AN AUDIENCE WITH…

Alan Trounson


CIRM

Since the California Institute for Regenerative Medicine (CIRM) was established in 2004, it has awarded nearly US$1.5 billion to foster stem cell research. As part of an institutional shift from basic to clinical development, however, it is now planning to spend more on translational research and is rolling out a $30 million Strategic Partnership Awards Initiative aimed at attracting biotech and pharmaceutical firms that can complete early-stage trials within the next 4 years. Alan Trounson, President of CIRM, discusses the latest initiative and the status of stem cell research with **Asher Mullard**.

What is the goal of your new initiative?

The first part of our funding strategy was really about building up basic stem cell research capacity and creating an environment that could drive a therapeutic pipeline. Then we started focusing on improving our translational capabilities to make sure that any findings we funded could be used to find candidates for clinical trials. We have already invested around US$400 million on translational sciences, and with the recent revision of our strategic plan we expect to focus even more effort and funding on translational research and clinical trial projects in the next 5 years. We also feel that now is the time to really engage our clinical aspirations, and so with these new strategic partnership awards we want the winners to complete early-stage clinical trials within 4 years.

We are looking really for companies with some maturity, that have enough financial stability for us to think that they can complete clinical development and provide patients with access to novel therapies. And because we feel that having skin in the game really does make a difference, we will be bringing them in on a genuine partnering basis — they, or a venture partner, have to provide at least 50% of the capital. Our main interest is on stem cells as therapeutics, but we are also allowing applications for products that will target cancer stem cells or shift a stem cell population into a regenerative mode.

By engaging with the companies that are likely to fill this role — and that have their own experience with trials and can provide guidance on clinical trial design — they can be sure they won't have to repeat critical components of the studies again if they want to take projects over.

[Full details of the initiative can be accessed at go.nature.com/GWUMTM.]

Is $30 million enough to catalyse clinical activity?

We have had a lot of preliminary discussions with prospective applicants, including major biotech and pharmaceutical companies. And although the board gave us $30 million, which is really up to $10 million for three projects, it has the capability to provide additional funding if we say that there are more really good applications.

How many therapeutics have your previous awards helped drive into clinical trials so far?

The only trial of a stem cell therapeutic that we specifically funded was Geron's GRNOPC1 [which has since been discontinued]. But there are clinical trials of small-molecule drugs that have come out of work that we funded. Stem cell assays were used to find genes of interest for certain diseases, and antagonists or agonists with activity in these pathways were then identified for further development. There are three or four of these — including Janus kinase 2 (JAK2) inhibitors and Notch inhibitors — that have gone into mid-stage trials with pharmaceutical companies.

What has been the fallout of Geron's decision not to pursue stem cell research?

There hasn't really been much. I think it is still in negotiations with other companies for the project and the intellectual property, and so we are still hoping that the work will be picked up. And it doesn't seem to have had any real effect on pharma's or biotech's interest in stem cells. I think it was taken for what it was: a financial decision to focus on one area of research rather than another because the company couldn't raise sufficient money to go for both. And that happens a lot in this industry.

What are the major regulatory sticking points for stem cell work at the moment?

In dealing with cells that we introduce into the body and that are likely to multiply, the issue of tracking where the cells are and how they migrate is difficult, especially in large animals such as humans. We are also still struggling with understanding the stability of stem cells when they expand, how well they retain their integrity and how much deviation is reasonable to accept. If only a few cells change, does that really have any influence?

From maybe a more basic biological standpoint, we are still trying to figure out whether stem cell therapeutics work in animals by inducing endogenous populations to respond over longer periods of time. What are the mechanisms by which cells seem to have their effects? It's a little hard to understand, for example, how mesenchymal stem cells can have an influence given that they are gone within a few weeks. We are trying to figure out these kinds of things because without an understanding of the mechanisms of action it is harder to improve a therapeutic or protect against adverse effects.

Where is the field at in terms of developing cells as drug discovery tools?

We've always expected the field to deliver drug discovery tools ahead of stem cell therapeutics. If we can use induced pluripotent stem cells to build disease models in dishes that can be used for high-throughput screening, for example, these should be ideal for finding drugs that can prevent certain phenotypes. And there is a lot of work in this area. But I actually haven't yet seen new drugs evolve from these studies. I would have expected them to come more quickly.