Harvard's Springer gets $51.5M from pharmas, others, from latest startup

Ben Fidler | June 30, 2016

Xconomy Boston — Inside our bodies, our cells move around, communicate, form new tissue, and heal wounds with the help of proteins called integrins. But when disease occurs, integrins get the wrong cues and do damage—they might help tumors grow, or promote inflammation or scarring inside the body. Several drugs to block bad integrin behavior and treat a range of maladies have come to market. But they have a record of going awry, too, with sometimes lethal side effects.

A key scientist involved in integrin research, Harvard University immunologist Tim Springer, is spinning out a biotech startup to develop a new generation of integrin-blocking drugs—pills instead of antibody-based injections—that he says will benefit from "a complete understanding" of these complex molecules.

The venture arms of GlaxoSmithKline, Pfizer, and AbbVie are leading a huge $51.5 million Series A to back Waltham, MA-based Morphic Therapeutics, a startup out of Springer's Harvard lab.

"I've been working on [integrins] since the early 1980s, and I'd say we only have complete understanding of how they work in the last year," says Springer (pictured), who has helped start several Boston-area companies, among them LeukoSite (sold to Millennium Pharmaceuticals for $635 million in 1999) and Scholar Rock.

Integrins are a family of proteins on the surface of cells that are involved in many biological processes, from blood clotting to cell migration. They help cells travel from one location to another to form tissues. Springer authored a number of peer-reviewed papers (here are twoexamples) which helped explain the function and activity of integrins.

The biological importance of integrins made them a drug target. They help traffic immune cells from one place to another, for instance, and when that process goes haywire the result can be the inflammation seen in maladies like inflammatory bowel disease. Springer formed LeukoSite in 1993, and that company ended up

developing an antibody drug for IBD, vedolizumab (Entyvio), that was eventually approved in 2014 and is now owned by Takeda Pharmaceutical. Other integrin-blocking drugs have been approved as well, such as natalizumab (Tysabri, for multiple sclerosis), eptifibatide (Integrillin, blood thinner), and alemtuzumab (Campath, leukemia). All of the approved integrin blockers are antibodies that have to be infused at hospitals and clinics. And some of them, like natalizumab, are linked to potentially deadly side effects.

There have been failures as well, among them a wave of blood thinning drugs tested more than a decade ago. These drugs, like sibrafiban, lotrafiban, and orbofiban, were found to actually increase the risk of strokes and heart attacks rather than prevent them, and they never came to market.

"They were abysmal failures," says Klaus Ley, an immunology professor at the La Jolla Institute for Allergy & Immunology, who isn't associated with Morphic. "They actually killed people."

Despite those dangers, the promise of targeting integrins has spurred Morphic, and another recently launched startup, to pursue improvements. Like Morphic, Pliant Therapeutics of Redwood City, CA, is developing integrin inhibitor pills instead of antibodies. Based on the work of scientists at UCSF, Pliant launched in February with $45 million from Third Rock Ventures.

But Morphic CEO Praveen Tipirneni, a former Cubist Pharmaceuticals executive, says while Pliant is focused on fibrosis, Morphic aims to treat other disorders like IBD and cancer as well.

Springer says the side effects in previous efforts were due to the ability of integrins to morph into different shapes depending on their functions. The failed blood thinning drugs binded to their integrin targets, Springer says, but when they wore off, they left those integrins locked into a different shape—one that led to the unintended side effects. Thanks in part to better structural biology tools, says Springer, "we think we understand the problem."

That's yet to be proven. Springer isn't disclosing Morphic's discoveries, and the company has yet to publish research in peer-reviewed journals about its work. Tipirneni estimates that Morphic is a few years away from testing drugs in clinical trials.

Ley, who published in January an article in Nature Drug Discovery about integrin drugs, cautions there's still much debate amongst scientists about how integrins work. "I don't think we fully know," Ley says. "So as good as [Morphic's plan] sounds, it is still a risky proposition."

The integrin alpha 4 beta 7, the target of vedolizumab, is on Morphic's list, which intrigues Ley. Vedolizumab generated about $530 million in sales last year, and Takeda has projected that it may top out at north of $2 billion a year.

"If they can make an a4b7 inhibitor that works as good as an antibody, power to them," he says. "But I want to see the evidence."

Morphic was formed by Polaris Partners and Leukon Investments in 2015. Some others investing in Morphic's Series A include Schrödinger and ShangPharma Investment Group. The company has 15 employees and is based in BioHub, a complex owned by AstraZeneca in Waltham.