Irv Weissman

An authority on hematopoiesis talks about the difficulties encountered in commercializing stem cell therapies.

Irv Weissman is Virginia and D.K. Ludwig Professor for Clinical Investigation and Cancer Research and Director of the Institute for Stem Cell Biology and Regenerative Medicine at the Stanford University Medical School. The first to isolate any stem cell, he has pioneered investigation of the hematopoietic system.

What challenges have you faced in translating your research to the clinic?

Irv Weissman: Shortly after 1988, when we isolated the mouse hematopoietic stem cell (HSC) and figured out how to make a mouse that had a human blood-forming and immune system, Mike McCune and I formed Systemix. Within two-and-a-half years we had isolated the human HSC. When we were about to go public in 1991, we started getting inquiries from big pharma. Soon after, Sandoz bought 60% of Systemix, and we started moving toward clinical trials. We wanted to isolate cancer-free HSCs from patients with breast cancer and non-Hodgkin's lymphoma and transplant them back to patients after very high-dose chemotherapy, rather than using bone marrow or mobilized blood cells, which are contaminated with cancer cells. We began clinical trials in 1996, but in that year Sandoz merged with Ciba to form Novartis, and Novartis made a business decision to shut down the trials. They were not going to be a stem cell isolation company for service. So the lesson with the first company was that the culture of big pharma isn't the culture of cell therapies. But the science was right. Fourteen years after the first patient got a stem cell transplant, we have just summarized our breast cancer experience, and I'll just say that the outcomes in our small number of patients have exceeded expectations. If it were a small molecule, it would be out there.

What about the two other companies you founded?

IW: Cellerant is still alive, but they don't do HSCs because they never got the money for a trial. At Cellerant I wanted to repeat the breast cancer trials with more patients but the length of time required wasn't acceptable to the VC [venture capitalist] investors. I also wanted to do SCID [severe combined immunodeficiency] with HLA [human leukocyte antigen]-matched sibling donors, or the mother as an HSC donor. Since the mid-50s, we knew that donor T cells, a component of bone marrow and blood, mediate an immune reaction against the host. But with pure HSCs there are no T cells, and there was no graft-versus-host disease (GvHD). So if you were lucky enough to cure SCID, you might be able to do sickle cell, thalassemia, and then diseases like diabetes, multiple sclerosis, lupus, all of which we've shown in mouse models are diseases of blood-forming cells that we can cure with HSCs from a disease-resistant donor. We had all of that in the mid-90s. When I proposed to the board at Cellerant that we do SCID first, the CEO blocked it, saying there's not enough money in SCID patients. I said, no, but we can do a world of good, providing HSCs without GvHD. I couldn't convince them. So this was a second lesson: if you try to do a phase 1 trial with VC backers and CEOs who control your destiny and whose function it is to make a profit in five years, the timelines are wrong.

Rusty Gage, David Anderson and I formed Stem Cells to look for stem cells outside the blood system, because with HSCs we could induce tolerance in mice to any organ transplant from the same donor, and it made sense that it would also induce tolerance to tissue or organ stem cells from the same donor. The company isolated human brain stem cells and worked on spinal cord injury and Batten disease. But the clinical trial for Batten disease, which is fatal in childhood, was turned down at a prominent medical center by its IRB [institutional review board] because it involved children, even though no adult exists with the disease. So Stem Cells did phase 1 trials elsewhere and now has approval to enroll early-stage patients. The point is that you don't learn about these kinds of barriers until you're actually trying to open a new field, the field of regenerative medicine with tissue-appropriate stem cell transplants. No current pharmaceutical company, no group of VCs know what the field of stem cell transplants is, and when they apply their culture and timelines and business parameters, you don't go forward.

If you were to start a company today, what would you do differently?

IW: I wouldn't start a company now unless I had a pretty high degree of control and, much more importantly, had progressed in the university through at least phase 1/2 trials. We have a CIRM [California Institute for Regenerative Medicine] disease team grant to take an anti-CD47 antibody to clinical trials in acute myelogenous leukemia [AML]. We are collaborating with the UK AML trials group, who have taken advantage of universal healthcare to organize clinical trials. In the old days we would have formed a company, but now neither we nor our university will grant licenses to form a company until we get through phase 1/2 trials. Because CIRM and the UK fund through phase 1, we are taking the place of a biotech. We've put together a great team that is moving these efforts forward.

But I've made mistakes trying to form a company, because I'm a scientist and a doctor in an institution that is trying to save people. Unfortunately, the VCs want a profit in five years, which excludes most of what I want to do. So how are we going to get around this dilemma, when the hospital and the medical school want to save lives, and the companies want to make a profit? Something new is needed. I can think of lots of reasonable business models that would charge appropriately for stem cell transplants that regenerate healthy tissues for life. For example, if Systemix had succeeded with its early plan to establish HSC separation units, it would have done this next to a hospital. So why not partner with the hospital to establish and run such units? The hospital and medical school could experiment with how to set up an efficient HSC isolation and transplant and clinical care service, and how to resolve issues of compensation. Should you do it in an outpatient setting? Should you have hospice units? As they explore these issues, I think a model will emerge. Somebody will then fund it when they see they can make money. I think it will happen first at places that have the whole collection of resources, and that will build the model.