

FIG. 1A

| ID Interna |                | CDR1                      | CDR2                      | CDR3                               |
|------------|----------------|---------------------------|---------------------------|------------------------------------|
| 312557     | SEQ. ID NO: 1  | GFTFDDYA<br>SEQ. ID NO:29 | ISWNSGSI<br>SEQ. ID NO:24 | AKDSRGYGDYRLGGAY<br>SEQ. ID NO:41  |
| 308261     | SEQ. ID NO: 2  | GFTFDDYA<br>SEQ. ID NO:29 | ISWNSGSI<br>SEQ. ID NO:24 | AKDSRGYGDYRLGGAY<br>SEQ. ID NO:41  |
| 308159     | SEQ. ID NO: 3  | GFTFDDYA<br>SEQ. ID NO:29 | ISWNSGSI<br>SEQ. ID NO:24 | AKDSRGYGDYSRGGAY<br>SEQ. ID NO. 42 |
| 308160     | SEQ. ID NO: 4  | GFTFDDYA<br>SEQ. ID NO:29 | ISWNSGSI<br>SEQ. ID NO:24 | AKDSRGYGDYSLGGAY<br>SEQ. ID NO:43  |
| 308256     | SEQ. ID NO: 5  | GFTFDDYA<br>SEQ. ID NO:29 | ISWNSGSI<br>SEQ. ID NO:24 | AKDSRGYGDYSLGGAY<br>SEQ. ID NO:43  |
| 312585     | SEQ. ID NO: 6  | GFTFANYA<br>SEQ. ID NO:30 | ISWNSGSI<br>SEQ. ID NO:24 | AKDSRGYGDYSRGGAY<br>SEQ. ID NO:42  |
| 312614     | SEQ. ID NO: 7  | GFTFNHYA<br>SEQ. ID NO:31 | ISWNSGSI<br>SEQ. ID NO:24 | AKDSRGYGDYSRGGAY<br>SEQ. ID NO:42  |
| 312583     | SEQ. ID NO: 8  | GFTFADYA<br>SEQ. ID NO:32 | ISWNSGSI<br>SEQ. ID NO:24 | AKDSRGYGDYSRGGAY<br>SEQ. ID NO:42  |
| 312586     | SEQ. ID NO: 9  | GFTFDNYA<br>SEQ. ID NO:33 | ISWNSGSI<br>SEQ. ID NO:24 | AKDSRGYGDYSRGGAY<br>SEQ. ID NO:42  |
| 312624     | SEQ. ID NO: 10 | GFTFDNYA<br>SEQ. ID NO:33 | ISWNSGSI<br>SEQ. ID NO:24 | AKDSRGYGDYSRGGAY<br>SEQ. ID NO:42  |
| 312578     | SEQ. ID NO: 11 | GFTFDDYA<br>SEQ. ID NO:29 | ISWNSGSI<br>SEQ. ID NO:24 | AKDSRGYGDYSRGGAY<br>SEQ. ID NO:42  |
| 312620     | SEQ. ID NO: 12 | GFTFDDYA<br>SEQ. ID NO:29 | ISWNSGSI<br>SEQ. ID NO:24 | AKDSRGYGSYSRGGAY<br>SEQ. ID NO:44  |
| 312634     | SEQ. ID NO: 13 | GFTFHNYA<br>SEQ. ID NO:34 | ISWNSGSI<br>SEQ. ID NO:24 | AKDSRGYGDYSLGGAY<br>SEQ. ID NO:43  |
| 312579     | SEQ. ID NO: 14 | GFTFDDYA<br>SEQ. ID NO:29 | ISWNSGSI<br>SEQ. ID NO:24 | AKDSRGYGDYSRGGAY<br>SEQ. ID NO:42  |
| 312630     | SEQ. ID NO: 15 | GFTFDNYA<br>SEQ. ID NO:33 | ISWNSGSI<br>SEQ. ID NO:24 | AKDSRGYGDYSLGGAY<br>SEQ. ID NO:43  |
| 312570     | SEQ. ID NO: 16 | GFTFDDYA<br>SEQ. ID NO:29 | ISWNSGSI<br>SEQ. ID NO:24 | AKDSRGYGDYRLGGAY<br>SEQ. ID NO:41  |
| 312567     | SEQ. ID NO: 17 | GFTFDDYA<br>SEQ. ID NO:29 | ISWNSGSI<br>SEQ. ID NO:24 | AKDSRGYGDYRLGGAY<br>SEQ. ID NO:41  |
| 312558     | SEQ. ID NO: 18 | GFTFDDYA<br>SEQ. ID NO:29 | ISWNSGSI<br>SEQ. ID NO:24 | AKDSRGYGDYRLGGAY<br>SEQ. ID NO:41  |

FIG. 1B

|                  |              |                          |                          |                              |
|------------------|--------------|--------------------------|--------------------------|------------------------------|
| 312325           | SEQ ID NO:19 | QSVSSN<br>SEQ ID NO:35   | GAS<br>SEQ ID NO:38      | QQYNNWPWT<br>SEQ ID NO:45    |
| 308902-bivalente | SEQ ID NO:20 | GFTVSSYG<br>SEQ ID NO:36 | IRGSDGST<br>SEQ ID NO:39 | AKQGENDGPDFH<br>SEQ ID NO:46 |
| 308902           | SEQ ID NO:21 | GFTVSSYG<br>SEQ ID NO:36 | IRGSDGST<br>SEQ ID NO:39 | AKQGENDGPDFH<br>SEQ ID NO:46 |

FIG. 1C

|        |                 |                            |                          |                                      |
|--------|-----------------|----------------------------|--------------------------|--------------------------------------|
| 304703 | SEQ ID<br>NO.22 | GGSISSGGHY<br>SEQ ID NO:37 | IHYSGST<br>SEQ ID. NO:40 | ARWRHDIFAAYPYYYYGMDV<br>SEQ ID NO:47 |
|--------|-----------------|----------------------------|--------------------------|--------------------------------------|

anti-CD3      antígeno  
                 antitumoral

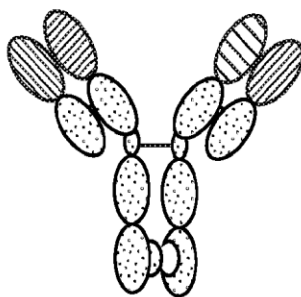


FIG. 2A

anti-CD3      antígeno  
                 antitumoral

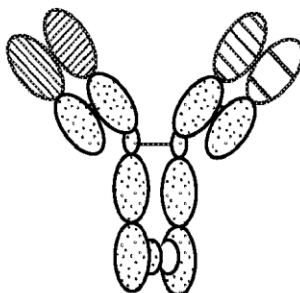


FIG. 2B

anti-CD3      antígeno  
                 antitumoral

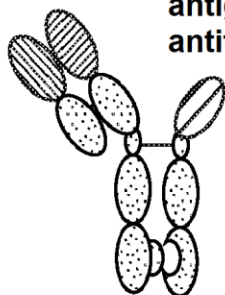


FIG. 2C

**anti-CD3**      **antígeno  
antitumoral**

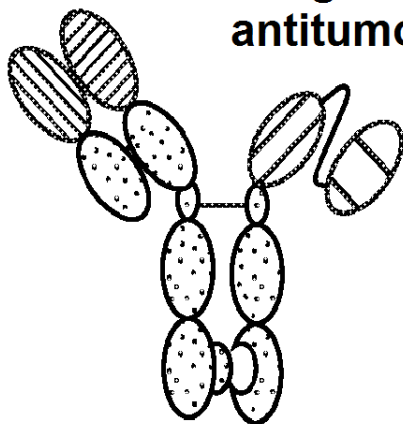


**FIG. 2D**

**antígeno  
antitumoral**      **anti-CD3**

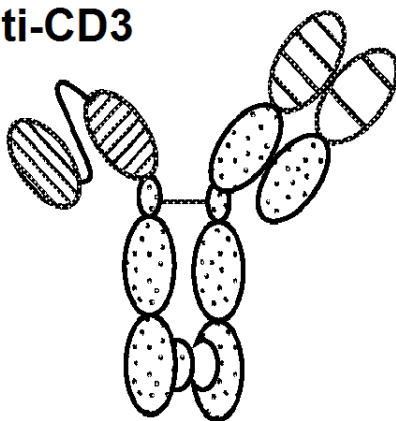


**FIG. 2E**

| Columna                      |                            |                               |                                            |      |      |       |              |              |                    |                       |         |                            |
|------------------------------|----------------------------|-------------------------------|--------------------------------------------|------|------|-------|--------------|--------------|--------------------|-----------------------|---------|----------------------------|
| 1                            | 2                          | 3                             | 4                                          | 5    | 6    | 7     | 8            | 9            | 10                 | 11                    | 12      | 13                         |
| ANTICUERPO ANTI-CD3 ORIGINAL |                            |                               | ANTICUERPO BIESPECIFICO ANTI-CD3/ANTI-BCMA |      |      |       |              |              |                    |                       |         |                            |
| ID de anti-CD3               | unión células Jurkat (MFI) | unión linfocitos T cyno (MFI) | con dosis de BxAb en ng/mL                 | IL-2 | IL-6 | IL-10 | IFN $\gamma$ | TNF $\alpha$ | EC50 dest. (ng/mL) | % de dest. (333ng/mL) | KD (nM) | unión células Jurkat (MFI) |
| 312624                       | 30.5                       | 1.4                           | CD3_F2E-BCMA                               | 130  | 1.0  | 24.1  | 705          | 1787         | 2.0                | 63                    | 227     | 296                        |
| 312585                       | 32.7                       | 0.9                           | CD3_F2C-BCMA                               | 93   | 0.5  | 19.2  | 751          | 1821         | 2.1                | 68                    | 44      | 513                        |
| 312614                       | 32.4                       | 0.9                           | CD3_F2D-BCMA                               | 294  | 1.5  | 89.9  | 1185         | 2387         | 6.1                | 63                    | 86      | 357                        |
| 312634                       | 21.4                       | 1.1                           | CD3_F2F-BCMA                               | 44   | 0.5  | 2.4   | 333          | 485          | 9.8                | 51                    | 714     | 67                         |
| 312608                       | 25.9                       | 1.0                           | CD3_F2A-BCMA                               | 96   | 0.5  | 3.3   | 505          | 1161         | 22.2               | 59                    | 199     | 110                        |
| 312557                       | 6.1                        | 1.0                           | CD3_F2B-BCMA                               | 8    | 0.5  | 0.6   | 154          | 553          | 150.1              | 38                    | 1000    | 31                         |
| 312568                       | 4.1                        | 1.2                           | CD3_F2G-BCMA                               | 1    | 0.5  | 0.5   | 29           | 231          | 352.0              | 12                    | ND      | 9                          |
| 304703                       | 15.9                       | 26.2                          | CD3_F1A-BCMA                               | 212  | 0.8  | 48.5  | 726          | 1844         | 6.4                | 71                    | 98      | 149                        |

FIG. 3

FIG. 4

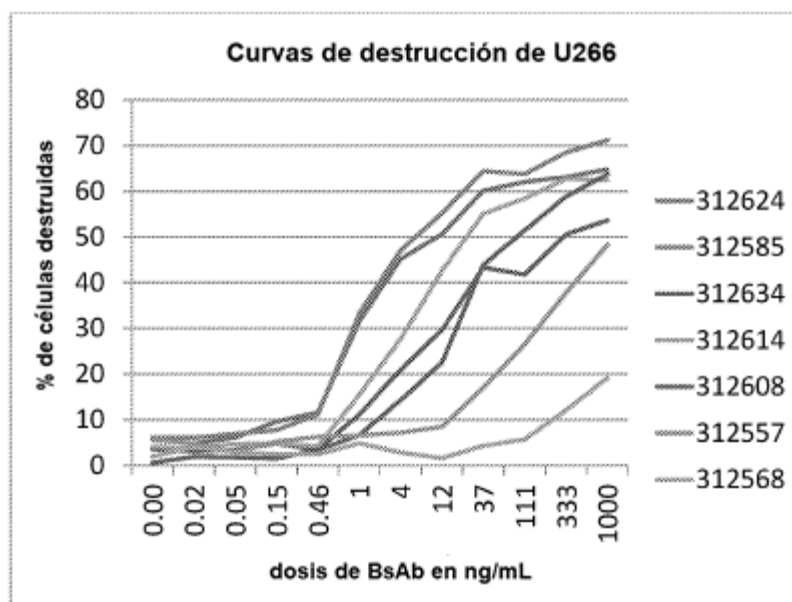


FIG. 5

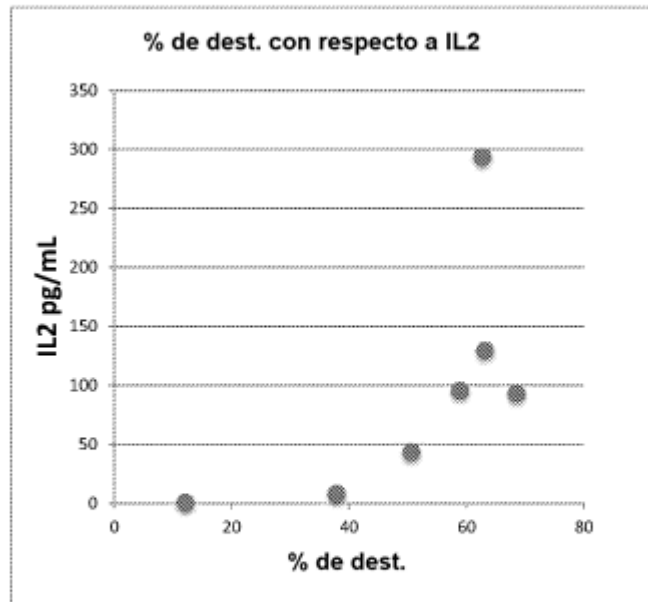


FIG. 6

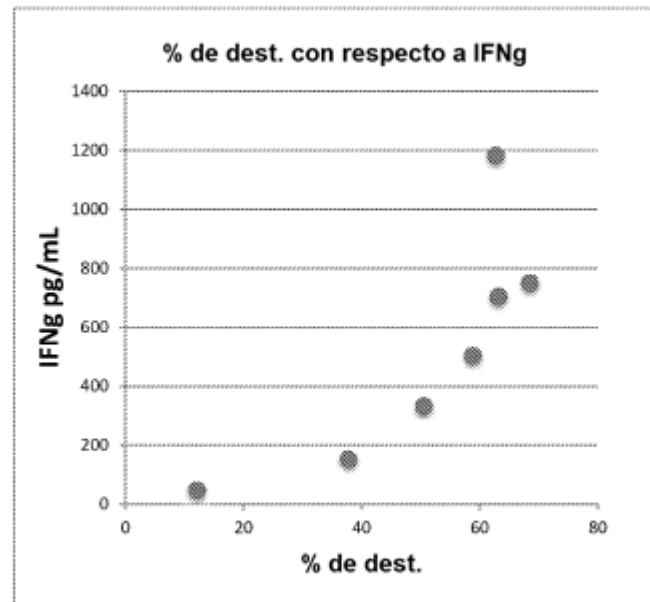


FIG. 7

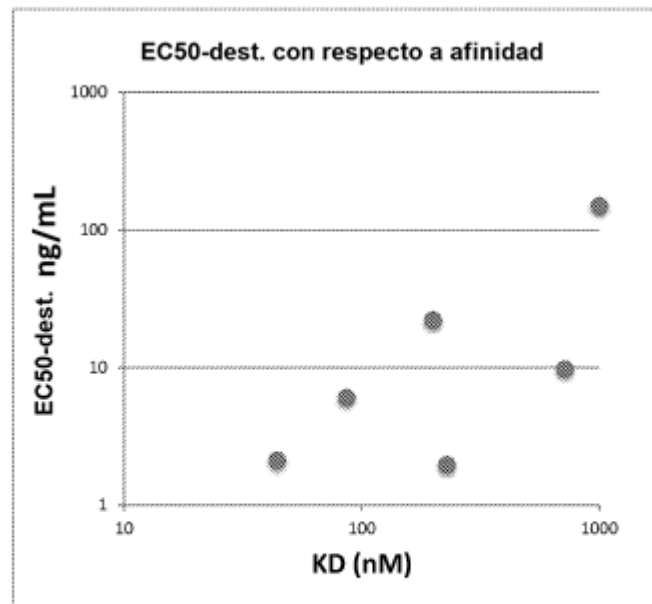


FIG. 8A

RPMI-8226

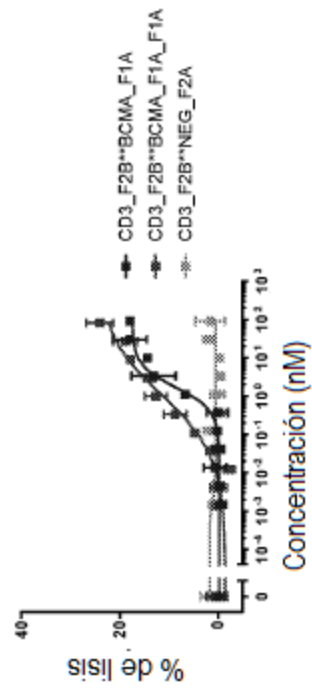


FIG. 8B

NCI-H929

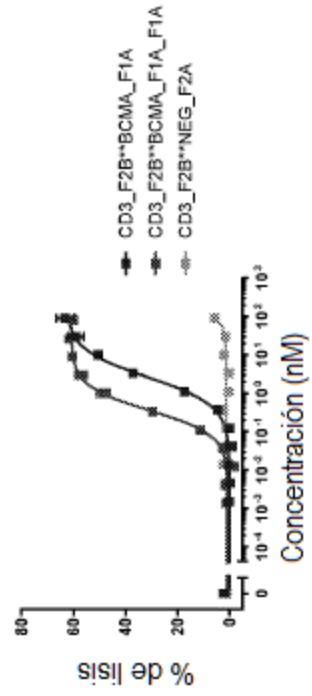


FIG. 8C

U-266

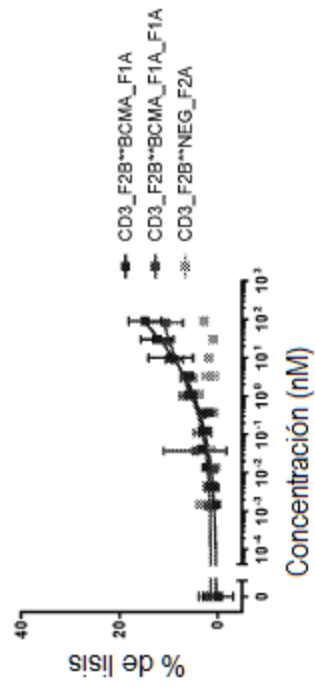


FIG. 8D

K562

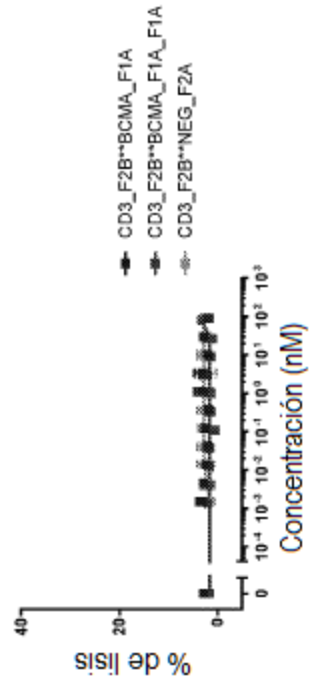


**FIG. 9A** RPMI-8226

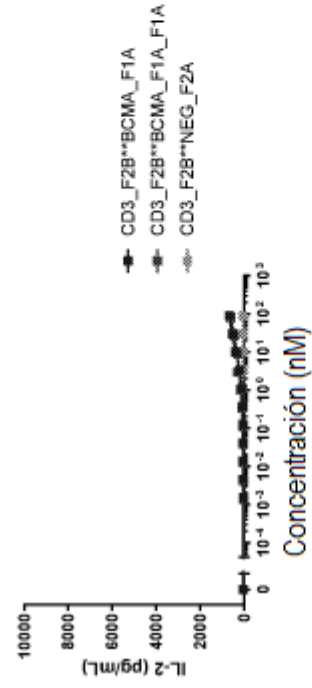


**FIG. 9B** NCI-H929

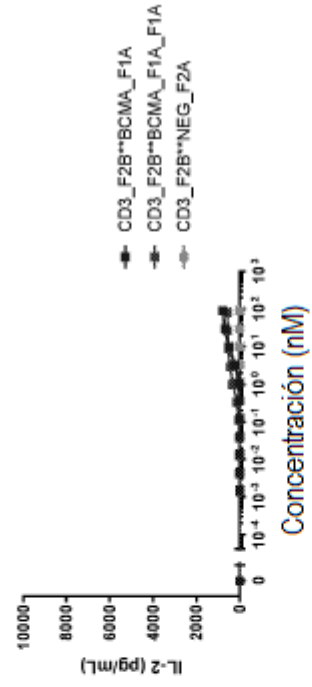


**FIG. 9C** U-266

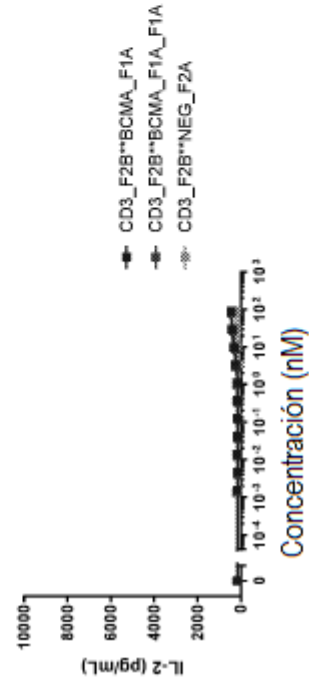


**FIG. 9D** K562

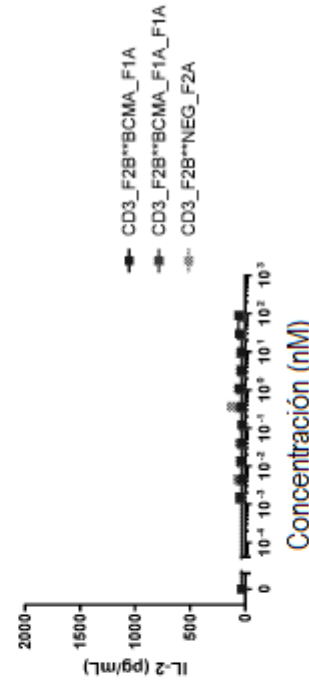


FIG. 10A

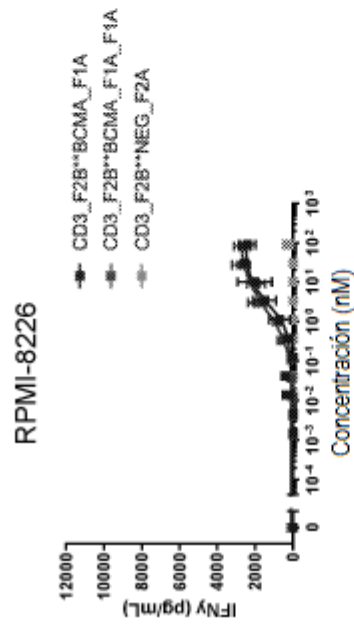


FIG. 10B

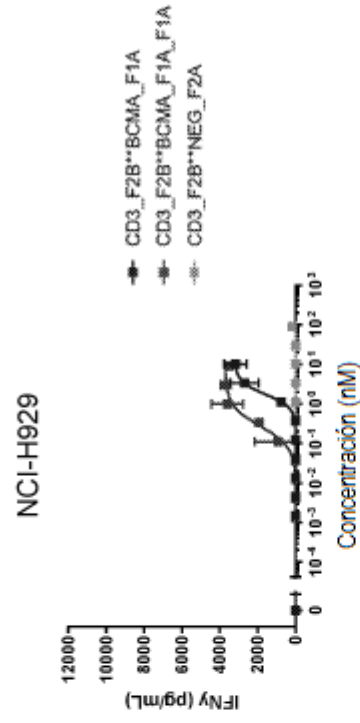


FIG. 10C

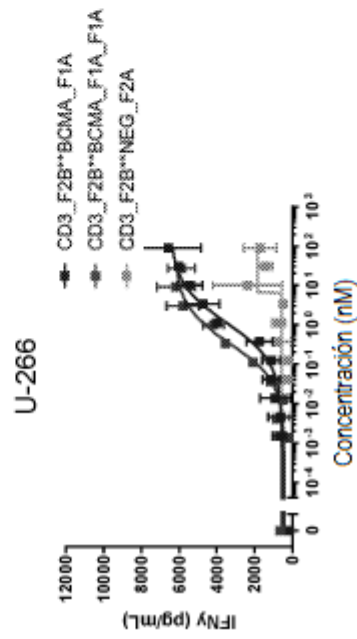


FIG. 10D

