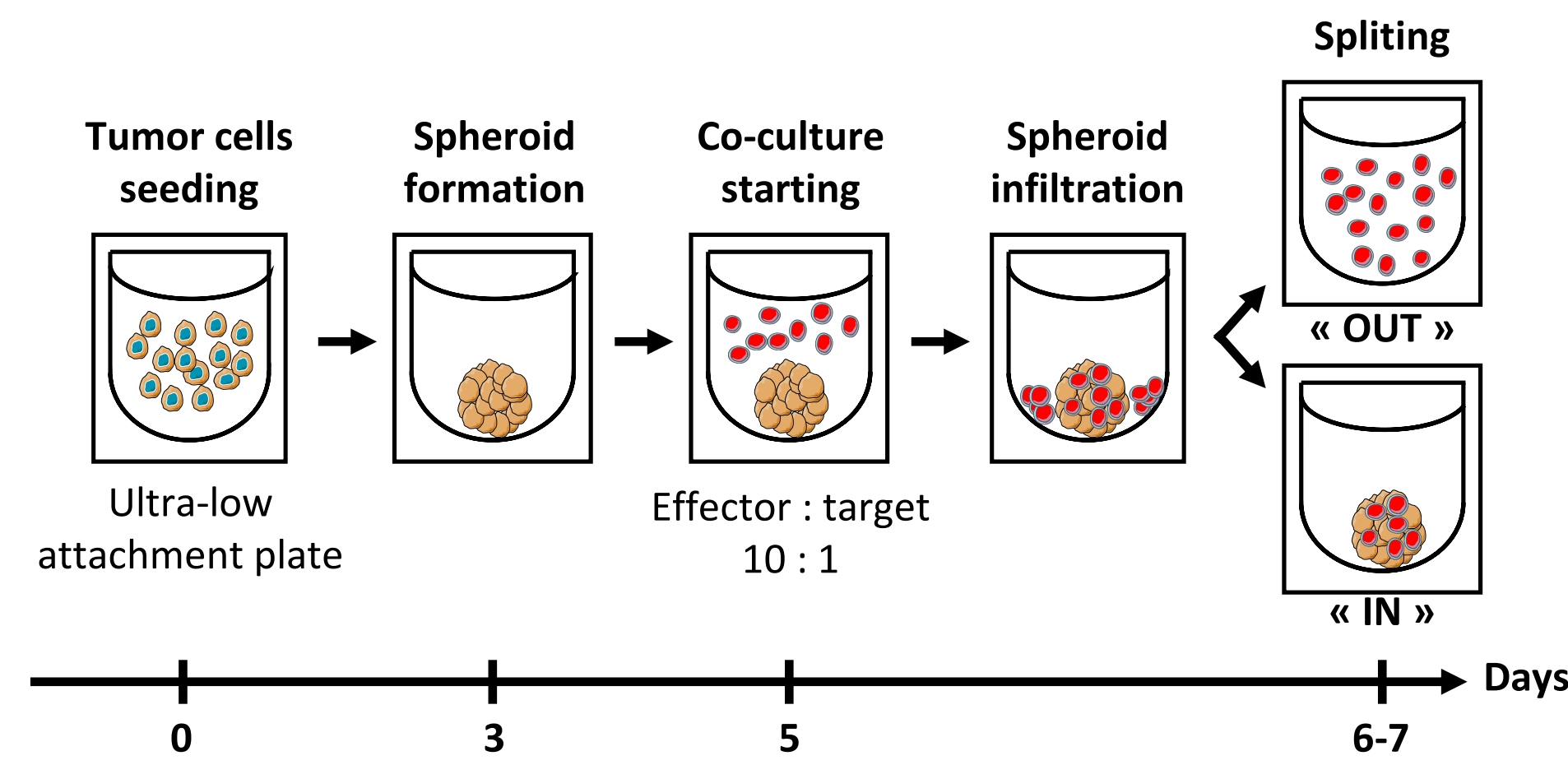


Co-cultures of human colorectal tumor spheroid with immune cells reveal therapeutic potential of anti-MICA/B cytotoxic antibodies

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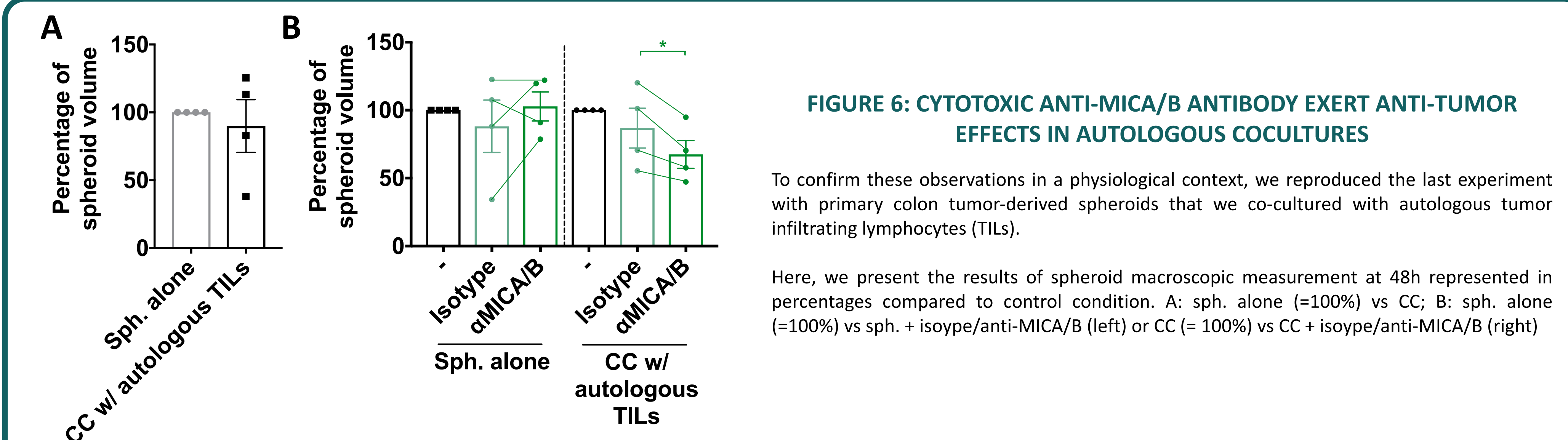
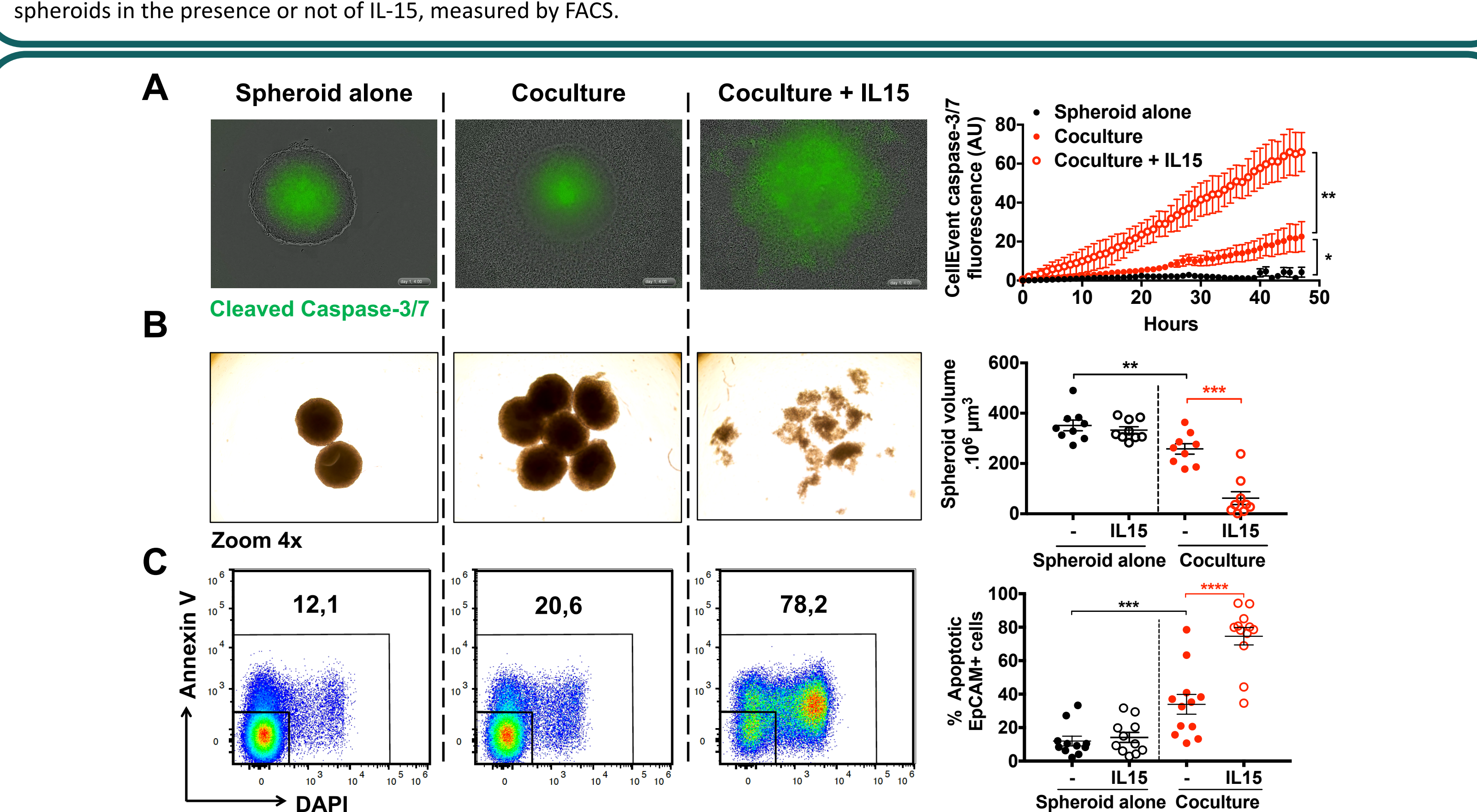
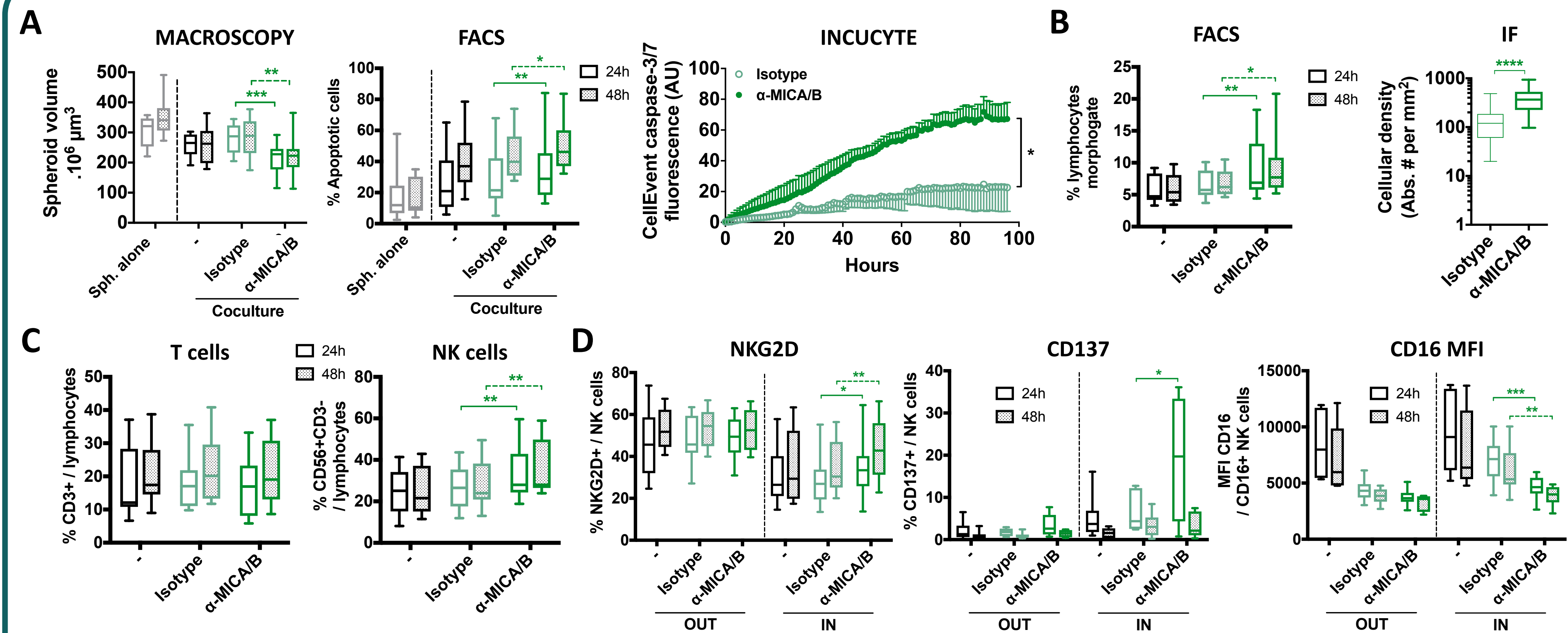
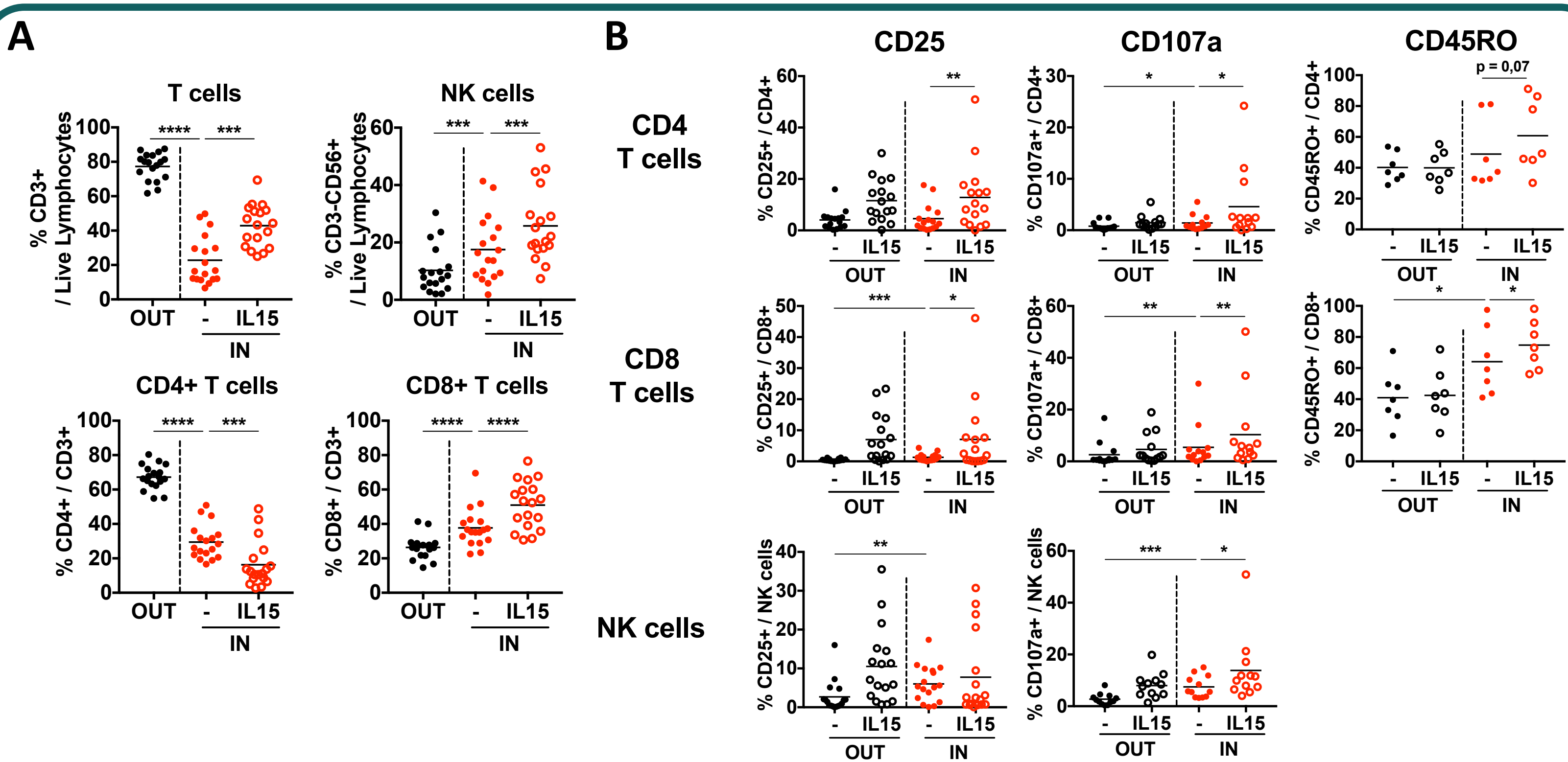
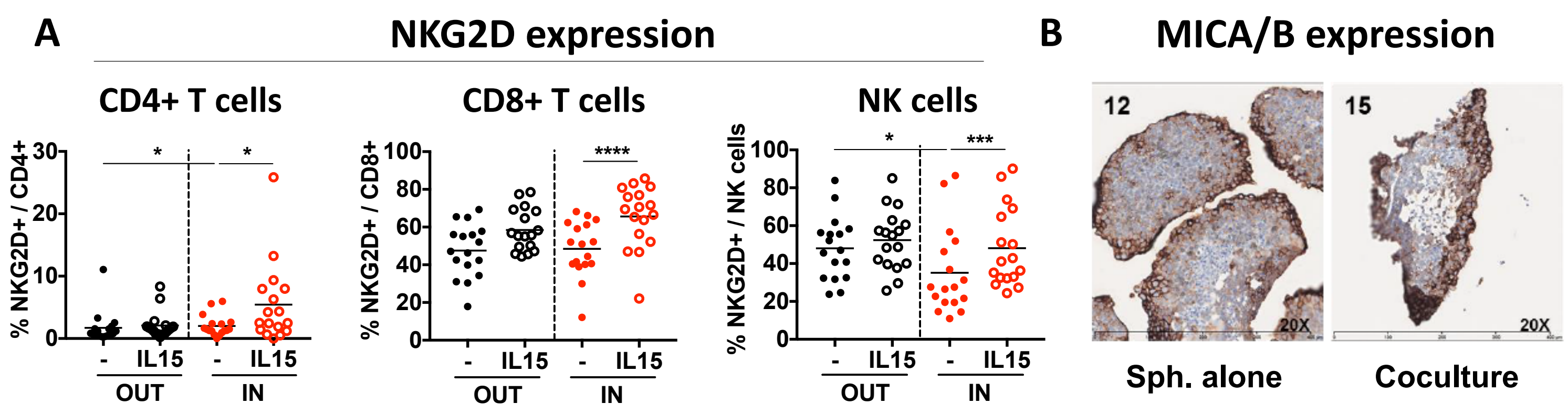
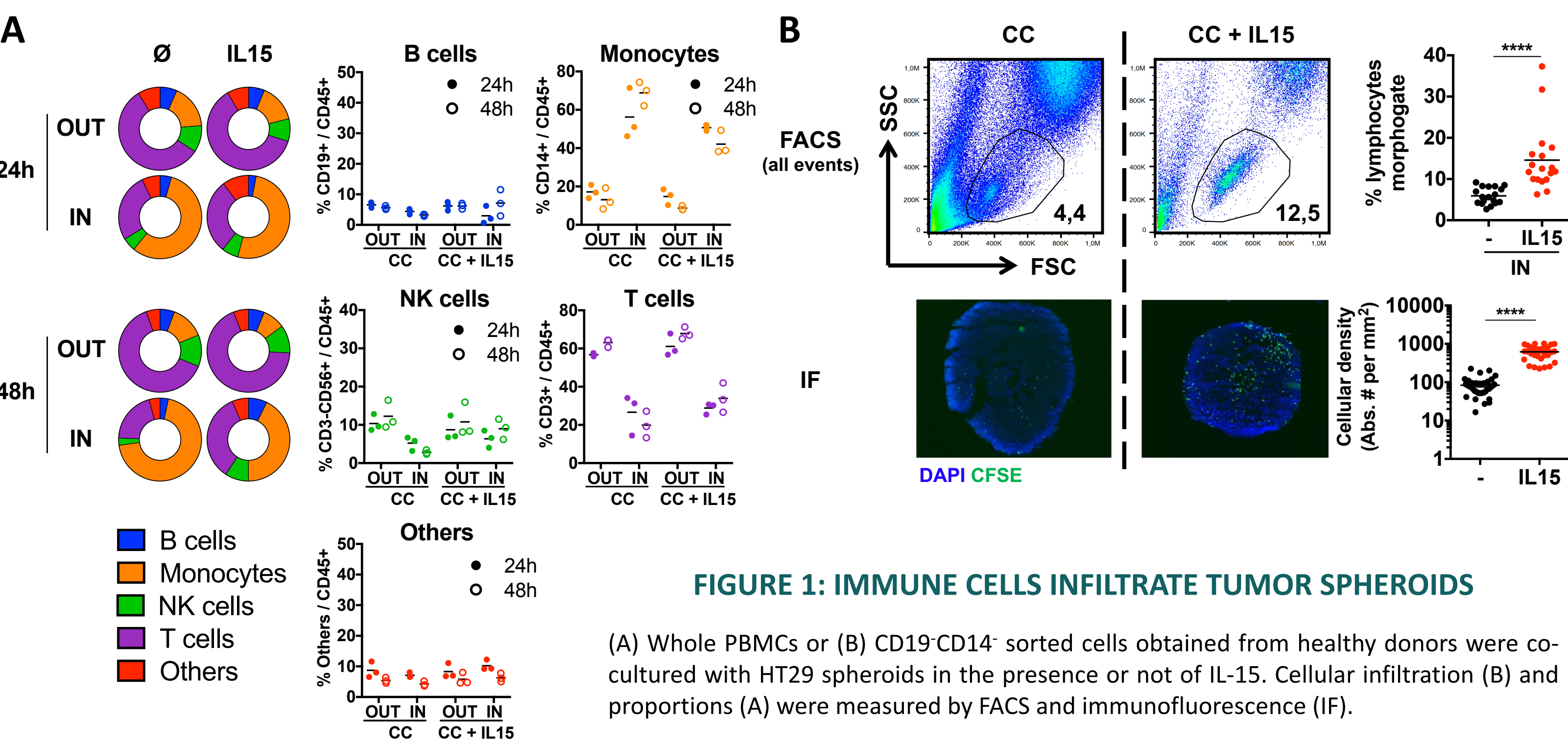


Tumor spheroids (3D tumor cultures) represent interesting models to study cancer treatments. Here, we developed co-culture systems with HT29 tumor cell line as well as primary colon tumor-derived spheroids to quantify by flow cytometry and live-cell imaging the infiltration, activation and function of immune cells toward tumors.

Monocytes, T and NK cells from donor peripheral blood rapidly infiltrated HT29 spheroids, in which we found increased activated/effector cells compared to outside the spheroids. This infiltration induced immune-mediated tumor cell apoptosis, and adding of stimulatory cytokine IL-15 enhanced both immune infiltration and activation, leading to increased tumor cell apoptosis and spheroid destruction.

In these settings, MICA/B is expressed by tumor cells and its ligand NKG2D is engaged on infiltrating cells. We thus used these co-cultures to assess the therapeutic potential of a cytotoxic antibody specific for MICA/B. Anti-MICA/B strongly increased immune-dependent destruction of tumor spheroid in allogeneic as well as autologous conditions. NK cell infiltration was increased and their Fc receptors were engaged, advocating for an antibody dependent cell-mediated cytotoxicity process.

ABSTRACT & METHODS:



CONCLUSIONS & PERSPECTIVES:

Altogether, we show that co-culturing tumor spheroids with immune cells represent a relevant tool to study tumor-lymphocyte interactions and testing of immunotherapies, such as anti-MICA/B cytotoxic antibodies.

In allogenic settings, this model can easily be set up with tumor cells lines and healthy donors to test anti-tumor potential of new targets at the pre-clinical level on human cells.

Autologous settings, meanwhile, can ultimately determine anti-tumor treatments efficacy in physiological conditions and anticipate treatment resistance in patients.