Predicting who might benefit from T cell immunotherapy in type 1 diabetes

The immune system varies enormously from person to person. This is evident in people's response to the current coronavirus – some clear the virus without so much as a sniffle; others mount a vigorous immune response that can cause damage.

The same is true when it comes to drugs that target the immune system - one immunotherapy may work well in one person and not at all in another. **Understanding which drug to use in which person is critical**.

Type 1 diabetes is caused by immune cells called T cells, and an immunotherapy that suppresses T cells (CTLA-4-Ig, Abatacept) was tested in people newly diagnosed with this condition. It delayed diabetes progression by about 9.6 months. At first glance this does not sound very impressive – but a closer look at the data shows some people had no deterioration of pancreas function for the whole 2-year trial period, while others deteriorated as quickly as those on placebo. **If we could predict in advance who would respond well, CTLA-4-Ig could potentially be a useful therapy**.

My team, in collaboration with researchers from Kings College London and AstraZeneca, looked at blood samples from people who took part in this trial. These precious samples had been carefully frozen and stored for years by TrialNet, a large international type 1 diabetes research consortium.

Our analysis provided new information about which type of T cells are targeted by this therapy. It showed that **the drug strongly suppressed Follicular helper T cells**, cells my group had previously found were involved in type 1 diabetes.

Surprisingly, it suggested that **analysing Follicular helper T cells before treatment could provide information on how a person would respond to this drug**. We confirmed this via an independent approach, using "machine learning" to analyse the samples with less bias (without specifying in advance which T cells we were interested in).

We now need to test this approach in more people to see whether it's a useful way to predict who should be treated with this drug. If it holds up, **it could reignite interest in a drug we thought might not be effective in type 1 diabetes**. New improved versions of CTLA-4-Ig drugs are also being developed and it will be particularly exciting to see if our biomarker approach is applicable to these.

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Link to the publication in Nature Immunology here: https://rdcu.be/b53pZ

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