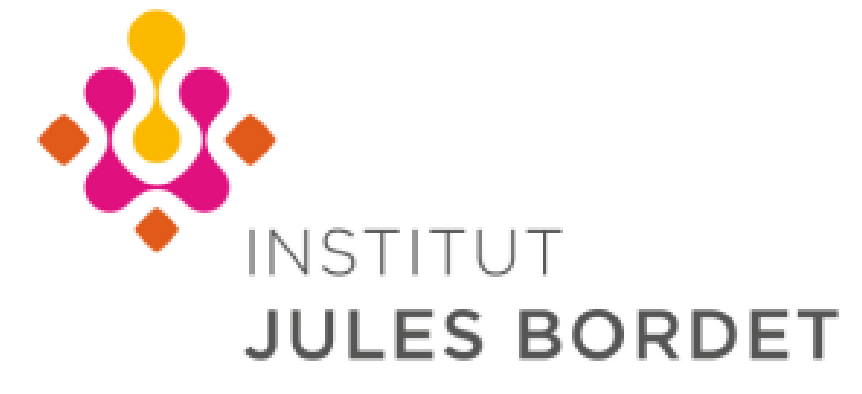


CLL extracellular vesicles induce the differentiation of monocytes into nurse-like cells



Dubois N*, Van Morckhoven D, Tilleman L, Van Nieuwerburgh F, Bron D, Meuleman N, Lagneaux L, Stamatopoulos B.
 Laboratory of Clinical Cell Therapy, Université Libre de Bruxelles (ULB), Jules Bordet Institute, Brussels, Belgium *nathan.dubois@ulb.be

Introduction

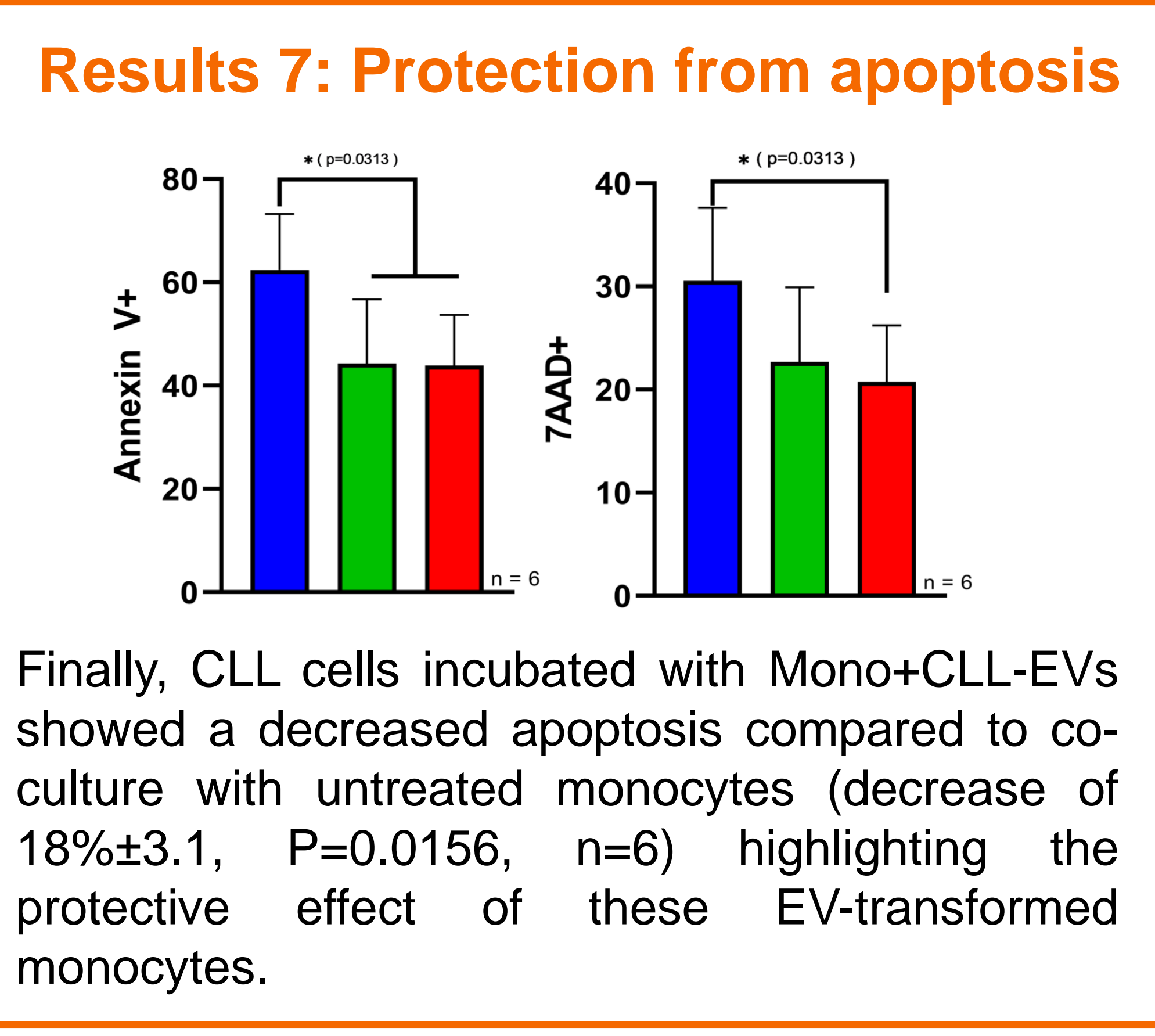
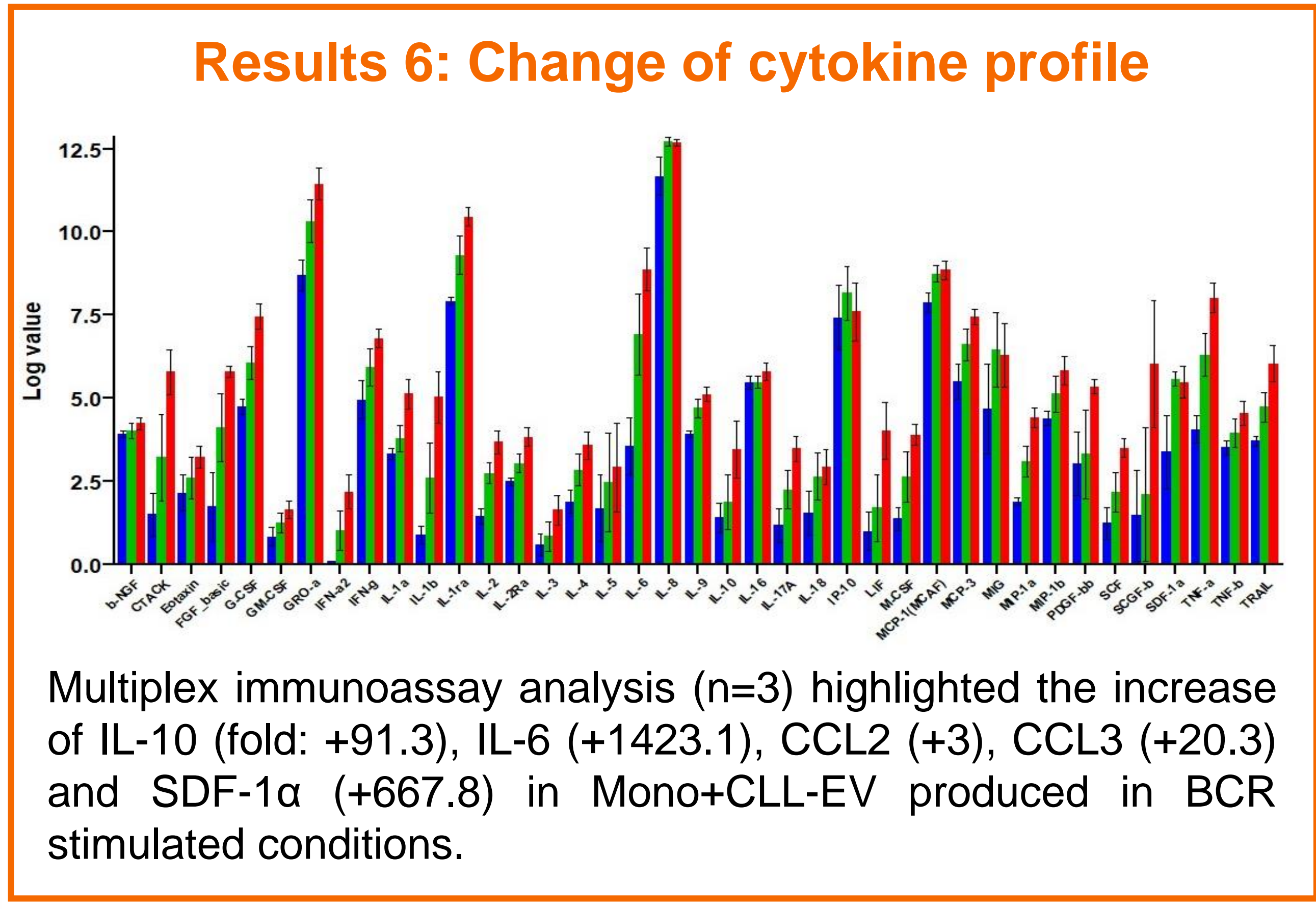
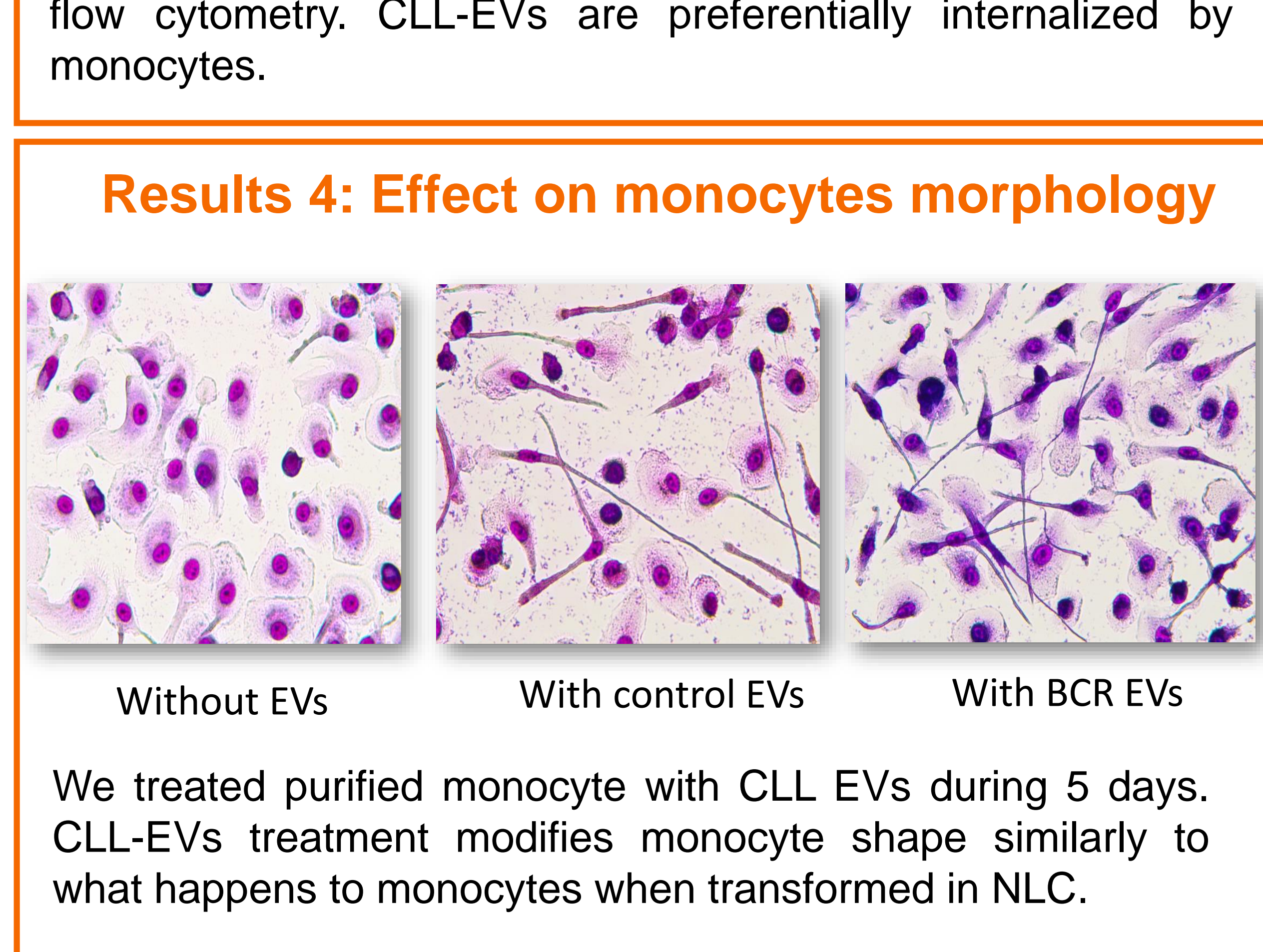
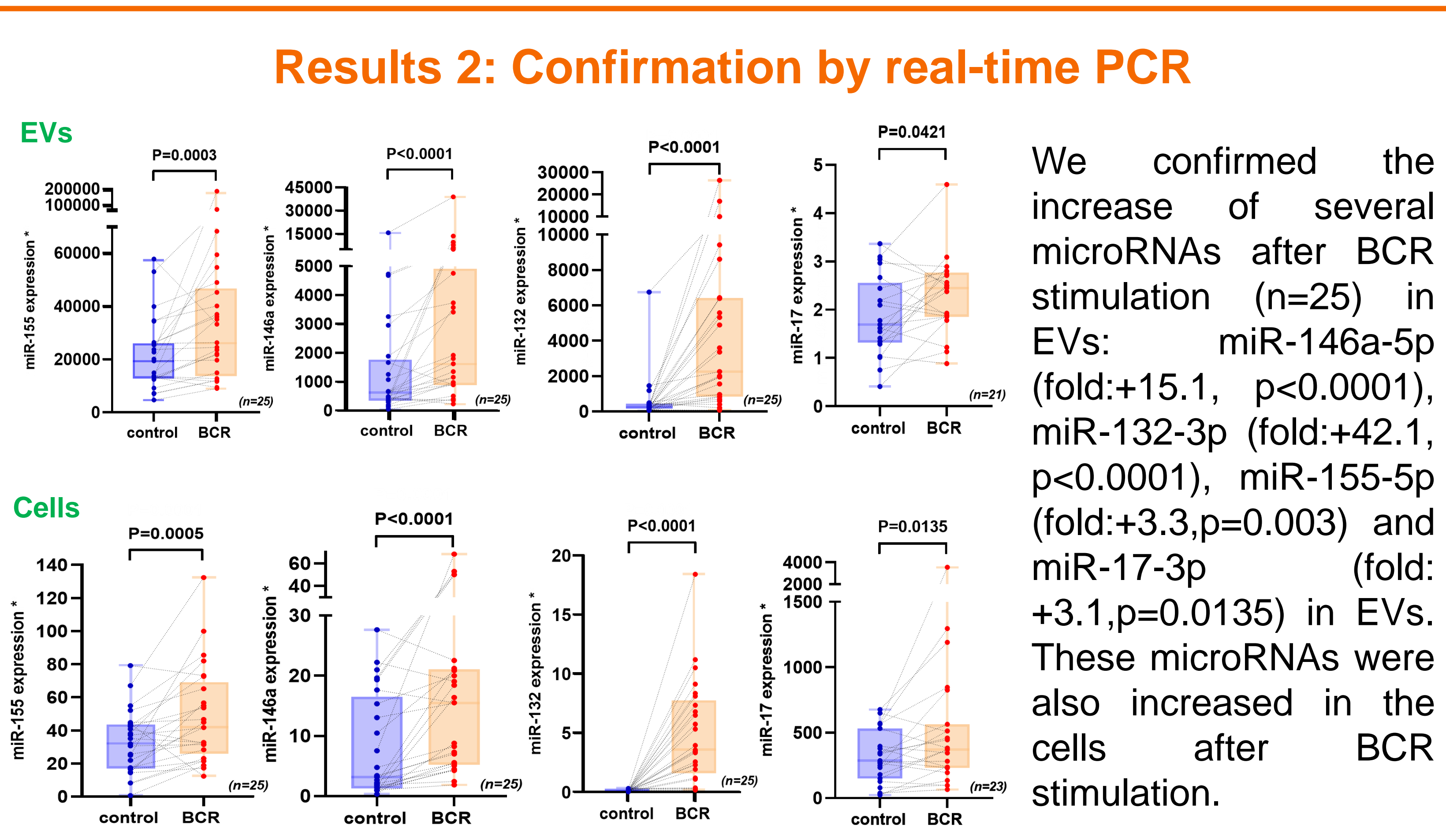
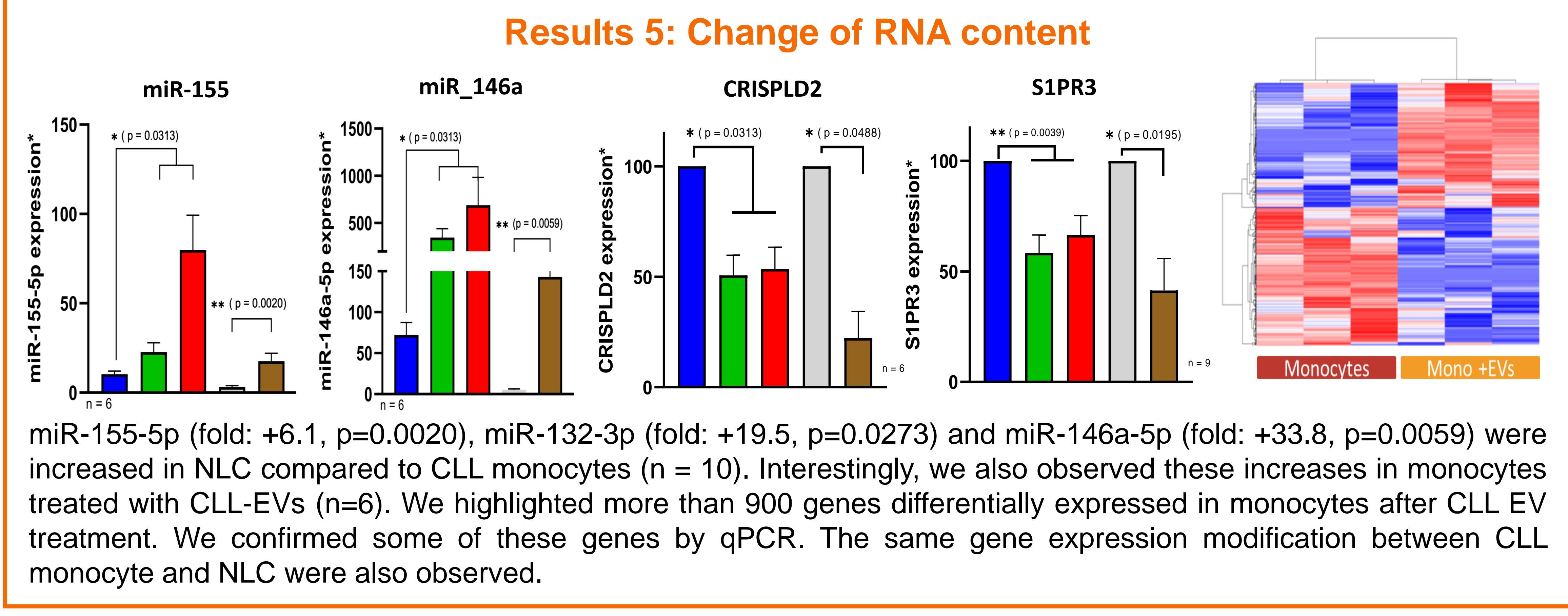
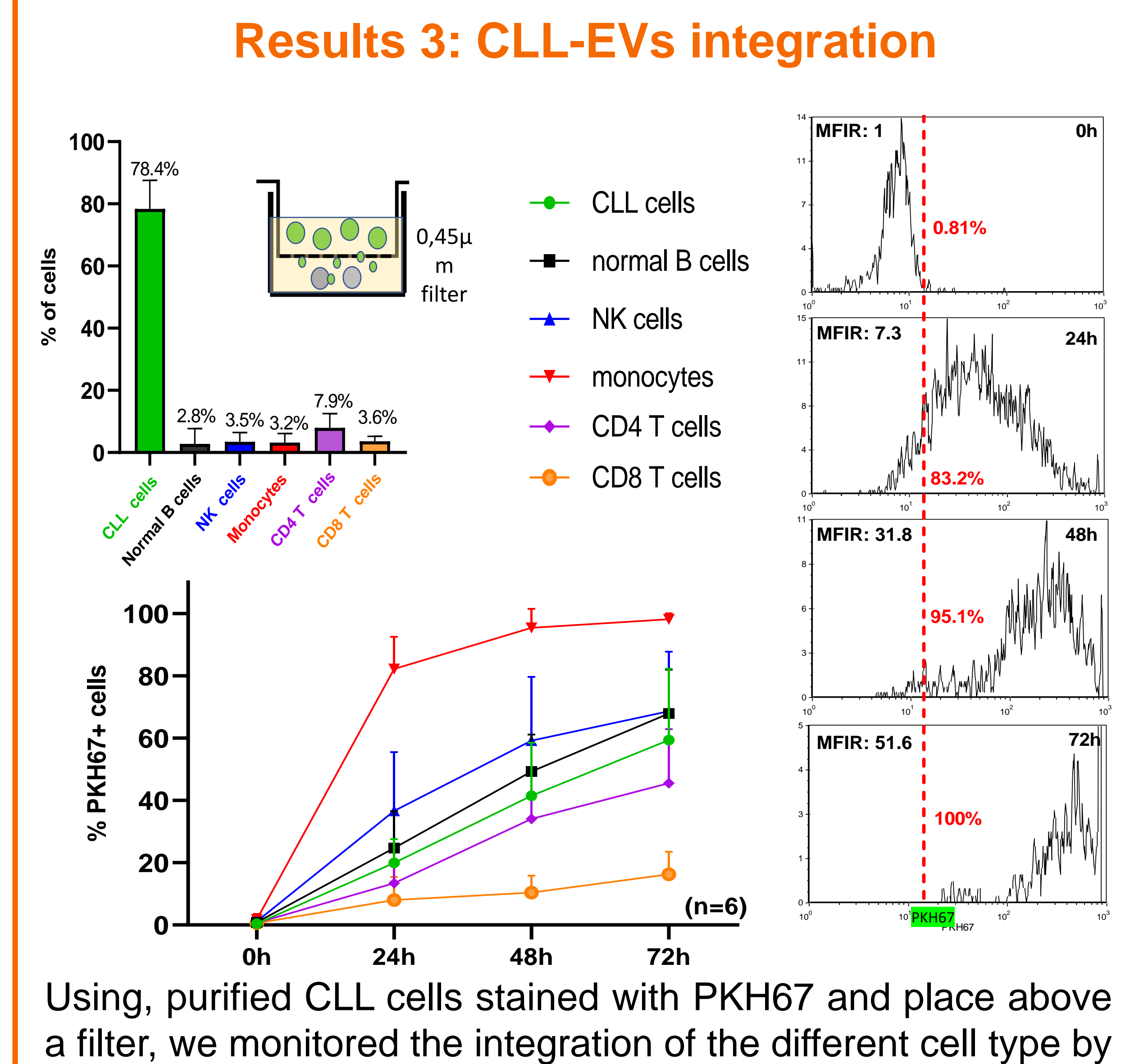
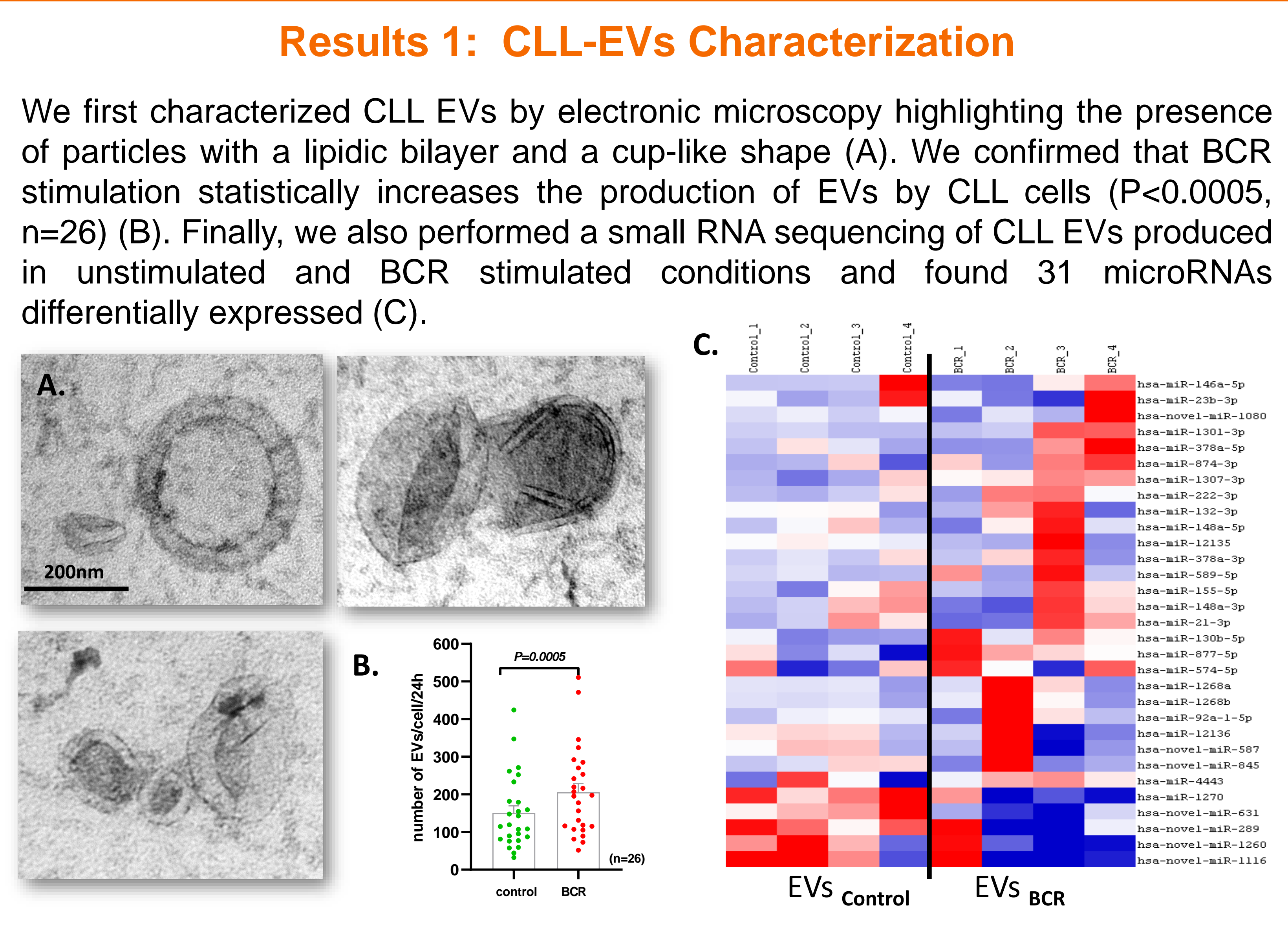
Chronic Lymphocytic Leukemia (CLL) cells are dependent of their microenvironment (ME) that could activate BCR pathway leading to their survival. In return, CLL cells could manipulate the immune ME in order to promote their own survival. Recently, Extracellular Vesicles (EVs) have been described as a new manner of cell-to-cell communication.

Objectives

Here, we will study the impact of BCR stimulation on microRNA content in CLL cells and EVs as well as the impact of CLL-EVs on monocytes. Finally, we will compare the monocytes profile incubated with CLL-EVs and NLC and study the biological induced changes

Methods

CLL-EVs were obtained from CD19+ purified patient leukemic cells cultured with/without BCR stimulation. microRNA profile analyzed by NGS and validated by qPCR in cells and EVs. Monocytes were treated with CLL-EVs (Mono+CLL-EVs) and microRNAs were quantified in Mono+CLL-EVs, in CLL-transformed monocytes ("nurse-like cells" – NLC) and untreated monocytes. Several mRNAs (targeted by these microRNAs or specific to NLC) were quantified by qPCR. To study CLL-EV functional effect, co-cultures of CLL-cells with monocytes treated or not with EVs for 5 days were performed and leukemic cells apoptosis was analyzed using Annexin V / 7AAD staining.



Conclusions

We showed that BCR stimulation modifies CLL-EVs microRNA content. The addition of EVs on monocytes lead to a shape change, an increase of several microRNAs, a decreased expression of some of their targets, an increase of several cytokines and an increased ability to rescue CLL cells from spontaneous apoptosis. All together, our data indicate that CLL-EVs induce the differentiation of monocytes into NLC supporting CLL cell survival.