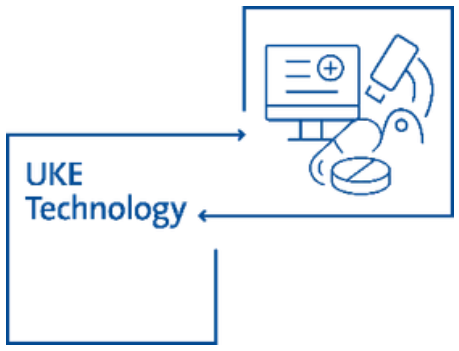
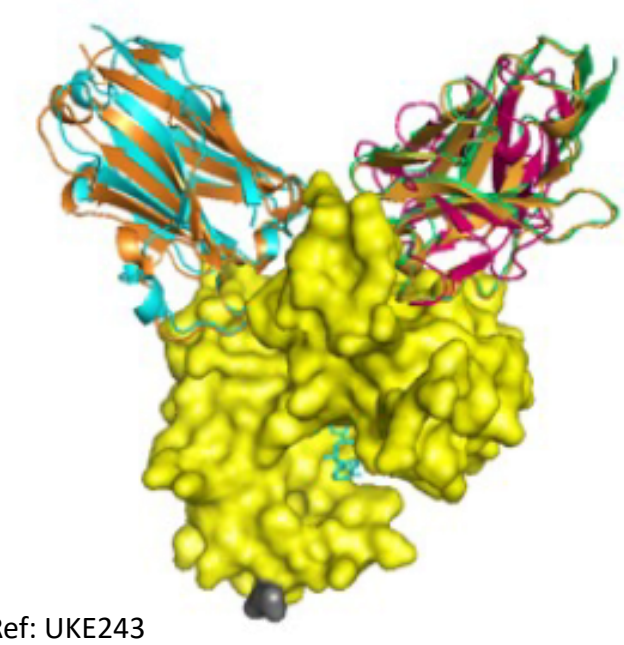
CD38-Specific Biparatopic Nanobodies for Diagnosis and Therapeutic Treatment of Diseases



Background & Innovation

CD38 is a transmembrane glycoprotein mainly expressed on the surface of cells of the immune system. It is upregulated in many **hematopoietic disorders** such as multiple myeloma, malignant lymphoma, leukemia or HIV. Therefore CD38 is clinically used as marker for e.g. CLL and HIV and monoclonal CD38 antibodies such as Daratumumab are used in the treatment of e.g. multiple myeloma.
Disadvantages of these monoclonal antibodies (mAb) result from their often insufficient stability after medical administration, high production costs and limited tissue penetration due to their size. Alternatively, fragments of full IgG antibodies, e.g. Fv or Fab, have been used but showed a reduced specificity and/or affinity for the antigen as well as a low water solubility. While some nanobodies linked to an Fc portion showed potent cytotoxicity for immunotherapy, it remained unclear which epitopes on CD38 targeted by particular nanobodies are especially advantageous for therapeutic purposes. Therefore, there is a need for improved therapeutic CD38 binders which are more effective in treating and diagnosing relevant diseases.

Here, we present **biparatopic anti-CD38 nanobodies** with high specificity and greatly improved cytotoxicity which makes them particularly suitable for the use in the **diagnosis** and/or **therapeutic treatment** of relevant diseases.



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Technical Description

We present novel biparatopic anti-CD38 nanobodies that recognize different, non-overlapping epitopes of the extracellular domain of CD38.
Two distinct nanobodies were genetically fused into heteromeric dimers via a flexible peptide linker and then fused these nanobody dimers to the hinge, CH2 and CH3 domains of human IgG1, yielding highly soluble, biparatopic nanobodies.
We analyzed the capacity of these nanobodies to mediate complement-dependent cytotoxicity (CDC) to CD38-expressing human multiple myeloma and Burkitt lymphoma cell lines. The biparatopic nanobodies elicited CDC toward CD38-expressing myeloma cells more effectively than Daratumumab.
Our results emphasize the advantage of nanobodies for constructing bispecific antibodies. Moreover, our biparatopic anti-CD38 nanobodies represent potential new powerful therapeutics for **treatment of multiple myeloma**.

Competitive advantage

Our biparatopic anti-CD38 nanobodies feature:

- greatly **improved cytotoxicity** vs. conventional antibodies (Daratumumab)
- faster and better **tissue penetration** than conventional antibodies
- better biodistribution
- **lower costs** than monoclonal antibodies
- higher stability and solubility
- smaller size
- lower immunogenicity
- better suited for in vivo imaging applications and for galvanization

FOCUS SECTORS

- Therapeutics
- Hematopoietic diseases
- Nanobodies for diagnosis
- Nanobody therapy

PROJECT KEY WORDS

- complement-dependent cytotoxicity
- Heavy chain antibody / nanobody
- Biparatopic nanobodies

DEVELOPMENT STATUS

- In-vitro experiments

PATENT PROCEDURE STATUS

- Patent application filed in CA, EP, US

POTENTIAL FOR COOPERATION

- R&D Cooperation
- Transfer of rights
- Licensing

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