

INNOVATIVE NANO-ANTIBODIES FOR A NEW GENERATION OF DIAGNOSTIC TESTS TO MONITOR CD38 IN MULTIPLE MYELOMA

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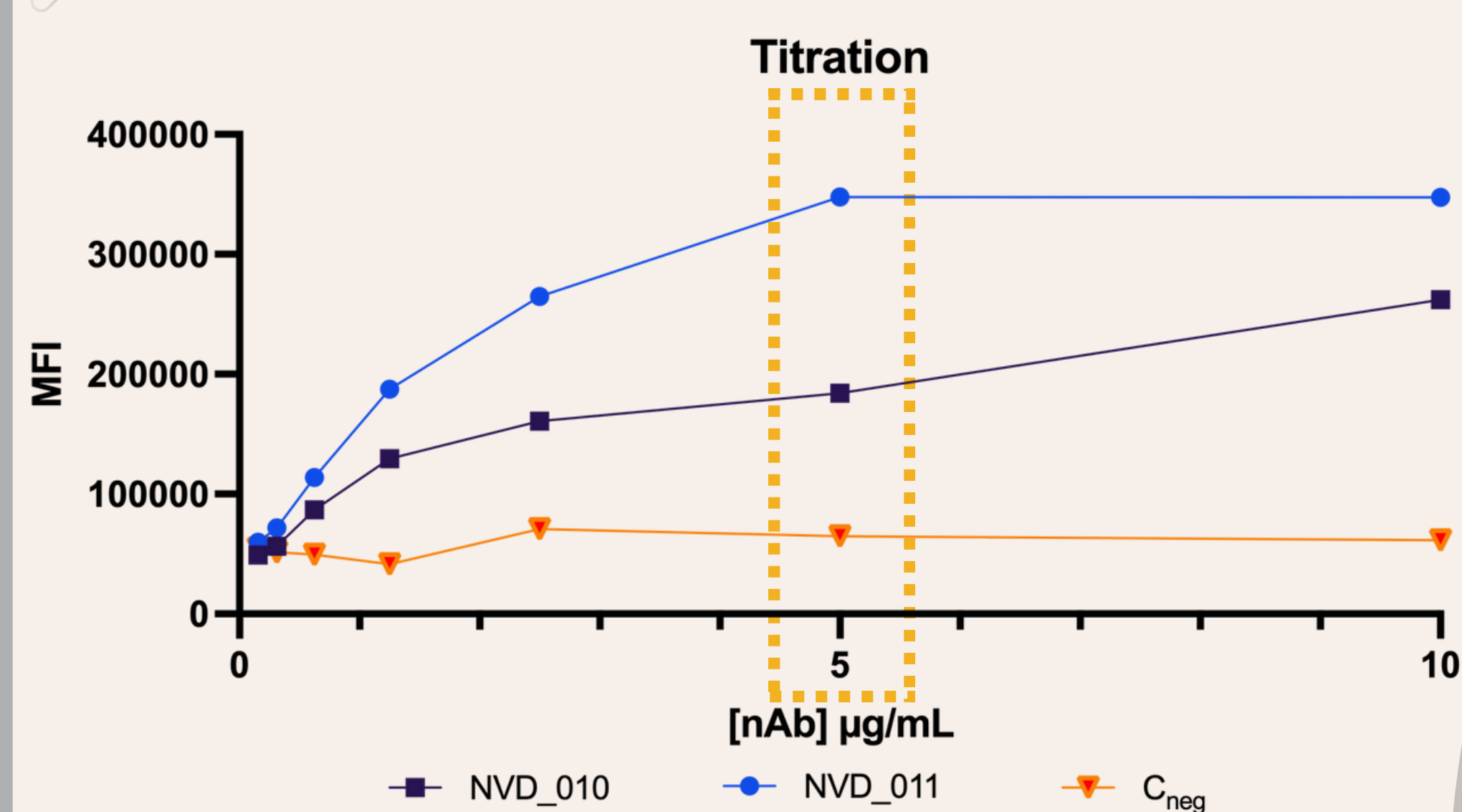
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INTRODUCTION

Multiple Myeloma (MM) is the second most common hematological cancer and is characterized by proliferation of malignant plasma cells (PC) in the bone marrow (BM). For several years now, the field of immuno-oncology has been trying to identify promising targets for the design of new immuno-therapies. In this context, CD38 has emerged as a hopeful one due to its high and uniform expression on malignant plasma cells, while being relatively low on normal lymphoid and myeloid cells, as well as on non-hematopoietic tissues. Daratumumab and Isatuximab are two therapeutic monoclonal antibodies (mAb) currently available for patients. In this context, we aim at developing CD38-specific nano-antibodies that are non-competitive with therapeutic mAbs for the development of CD38RO assays for monitoring treatment. This work was performed using the native conformation of CD38, thanks to NVDIAG technology (Cf. Abstract #33093 - SP9-O1).

TITRATION

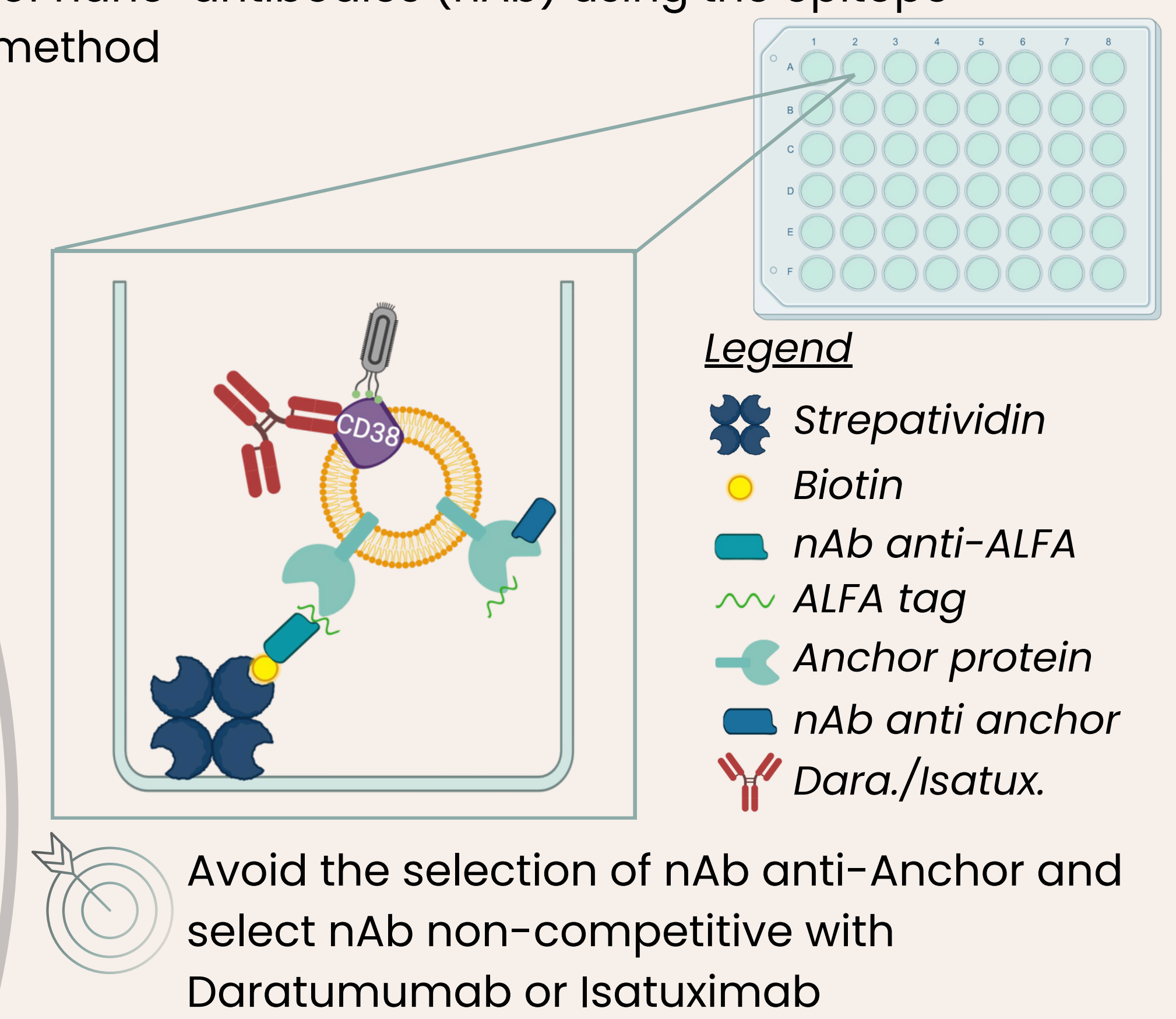
Determination of saturating concentration of nAb



nAb are specific for CD38 and can be used at low concentrations (5 µg/mL) due to high affinity

SELECTION

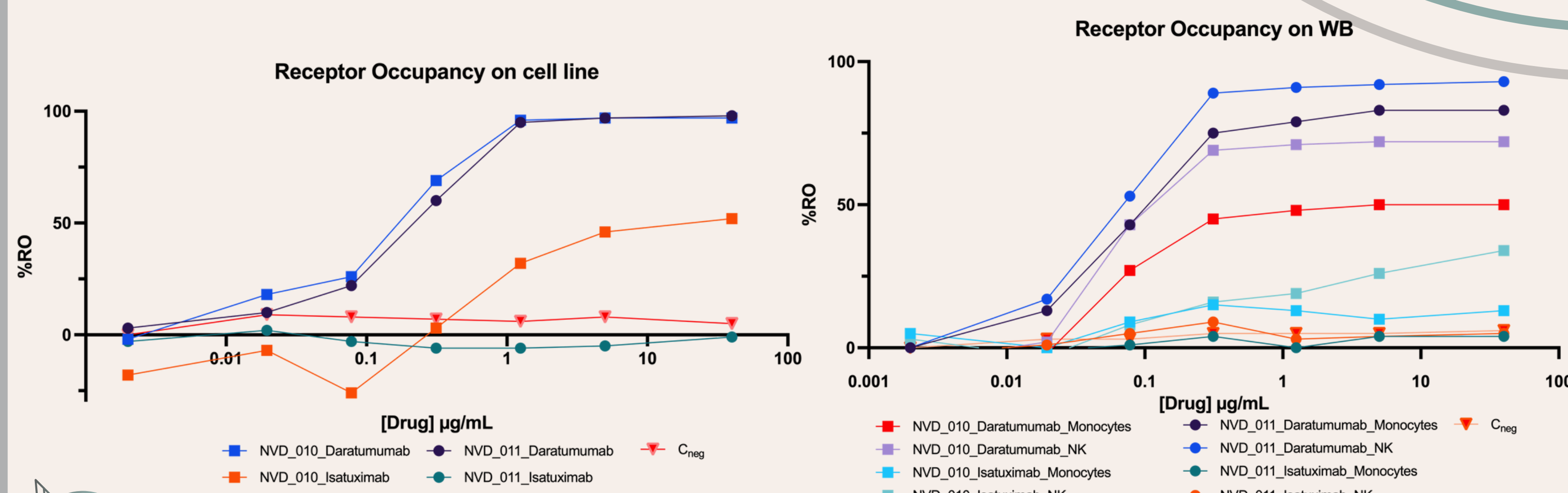
Selection of nano-antibodies (nAb) using the epitope masking method



Avoid the selection of nAb anti-Anchor and select nAb non-competitive with Daratumumab or Isatuximab

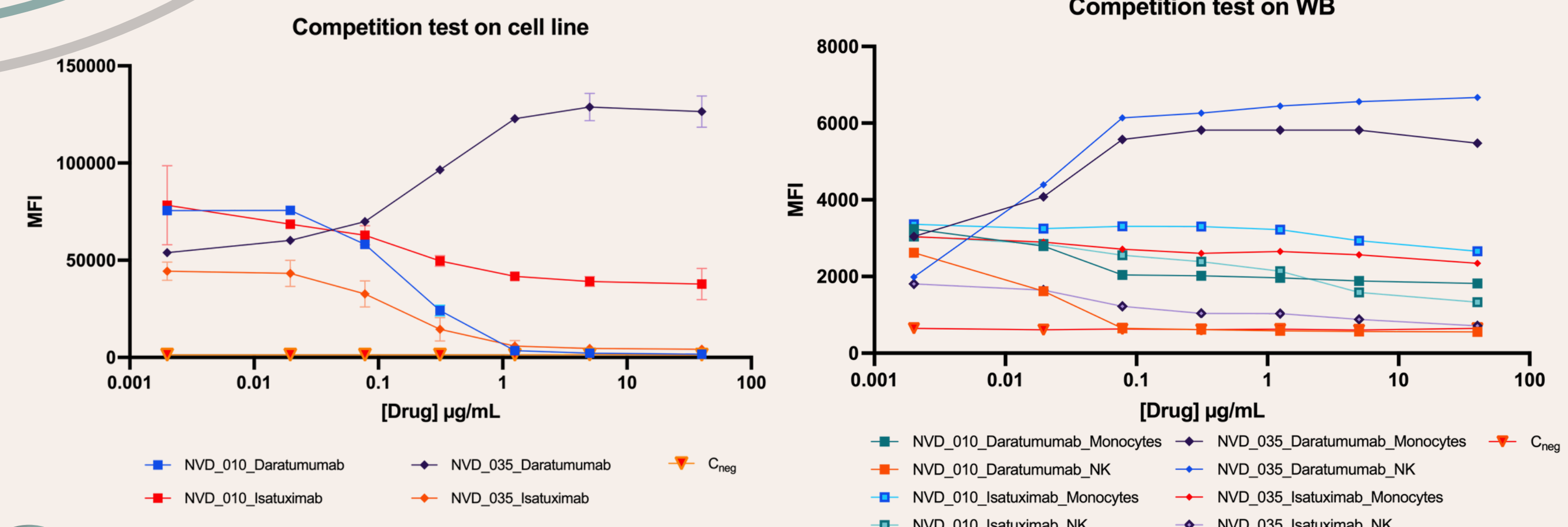
RESULTS

Competition tests were carried out on cell line homogeneously expressing CD38 and on whole blood (WB) in which 60% of monocytes and NK cells express CD38



NVD_011 is competitive with Daratumumab but non-competitive with Isatuximab, and represents a good candidate to develop a diagnostic test

Competition tests of NVD_035 selected with an optimized phage display method using epitope masking



Potential of CD38 detection when the saturating concentration of Daratumumab is exceeded

CONCLUSION

Due to a dynamic expression the down-regulation of CD38 at the surface of PC is heterogenous accross patients.

As shown in the literature, Isatuximab internalizes CD38, explaining that the majority of anti-CD38 Abs are slightly competitive with this mAb. Remarkably, we showed here that NVD_011 nAb is totally non-competitive with Isatuximab.

Our NVD_035 evidenced that a high dose of Daratumumab tends to potentiate its detection of CD38, potentially by making the epitope targeted by NVD_035 more accessible. In conclusion, both newly developed nAb offer a great opportunity for BioCytex to develop new generation diagnostic tests for monitoring disease progression in patients undergoing immunotherapy.

References

- Human CD38: a glycoprotein in search of a function - *F Malavasi et al.*
- Multiple myeloma - *Antonio Palumbo, Kenneth Anderson*
- CD38: A Target for Immunotherapeutic Approaches in Multiple Myeloma - *Fabio Morandi et al.*
- Tetrameric interaction of the ectoenzyme CD38 on the cell surface enables its catalytic and raft-association activities - *Miki Hara-Yokoyama et al.*