An autoimmune upstart turns PD-L1 around to blaze a new approach to diabetes, multiple sclerosis

by JOHN CARROLL — on September 24, 2018 06:00 PM EDT

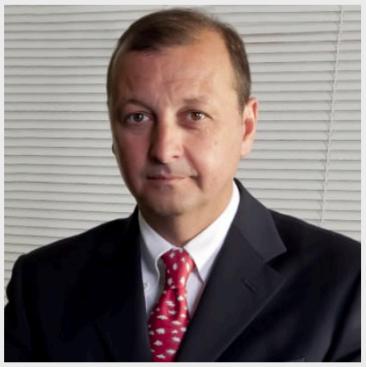
PD-L1 has become one of the most familiar targets in the global cancer research world, a key player in mediating a coordinated immune system assault on cancer cells.

But what if you could also turn it around, use elevated PD-L1 to muffle an autoimmune response by T cells, hitting the brakes on the immune system and avoiding an assault on healthy tissue — rather than taking your foot off the brake and targeting cancerous cells?

A prominent Italian investigator named Paolo Fiorina based, in part, at Boston Children's put that idea to the test in PD-L1 deficient mice last year — adapting blood stem cells — and found that it could coordinate an effective reversal of hyperglycemia and Type 1 diabetes, the inherited form of the disease in which the immune system attacks insulin-producing cells in the pancreas.

He published his work in *Science Translational Medicine.*

In this case, Fiorina and his team used different approaches, one of which involved delivering a gene with a healthy copy of PD-L1 into stem cells to reengineer them for a new role playing defense. Now, they're using that successful animal experiment to start a new biotech — dubbed Altheia Science — which will look to try it in humans in about 2.5 to 3 years.



Paolo Rizzardi

This isn't the first time diabetes has been cured in mice. Humans still face plenty of obstacles, so some healthy skepticism is always warranted. But Paolo Rizzardi, who heads up the Milan-based tech transfer group AurorA-TT, is a believer.

Rizzardi has just lined up an $11 million launch round to complete the translational work needed to develop an effective, commercially viable, gene therapy approach that could adapt patient stem cells to do the work with PD-L1.

"I like the idea," Rizzardi tells me. "The concept was quite simple," where the scientists recognized a common biologic mechanism that worked across multiple indications.

And they are by no means limiting the approach to diabetes. Altheia's team is working on the belief that multiple sclerosis should be an early focus at the company. And rheumatoid arthritis as well as other autoimmune conditions could be added later.

Diabetes, MS, rheumatoid arthritis; these are all diseases with major populations. But Rizzardi believes that the experts in the field are giving birth to generation 2.0 of gene therapy, which can be adapted to large numbers with an economy of scale.

Milan, which was home to the gene therapy work that GlaxoSmithKline recently spun out to Orchard, has a broad group of experts in gene therapy operating at the San Raffaele Scientific Institute. But with gene therapy expertise lined up along the East Coast, a group of potential partners along with investors who are happy to back preclinical work like this, Rizzardi felt the 3-member team doing the initial work should have an office in New York.

Some private investors joined the Rovati family's Fidim/Rottapharm Biotech group in providing the first $11 million, which could range up to $17 million as the project develops.

"These numbers are not that fascinating for the US," Rizzardi readily concedes, but they are "pretty good" for Europe. And it's enough for a lean-and-mean team to get through the proof-of-concept stage for this, when they'll know if they have something that could completely disrupt major markets.

That's pretty good, too.