

**Supplementary Table S3.** Effect of the cannabinoids on the molecular entities, participating in the interaction between NK and target cells.

| Receptor  | Ligand             | Activity | Effect of cannabinoids   | Reference    |
|-----------|--------------------|----------|--|--------------|
| KIR       |                    |          |  |              |
| KIR2DL2/3 | HLA-C1             | I        | THC upregulates KIR2DL2 RNA levels   | 151          |
| KIR3DL1   | HLA-Bw4, HLA-A     | I        | THC (0.03 mg/kg) upregulates HLA-A expression  | 151          |
| CD94-NKG2 |                    |          |  |              |
| NKG2C     | HLA-E              | A        | THC increases NKG2 RNA expression  | 151          |
| NKG2E     | HLA-E              | A        |  |              |
| NKG2D     | MIC-A, -B; ULBP1-4 | A        | Exposure to SR141716 increases glioma cells susceptibility to NK cell mediated cytotoxicity through the upregulation of NKG2D ligand MICA/B. NK cells exposed to CBD (10 $\mu$ M) does not exhibit any change in NKG2D   | 29, 148, 149 |
| NCR5      |                    |          |  |              |
| NKp30     | BAT-3, HSPG, B7-H6 | A        | THC (75 mg/kg) downregulates B7 (CD86) expression in lung mice cells.  | 152          |
| NKp44     | VIRAL HA           | A        |  |              |
| NKp46     | VIRAL HA, HSPG     | A        | CB2 KO favors NK cell NKp46 expression within the tumor microenvironment   | 25           |
| LILR      | MHC-I UL18         | I        | Cannabinoids differentially induce MHC-I expression in colorectal cancer cells: THC (27 $\mu$ M) 6.1-fold, CBDV (20 $\mu$ M) 5.5 fold, CBV (20 $\mu$ M) 3.9 fold, CBD (11 $\mu$ M) 3.3 fold, CBG (38.9 $\mu$ M) 2.7 fold, CBN (28 $\mu$ M) 1.8 fold, CBC (26 $\mu$ M) 1.6 fold. Synthetic cannabinoid SR141716 does not affect MHC-I in glioblastoma cells WIN55212-2 increases MHC-I in target cell | 148, 153     |
| KLRG1     | Cadherins          | I        | KLRG1 expression is downregulated in cannabis consumers. KLRG1 expression is dependent on CB2 expression   | 154, 155     |
| PILR      | CD99               | A        | CBD (5 $\mu$ M) downregulates CD99 expression in MSCs  | 156          |
| PD1       | PD1L               | I        | WIN55-212-2 increases PD-L1 in cancer cells  | 149          |
| CD69      |                    |          | O1602 favor CD69 overexpression, a functional marker triggering the NK cytotoxicity  | 31           |
| FasL      | Fas                | A        | AEA induced FAS recruitment to plasma membrane in cancer cell; CBD promotes FasL expression; THC; JWH133 and SR141716 decreases Fas and FasL expression  | 157-160      |
| TRAIL     | DR5                | A        | WIN55212-2 favors DR5 expression in TRAIL resistant cancers; CBD substantially upregulates TNF/TNFR1 and TRAIL/TRAIL-R2 signaling by modulation of both ligand and receptor levels   | 161, 162     |