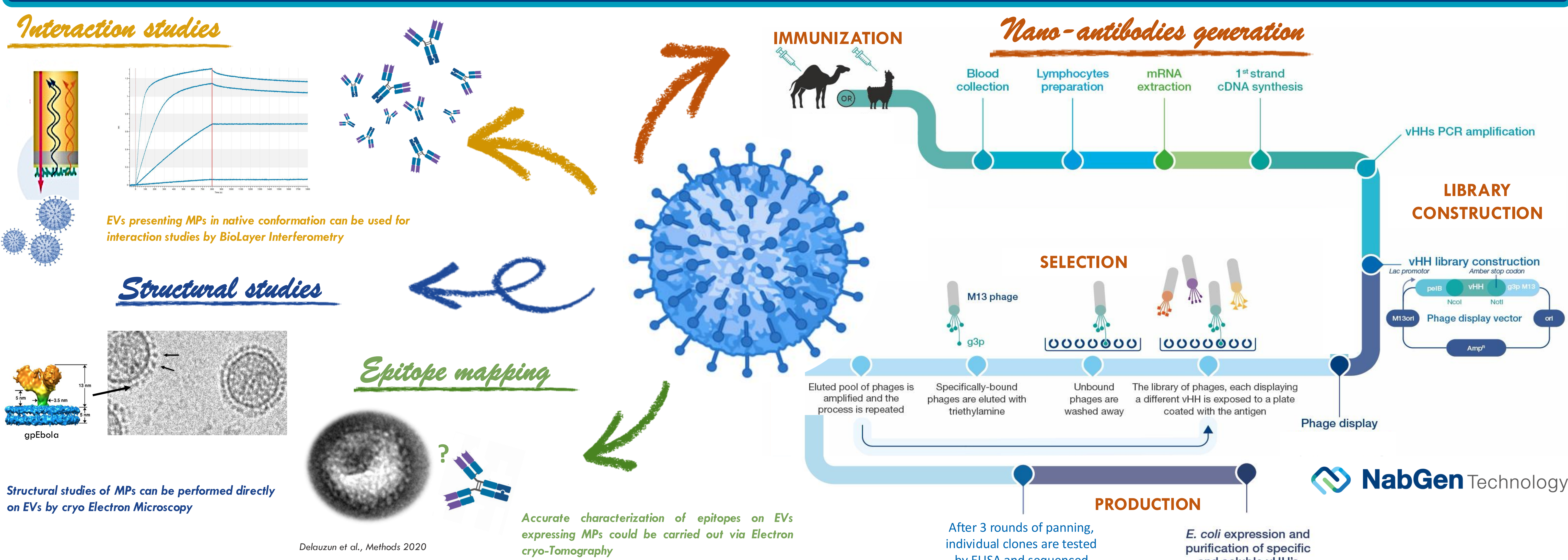


ABSTRACT

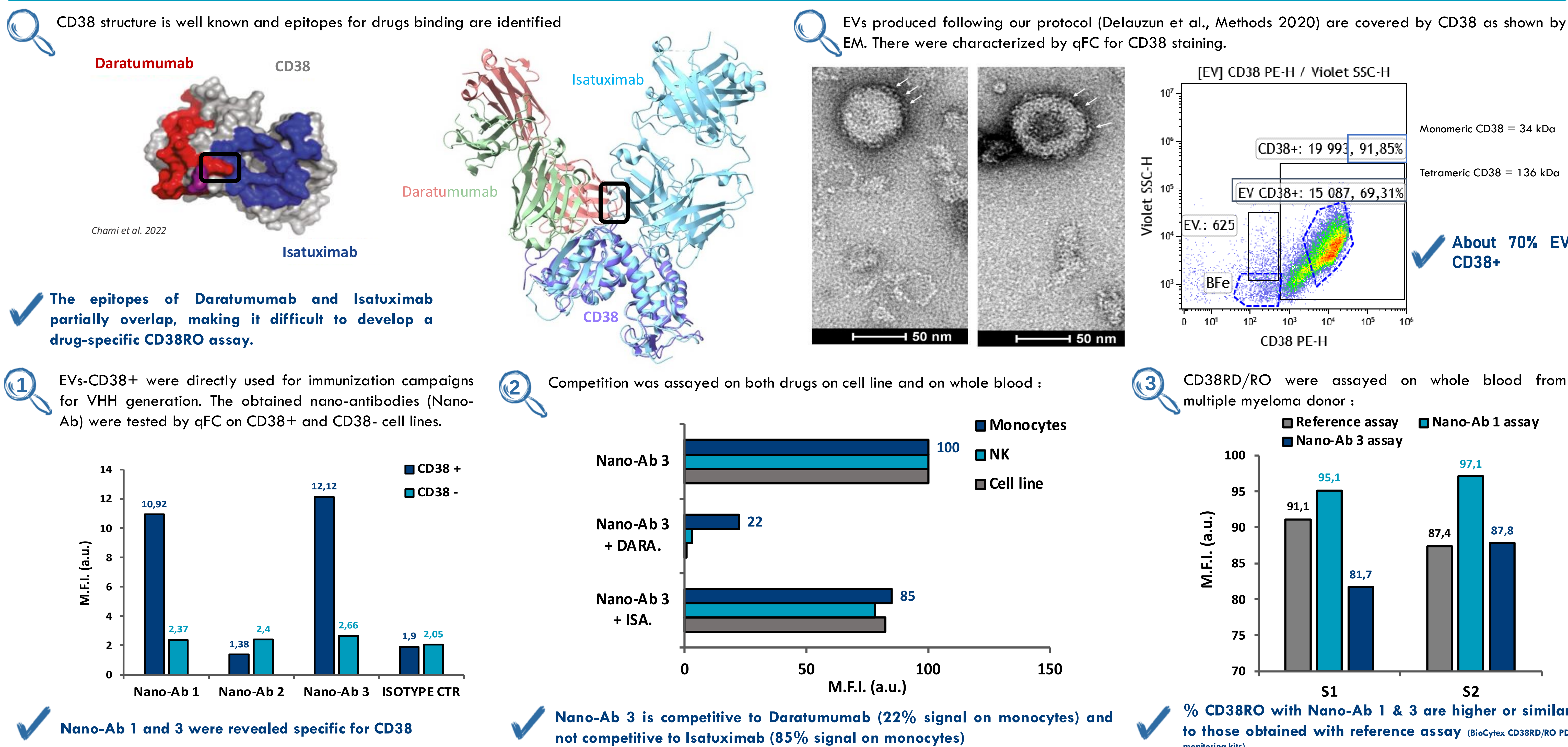
The **NVDIAG LabCom** is a partnership between the HPI team (Host-Pathogen Interaction) from the **LISM (CNRS-AMU)** and the company **BioCytex**. Most of the markers used in medical diagnostics are surface membrane proteins (MPs). Our team has demonstrated, through structural studies using electron microscopy, that the use of extracellular vesicles (EVs) makes it possible to obtain MPs in a native conformation (glycosylation, oligomerisation state). In parallel, LISM operates the **Nabgen platform** dedicated to the generation of **nano-antibodies (Nano-Ab)** derived from camelid heavy chain antibodies. **MPs** produced at the surface of EVs in **native conformation reveal original epitopes** that do not exist when, for example, soluble extracellular domains are used. We believe that these original epitopes offer the potential to develop **innovative Nano-Ab** against a wide range of targets, even those known to be particularly difficult. We also focus on the development of Nano-Ab that are **non-competitive with therapeutic antibodies**, which could then be used in **quantitative Flow Cytometry- (qFC) and ELISA-based companion diagnostic tests** for monitoring treatment, particularly in **cancer immunotherapy**.

The development of biotherapeutic drugs targeting **CD38** has been shown to be successful for **multiple myeloma (MM)** patients. The plasma cells (PC) from MM patients highly express CD38 on PC surface, making CD38 an attractive target. So far, 2 therapeutic monoclonal antibodies **Isatuximab** and **Daratumumab** are currently available for patients. Nevertheless, down regulation of CD38 on cell surface remains controversial since there is no commercial antibodies that bind to CD38 independently to Isatuximab and Daratumumab. Here we show that using NVDIAG strategy can lead to **suitable Nano-Ab for monitoring the total number of CD38 molecules on PC** in real time. Such a Nano-Ab would be used in **qFC for assessment of the total CD38 receptor density (CD38RD)**. In combination with a competitive antibody, the **CD38 receptor occupancy (CD38RO)** can be monitored.

USE OF EXTRACELLULAR VESICLES TO OBTAIN NATIVE MEMBRANE PROTEINS



EVs EXPRESSING CD38 AS AN OPPORTUNITY TO DEVELOP COMPANION DIAGNOSTIC TESTS



CONCLUSION

EVsCD38+ used for antigen presentation in the llama immunization campaign enabled us to generate Nano-Ab against new CD38 epitopes. As a matter of fact, it resulted in Nano-Ab that do not compete with Isatuximab giving promising candidates for designing a new generation of CD38RO assay.

On the strength of this proof of concept, the LabCom NVDIAG plans to target other cancer biomarkers (CD19 and CD33), as well as other MPs involved in cardiovascular diseases (CD63) in partnership with BioCytex.

In addition, NVDIAG is willing to offer its services to the entire academic and industrial community for future developments.