degranulation (Figure 1c and 2), and leading to the identification of the reference mAb 107G3. Sequencing of VH and VL regions of these subclones was performed (see Table ~~2~~ 9 below).

Anti-BTN2A1 107G3 antibody induces Vγ9Vδ2-T cell degranulation against different cancer cell targets

Purified Vγ9/Vδ2 T cells were expanded from PBMCs of healthy donors and co-cultured with different cancer cell lines, including Daudi (Burkitt's lymphoma), Jurkat (acute T cell leukemia), L-IPC (pancreatic adenocarcinoma) and MDA-MB-134 (breast carcinoma) as target cells, with or without anti-BTN2A1 107G3 hybridoma culture supernatant. As shown in Figure 2 and Table 3, the addition of anti-BTN2A1 107G3 hybridoma supernatant lead to an induction of the cytolytic function of Vγ9/Vδ2 T cells, as measured by the percentage of CD107+ degranulating cells, compared to co-cultures with target cells alone, or in the presence of control hybridoma culture medium. PMA/ionomycin treatment of Vγ9/Vδ2 T cells lead to a maximum induction of their cytolitic function independently of the target cell, as expected.

The percentage of CD107+ cells induced by anti-BTN2A1 107G3 hybridoma supernatant ranged from 71.1 ± 7.4% in Daudi cells to 17.1 ± 2.9% in MDA-MB-134 cells vs. 24.9 ± 4.7% and 4.9 ± 0.4%, respectively, in co-cultures with control hybridoma culture medium. In co-cultures of Vγ9/Vδ2 T cells, with all of the cancer cell lines tested as targets, anti-BTN2A1 107G3 induced between 2-fold and 8-fold more Vγ9/Vδ2 T cell degranulation compared to the same co-cultures in the presence of control hybridoma culture medium.

Purified anti-BTN2A1 mAb 107G3 displayed an EC50 of 0.77 µg/mL (95%IC 0.32 – 13.22 µg/mL) for the induction of Vγ9/Vδ2 T cell degranulation, as depicted by the percentage of CD107+ cells, co-cultured with Daudi cells as targets in the presence of increasing concentrations (0 to 18 µg/ml) of the anti-BTN2A1 107G3 mAb (Figure 2b).

Table 3

	Anti-BTN2A1 107G3	Control hybridoma supernatant
EC_{50} on HEK-293T BTN2 KO + BTN2A1	0.32 (95%IC 0.21-0.46) µg/mL	not applicable

CLAIMS

1. An anti-butyrophilin-2A (BTN2A) antibody characterized in that it has at least one of the following functions:
   i. it inhibits the polarization of monocytes towards M2 macrophages,
   ii. it induces reversion of M2 macrophages towards anti-tumoral M1 macrophages,
   iii. it triggers NK cells activation directly,
   iv. it enhances NK cell-mediated cytotoxicity.

2. The anti-BTN2A antibody of ~~Claim~~ claim 1 which competes for binding to BTN2A1 with
   - the reference antibody mAb 107G3 comprising (i) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:1 and (ii) a light chain variable region comprising the amino acid sequence of SEQ ID NO:2, or
   - the reference antibody mAb 101G5 comprising (i) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:19 and (ii) a light chain variable region comprising the amino acid sequence of SEQ ID NO:20.

3. The antibody of any one of ~~Claim~~ claim 1 or 2, which binds an epitope comprising residues located in positions: 65, 68, 69, 72, 78; 84, 85, 95, 97, and 100 of SEQ ID ~~Nº~~NO:17.

4. The antibody of any one of ~~Claim~~ claim 1 or 2, which binds an epitope comprising residues located in positions 212, 213, 218, 220, 224, and 229 of SEQ ID ~~Nº~~NO:17.

5. The antibody of any one of ~~Claim~~ claim 1 to 4, which does not cross-react with the human BTN3 isoforms, and/or which cross-react with the cynomolgus BTN2A1 ortholog.

6. The anti-BTN2A~~1~~ antibody of any one of the preceding claims comprising:
   - a heavy chain variable region CDR1 comprising SEQ ID NO:3, a heavy chain variable region CDR2 comprising SEQ ID NO:4, a heavy chain variable region CDR3 comprising SEQ ID NO:5, a light chain variable

region CDR1 comprising SEQ ID NO:6, a light chain variable region CDR2 comprising SEQ ID NO:7, and a light chain variable region CDR3 comprising SEQ ID NO:8, or

- a heavy chain variable region CDR1 comprising SEQ ID NO:21, a heavy chain variable region CDR2 comprising SEQ ID NO:22, a heavy chain variable region CDR3 comprising SEQ ID NO:23, a light chain variable region CDR1 comprising SEQ ID NO:24, a light chain variable region CDR2 comprising SEQ ID NO:25 and a light chain variable region CDR3 comprising SEQ ID NO:26.

7. The anti-BTN2A~~1~~ antibody of any one of the preceding claims which comprises:

   - a heavy chain variable region comprising a sequence having at least 90 % identity with the amino acid sequence of SEQ ID NO:1 and a light chain variable region comprising a sequence having at least 90 % identity with the amino acid sequence of SEQ ID NO:2, or
   - a heavy chain variable region comprising a sequence having at least 90 % identity with the amino acid sequence of SEQ ID NO:19 and a light chain variable region comprising a sequence having at least 90 % identity with the amino acid sequence of SEQ ID NO:20.

8. The anti-BTN2A antibody of any one of claims 1-7, wherein said antibody further has at least one of the following functions:

   i. it activates secretion of cytolytic molecules of γ9Vδ2 T cells,
   ii. it activates the cytolytic function of Vγ9Vδ2 T cells, and/or
   iii. it activates the proliferation of Vγ9Vδ2 T cells.

9. The anti-BTN2A antibody of claim 8, which competes for binding to BTN2A1 with the reference murine antibody mAb 107G3 comprising (i) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:1 and (ii) a light chain variable region comprising the amino acid sequence of SEQ ID NO:2.

10. The anti-BTN2A antibody of any one of claim 8 or 9, which comprises:
    - a heavy chain variable region CDR1 comprising SEQ ID NO:3, a heavy chain variable region CDR2 comprising SEQ ID NO:4, a heavy chain variable region CDR3 comprising SEQ ID NO:5, a light chain variable region CDR1 comprising SEQ ID NO:6, a light chain variable region CDR2

comprising SEQ ID NO:7, and a light chain variable region CDR3 comprising SEQ ID NO:8, or

- a heavy chain variable region comprising a sequence having at least 90 % identity with the amino acid sequence of SEQ ID NO:1 and a light chain variable region comprising a sequence having at least 90 % identity with the amino acid sequence of SEQ ID NO:2, or
- a heavy chain variable region comprising a sequence having at least 90 % identity with the amino acid sequence of SEQ ID NO:1 and a light chain variable region comprising a sequence having at least 90 % identity with the amino acid sequence of SEQ ID NO:2.

11. The anti-BTN2A antibody of any one of claims 8-10 having specificity for the human BTN2A1 isoform.

12. The anti-BTN2A antibody of any one of the preceding claims, which is a human, chimeric or humanized antibody.

13. A nucleic acid molecule, which encodes a heavy chain and/or a light chain of the anti-BTN2A antibody of any one of ~~Claims~~ claims 1-10.

14. A host cell comprising the nucleic acid of claim 13.

15. The anti-BTN2A antibody of any one of ~~Claims~~ claims 1-12, for use in therapy.

16. Use of the anti-BTN2A antibody of any one of ~~Claims~~ claims 1-12, in the manufacture of a medicament for treating cancer or infectious diseases.

17. A pharmaceutical composition comprising the anti-BTN2A antibody of any one of ~~Claims~~ claims 1-12, and at least a pharmaceutically acceptable carrier.