

The therapeutic potential of anti-CD25 antibodies

CD? Did you say CD?

In immunology, it is really useful to identify the different types of leukocytes within a sample. But distinguishing leukocytes according to their morphological or functional characteristics is not an easy job.

However, scientists discovered that leukocytes express on their surface a large number of molecules which can be used as markers for their specific identification. The concept of cell immunophenotypic identification was born.

This identification is based on the detection of these membrane markers using monoclonal antibodies followed by analysis in flow cytometry. Since 1982, these markers have been designated according to the cluster of differentiation nomenclature or CD, followed by a number. And the combination of present (CD+) and absent (CD-) markers allows the identification of the state of maturation of the cells.

CD25: a difficult youth

As early as February 1988, a Diaclone monoclonal antibody anti-CD25, the B-B10 clone (now known as Inolimomab or Leukotac) was used *in vivo* to treat a severe case of acute Graft versus Host disease.

CD25, also known as the interleukin-2 high-affinity receptor alpha chain (IL-2R α), has been observed on activated B, T lymphocytes and macrophages. Alternative names for the antigen are often used: IDDM10, IL2R, TCGFR, p55 or Tac.

Inhibiting the binding of IL-2 to CD25, anti-CD25 monoclonal antibodies were first developed as therapeutic agents to treat organ transplant rejection (Basilixumab, a Novartis chimeric mouse-human CD25 antibody, 1998 approval) and multiple sclerosis (Daclizumab, a Biogen humanized CD25 antibody, 1997 approval then withdrawn due to safety issues).

But since - as CD25 is constitutively and highly expressed on Treg cells - this marker was rapidly investigated as a potential target for inflammatory, auto-immune and cancer immunotherapies.

In 2013, ADC Therapeutics and Genmab partnered to develop a new antibody format, an Antibody Drug Conjugate (ADC), offering anti-CD25 a second life, this time in the oncology field. Camidanlumab was in the pipeline.

But tackling cancer with a Treg cell depletion tactic - like companies such as Hifibio Therapeutics have promoted since the beginning - was quite a contested therapy approach. So far, clinical trials have proven these strategies wrong. Until recently...

CD25: an oncology boat with the wind in its sails

- Anne Goubier and her team at Tusk Therapeutics made the headlines when they showed that a blockade of IL-2 signalling limits Teff responses. They consequently decided to develop a new version of anti-CD25 antibody that does not block the IL-2 signalling in order to deplete Treg and stimulate Teff at the same time. This promising antibody is going to be tested in cancer. But not by Tusk itself. At the end of 2018, Roche paid €70 million (\$81 million) upfront to buy Tusk Therapeutics and in doing so getting complete control on this promising anti-CD25 antibody.
- In 2019, NIH conjugated a near infrared silica-phthalocyanine dye to a monoclonal antibody. This process led to a new cell-specific cancer therapy that locally kills specific cells in the tumour. In this particular context, comparing full length anti-CD25 antibody with its fragment version, it appears that the absence of the Fc portion leads to faster clearance and therefore promotes a superior activated T cell response in tumours.
- January 2020, Alderaan Biotechnology, a preclinical company focused on the development of anti-CD25 monoclonal antibodies for the treatment of cancer, announced that it raised €18.5 million in a Series A financing.

And any recent updates on dysregulated inflammatory response?

In 2019, a Japanese team from Kyoto University and Asahi Kasei Corporation paved the way to a new approach. Apheresis is a technique that makes it possible to take, via a machine, one or more blood components depending on the needs. The team demonstrated that the removal of Tregs from septic patients by apheresis was a good relief solution. However, the removal of cells other than Tregs caused the adverse effect of lowering the immune response against microbes. So, they decided to immobilise an anti-CD25 antibody on a polyethylene fibre to specifically remove Tregs without impacting the other components of PBMCs.

We might agree that it is not a definitive therapeutic solution like those described above for cancer, but this nice creativity - combining immunoaffinity purification with the apheresis technique - must be applauded and encouraged!

Do you have a current project on CD25? Do you want to specifically target Treg?

Diaclone has developed several anti-CD25 monoclonal antibodies for your research:

Clone **B-B10**: anti-IL2Ra, a biologically active mAb

Clone **B-F2**: anti-IL2Ra

Clone **B-G3**: anti-IL2Ra

CD25 ELISA Pair:

Clone **B-G3**: Capture antibody

Clone **B-F2**: Revelation antibody