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First human Crispr trial is a go, but don’t ask about the IP

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Yesterday’s near-unanimous expert vote brings the West’s first human trial to use the Crispr gene-editing technique a step closer to reality. But the riddle of who from a complex web of interested parties stands to benefit, and who precisely will own any resulting intellectual property, remains unanswered for now.

Still, the proceedings will have reminded investors, many of whom have thrown huge amounts of cash at Crispr over the past year, that the technology itself has no IP protection, and that its lab use is widespread. This might explain why Editas Medicine, a company specifically focusing on Crispr, fell 7% yesterday.

Another reason is that at one point Editas was thought to be on track to become first to start a clinical trial involving Crispr (*Crisp financing and partnering in gene editing space, September 2, 2015*). Based on yesterday’s vote, at a meeting of the NIH’s recombinant DNA advisory committee, this honour will likely belong to Dr Carl June’s group at the University of Pennsylvania.

Clear support

The expert panel made it clear that it was not giving the study the go-ahead – that was the job of the FDA under an IND application – but its support was evident: except for one abstention all panellists voted in favour.

The safety trial, in up to 15 patients with myeloma, melanoma and sarcoma, proposes to test autologous T cells with an engineered T-cell receptor (TCR) against the NY-ESO-1 antigen. It is to be sponsored by Penn, with Dr June as advisor, and will also include centres at MD Anderson and University of California, San Francisco.

It would not be the first to target NY-ESO-1 with an engineered TCR, but what makes it interesting is the use of Crispr to edit out the T cells’ immune checkpoint PD-1, as well as their endogenous TCRs. The point of the former is clear – to release a potential brake on immune system activity – but the latter less so.

Editing out endogenous TCRs, using Talen nucleases rather than Crispr, forms the basis of Cellectis’s approach to CAR-T, though here it is geared towards eliminating the potential for graft-versus-host disease in an allogeneic product.

As the Penn approach is autologous the risk of GvHD would normally not arise, but it might do with PD1 also edited out. And the panellists suggested another reason for deleting endogenous TCRs: to avoid the risk of subunit mispairing caused by a single T cell having TCRs directed at two different antigens.

It is interesting that rival studies of engineered TCRs, including those run by the NCI, Juno, Adaptimmune and University College London, have not sought to edit out endogenous TCRs.

Penn’s future use of Crispr as the basis for an allogeneic adoptive cell therapy to rival Cellectis remains an intriguing possibility, and preclinical work, over which Novartis will presumably have a claim, is already under way. As for problems, Dr June accepted that T cells without PD-1 might exhibit relatively short persistence.

Financial conflicts

But Dr June became cagey when asked about his financial conflicts of interest, saying only that these would become clear if and when the study was allowed to start.

His work is licensed to Novartis and Thermo Fisher (via its Life Technologies business, a partner of Adaptimmune), and he is also behind the Penn spinout Tmunity Therapeutics. But he told the panel that the Crispr study had no relationship to Novartis – that deal covers CAR-T projects active as at 2012 – or Life Technologies.

This suggests that patents arising out of it might be the property of Penn or Tmunity, with Dr June named as co-inventor. A further twist is that funding for the study appears to be coming from the tech entrepreneur Sean Parker, under one of the various “cancer moonshot” programmes that have sprung up of late.

Since Mr Parker's $250m commitment to this effort has been described as a gift his personal claim on any discoveries might be limited. But the various competing interests must already have the lawyers rubbing their hands with glee.

EP Vantage has published a broad overview of the current opportunities and risks in the CAR-T space. A free copy of the report is available by download.

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