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Takeda takes a plunge into the fringes of cell therapy

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Takeda jumped enthusiastically into a very early space in the cell therapy world yesterday, joining a $100m funding round for a UK start-up working with gamma-delta T cells. The partners ultimately hope to develop allogeneic immunotherapies to treat cancers and autoinflammatory diseases.

The Japanese company joined the venture firm Abingworth to back Gammadelta Therapeutics – which claims to have technology that for the first time can isolate large numbers of high-quality, tissue-resident gamma-delta T cells. These have important advantages over those found in blood, chief executive Paolo Paoletti tells *EP Vantage*, though he admits that work is a long way from the clinic.

Gamma-delta T cells, along with B cells and alpha-beta T cells, form part of the adaptive immune system. The inability to extract them in a reliable way has held back research, and as a result the mechanisms through which they work, and ultimately their full role, remain largely unknown.

Their potential is less in doubt: as well as being resident in many human tissues and blood, they can detect generic signals of dysfunction and respond apparently without the need of an antigen trigger. This means that they can recognise several tumour types but not be susceptible to antigen downregulation.

The prospect of allogeneic therapies is raised because gamma-delta T-cell recognition does not rely on antigen being presented on the major histocompatibility complex, and thus they might not cause alloreactivity. However, it is not clear how they recognise their targets.

Mr Paoletti stresses that the possibility of developing an off-the-shelf product remains to be proven, however. “The first things we are committed to do are optimise the process of isolation and replication of the cells, and go to clinic with autologous cell therapy,” he says.

Whether any therapy will be genetically modified, in the way that CAR-T therapies have been, for example, is something they are thinking about, says Raj Mehta, the company's head of IP and business development.

“It’s the logical next step but it’s too early say,” he says.

Tissue science

Gammadelta was founded last year by Abingworth and Cancer Research Technology to exploit work by Professor Adrian Hayday and Dr Oliver Nussbaumer at King’s College London and the Francis Crick Institute – the scientific founders of the company.

The ability to isolate these T cells from the tissue rather than the blood presents a unique opportunity, Mr Paoletti says, because much of the work with gamma-delta to date has focused on the blood-resident form. However, because these are not biologically primed to act outside the blood, the company believes that tissue-resident T cells could be more suitable for targeting solid tumours.

“That possibility gives us a starting point for a platform for research, and the agreement with Takeda will allow us in parallel to explore the biology from a different point of view,” he says.

Alongside working to take the cells into the clinic, he says the company will be further researching the biology, trying to discover how they behave differently to alpha beta T cells, and trying to work out what stops these cells from monitoring cancers, allowing them to grow and proliferate. Growing the cells ex-vivo in a manner that avoids T cell exhaustion will also be a priority.

In return for its contribution to the $100m funding round, the deal gives Takeda an equity stake and the exclusive right to purchase the company within four years. Further financial details were not disclosed and the Japanese company has no rights to any IP as the deal stands.

Testing the hypothesis

While it is undeniably very early stage, Gammadelta is not alone in the commercial world operating in this space – private European biotechs Gadeta and Lymphact have also conducted work.

The Belgian Gadeta seems to be the most active here – it has a therapy called TEG001 approaching the clinic that

comprises a gamma-delta derived T-cell receptor expressed on a conventional T cell.

These approaches both appear to be based on blood-resident gamma-delta T cells.

“With tissue-resident [gamma-delta], people just don’t know what they do, what they interact with, what is their role. But what is exciting is that we do know they don’t behave like alpha-beta T cells, there’s something different going on here,” says Mr Mehta.

“So we may have another weapon to fight cancer when the biology has been completely understood,” Mr Paoletti says.

That hypothesis will take some time to test. But with substantial R&D funding secured, Gammadelta is well tooled to get started.

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