

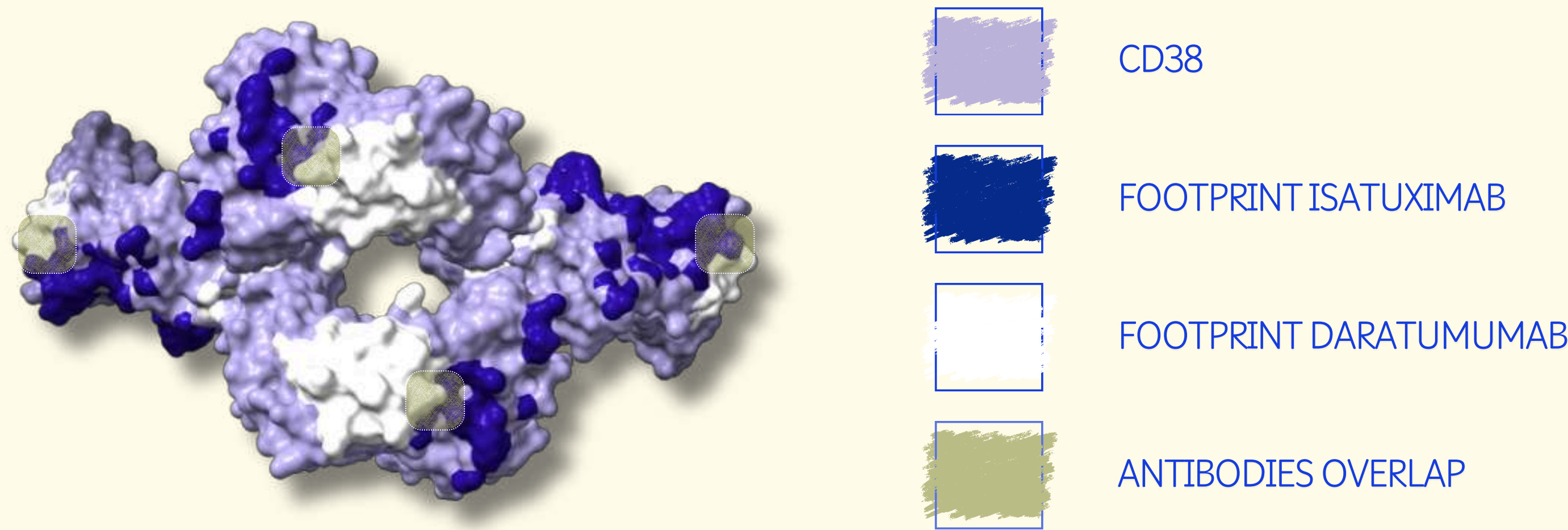
UNLOCKING NATIVE MEMBRANE PROTEIN EPITOPES WITH NANO-ANTIBODIES FOR ADVANCED DIAGNOSTIC AND MONITORING APPLICATIONS

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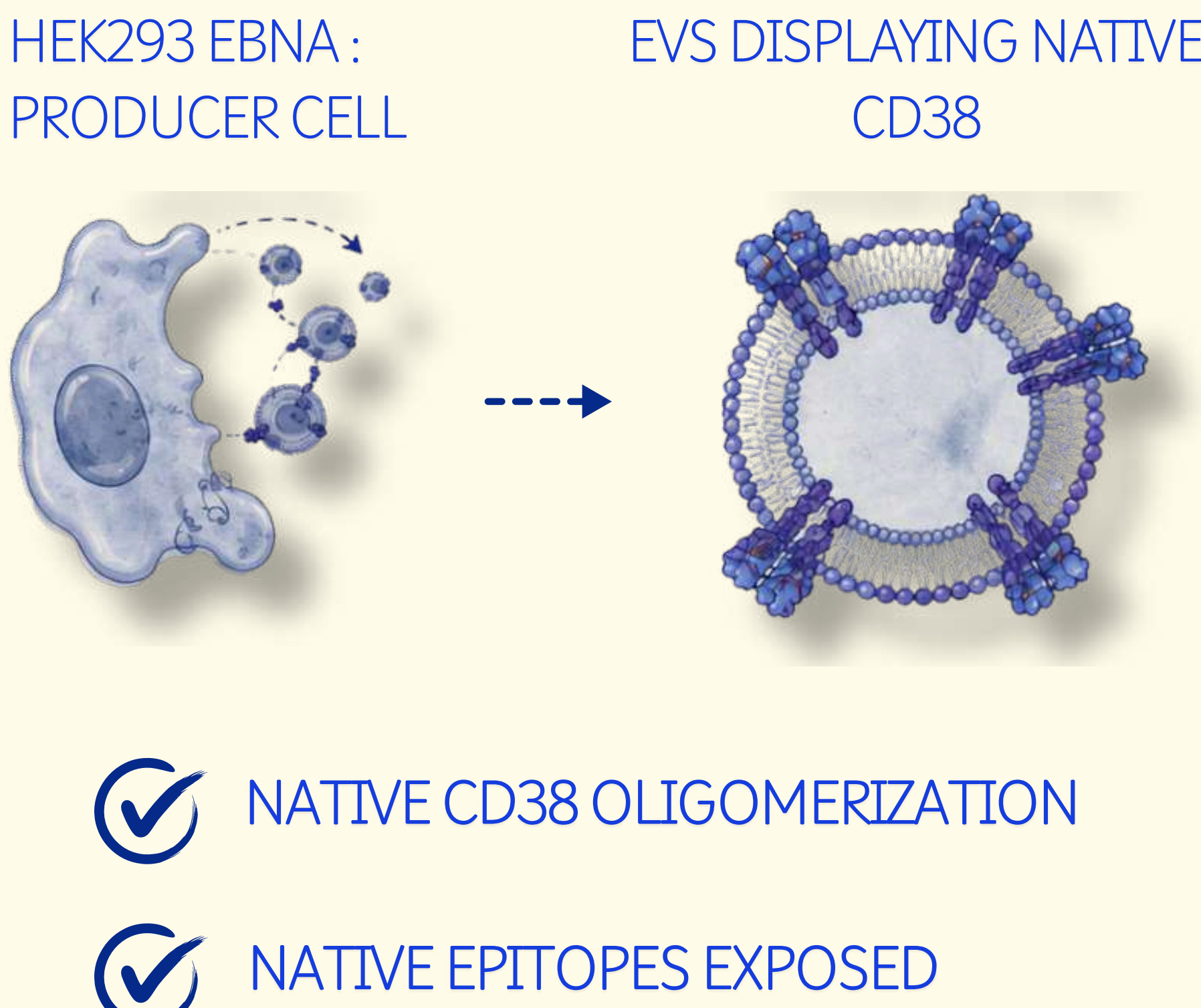
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CHALLENGE

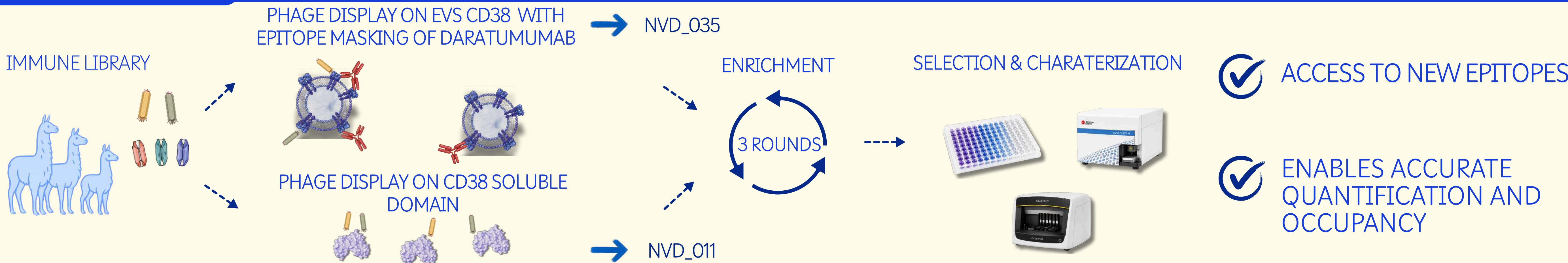
CD38 IS A DYNAMIC MEMBRANE TARGET, MAKING ITS NATIVE RECOGNITION AND QUANTIFICATION CHALLENGING, ESPECIALLY IN THE PRESENCE OF THERAPEUTIC ANTI-CD38 ANTIBODIES. WE USED EXTRACELLULAR VESICLES (EVS) TO PRESENT CD38 IN A NATIVE MEMBRANE CONTEXT AND GENERATE SINGLE-DOMAIN ANTIBODIES. THIS STRATEGY AIMS TO OBTAIN NON-COMPETITIVE BINDERS FOR RELIABLE CD38 MEASUREMENT DURING THERAPY.



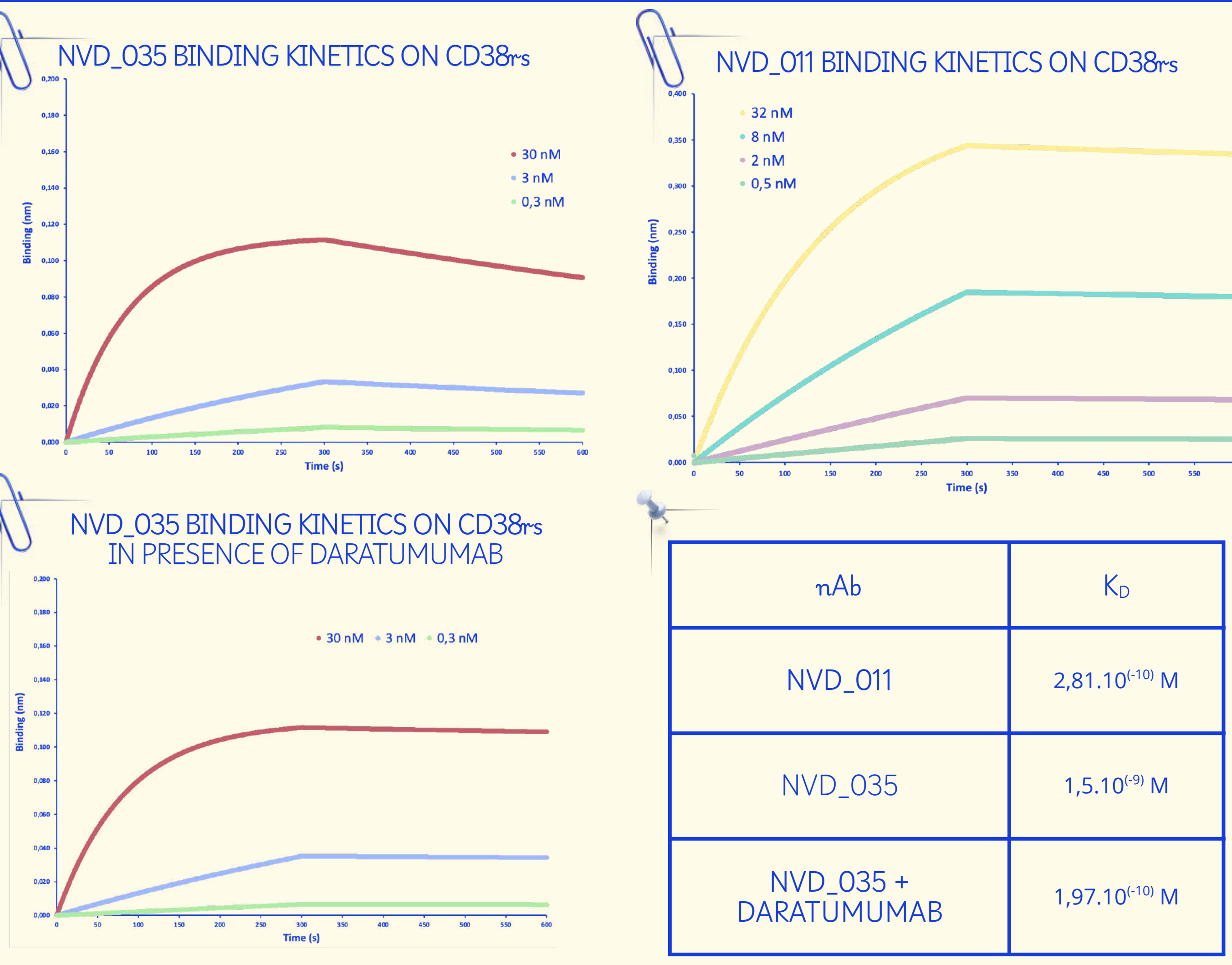
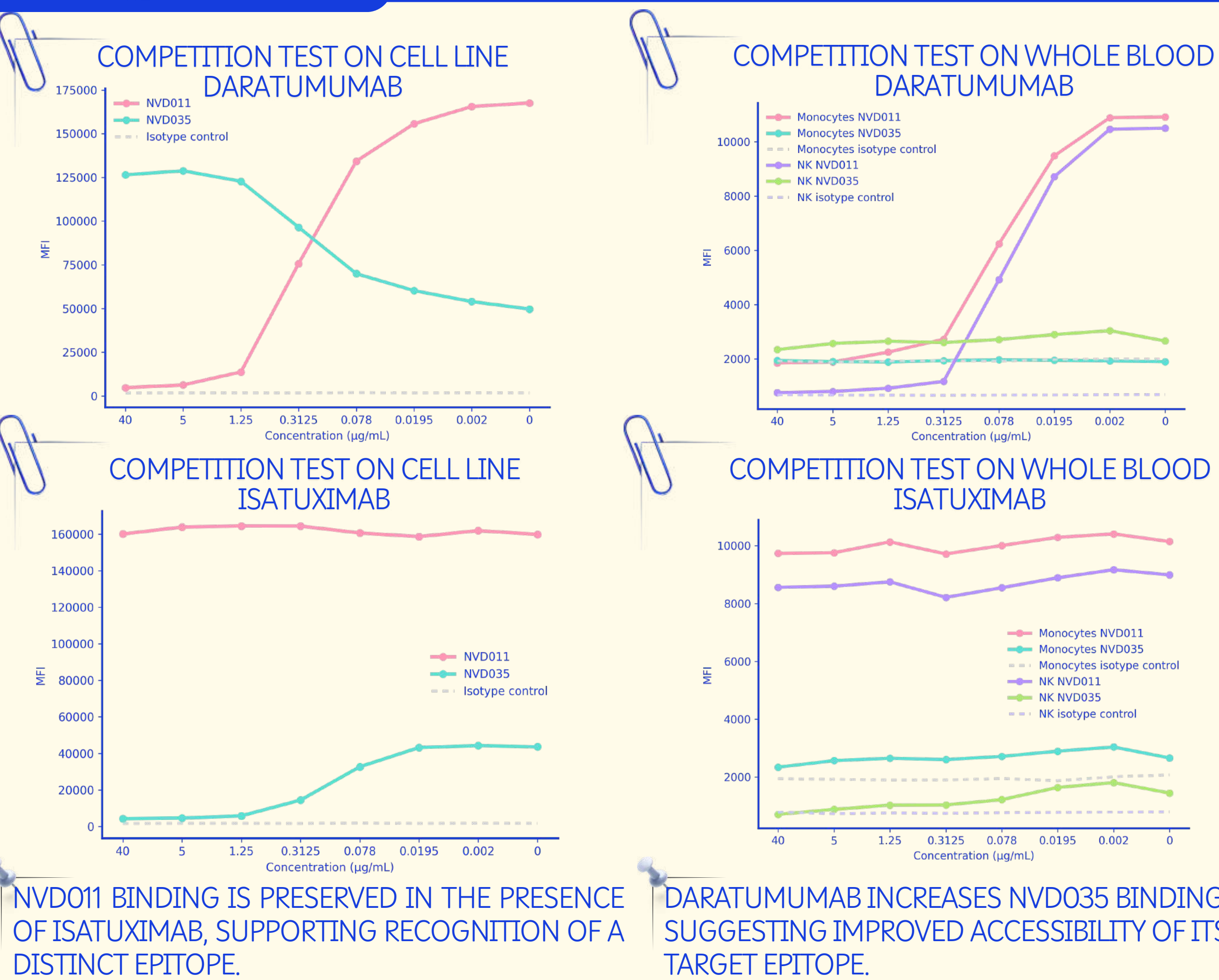
APPROACH



SELECTION



RESULTS



CONCLUSION

DUE TO THE DYNAMIC EXPRESSION OF CD38, ITS DOWNREGULATION AT THE SURFACE OF PLASMA CELLS IS HETEROGENEOUS ACROSS PATIENTS. IN THIS CONTEXT, WE DEVELOPED NEXT-GENERATION NABS TARGETING CD38 AS IT IS NATURALLY PRESENTED ON MALIGNANT CELLS BY LEVERAGING EXTRACELLULAR VESICLES (EVS) AS NATIVE ANTIGENIC PLATFORMS. WHILE ISATUXIMAB-INDUCED CD38 INTERNALIZATION LIKELY EXPLAINS THE PARTIAL COMPETITION OBSERVED FOR MOST ANTI-CD38 ANTIBODIES, NVD_011 WAS FULLY NON-COMPETITIVE WITH ISATUXIMAB. IN PARALLEL, NVD_035 ENHANCED CD38 DETECTION IN THE PRESENCE OF HIGH DARATUMUMAB DOSES, SUGGESTING IMPROVED EPITOPE ACCESSIBILITY. TOGETHER, THESE NABS REPRESENT PROMISING TOOLS FOR COMPANION DIAGNOSTICS AND THERAPEUTIC MONITORING IN MULTIPLE MYELOMA.

