Each year, of the approximately 49,000 patients that will develop RCC, a little over 40,000 of those will be diagnosed with ccRCC in the US (American Cancer Society: Cancer Facts and Figures final (2008). While some newer therapeutics have been approved for RCC over the last 4 years, the 5 year survival rate for patients with metastatic RCC remains dismal at 10-20% (National Caner Institute. SEER cancer statistics fact sheet: cancer of the kidney and renal pelvis -- accessed 2008) and significant unmet medical need remains. The projected yearly number of newly diagnosed ccRCC patients (U.S.) that are expected to express CD27L is approximately 36,000. There are an estimated 64,000 ccRCC patients currently with active disease.

Of the B-cell malignancies reported to aberrantly express CD27L, the B-NHL subsets of diffuse large cell B-cell lymphoma (DLBCL) and follicular lymphoma (FL) show the highest incidence of expression ranging from 33% for FL to 71% for DLBCL as assessed by IHC on frozen sections using a validated antibody (Lens et al., *Brit. J. Hematol.* 106, 491-503 (1999). 50-89 % of B-CLL tumors also express CD27L as assessed by IHC on frozen tumor sections or by flow cytometry on circulating tumor cells (Ranheim et al., *Blood* 85, 3556-3565 (1965); Trentin et al., *Cancer Res.* 57, 4940-4947 (1997)).

Of the 127,000 patients in the US currently with active B-NHL, approximately 50% of these patients present with the DLBCL (intermediate grade) sub-type (Morton et al., *Blood* 107, 265-276 (2002)). Despite Rituxan plus cyclophosphamide, adriamycin, vincristine, prednisone (CHOP) standard of care therapy for DLBCL patients, almost 50% relapse. Therefore an unmet medical need remains in this disease as well.

SUMMARY

The disclosure provides anti-CD27L antigen binding proteins, e.g., antibodies and functional fragments thereof. The anti-CD27L antigen binding proteins are particularly useful in methods of treating diseases and disorders associated with aberrant cell proliferation, e.g., cancer, and/or with inflammation.

In one aspect, the present disclosure refers to a CD27L antigen binding protein comprising a light chain variable domain and a heavy chain variable domain, wherein a) the light chain variable domain comprises an LCDR1 as set forth in SEQ ID NO: 74; an

LCDR2 as set forth in SEQ ID NO: 82; and an LCDR3 as set forth in SEQ ID NO: 90; and the heavy chain variable domain comprises an HCDR1 as set forth in SEQ ID NO: 28; an HCDR2 as set forth in SEQ ID NO: 36; and an HCDR3 as set forth in SEQ ID NO: 44; b) the light chain variable domain comprises the amino acid sequence SEQ ID NO: 66 but has an R24K-S26G mutation, and the heavy chain variable domain comprises the amino acid sequence SEQ ID NO: 20 but has an N31S-I34M mutation; c) the light chain variable domain comprises the amino acid sequence SEQ ID NO: 66 but has an R24K-S26G mutation, and the heavy chain variable domain comprises the amino acid sequence SEQ ID NO: 20; d) the light chain variable domain comprises the amino acid sequence SEQ ID NO: 66 but has an L55I-Y58F mutation, and the heavy chain variable domain comprises the amino acid sequence SEQ ID NO: 20; e) the light chain variable domain comprises the amino acid sequence SEQ ID NO: 66 but has a Q95N-T96S mutation, and the heavy chain variable domain comprises the amino acid sequence SEQ ID NO: 20 but has an N31S-I34M mutation; or f) the light chain variable domain comprises the amino acid sequence SEQ ID NO: 66 but has a Q95N-T96S mutation, and the heavy chain variable domain comprises the amino acid sequence SEQ ID NO: 20.

In another aspect, the present disclosure refers to a composition comprising a CD27L antigen binding protein as described herein, wherein the average number of DM1 molecules per CD27L antigen binding protein is between 1 and 10, preferably between 3 and 7, preferably between 4 and 6, or 4.0, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, or 6.0. In another aspect, the present disclosure refers to an isolated nucleic acid encoding a polypeptide, said polypeptide comprising: a) a light chain variable domain comprising an LCDR1 having the amino acid sequence set forth in SEQ ID NO: 74; an LCDR2 having the amino acid sequence set forth in SEQ ID NO: 82; and an LCDR3 having the amino acid sequence set forth in SEQ ID NO: 90; and a heavy chain variable domain comprising an HCDR1 having the amino acid sequence set forth in SEQ ID NO: 28; an HCDR2 having the amino acid sequence set forth in SEQ ID NO: 36; and an HCDR3 having the amino acid sequence set forth in SEQ ID NO: 44; b) light chain variable domain comprising the amino acid sequence SEQ ID NO: 66 but having an R24K-S26G mutation or a Q95N-T96S mutation; and a heavy chain variable domain

comprising the amino acid sequence SEQ ID NO: 20 but having an N31S-I34M mutation; or c) a light chain variable domain comprising the amino acid sequence SEQ ID NO: 66 but having an L55I-Y58F mutation; and a heavy chain variable domain comprising the amino acid sequence SEQ ID NO: 20.

In yet another aspect, the present disclosure refers to an expression vector comprising the isolated nucleic acid as described herein. In yet another aspect, the present disclosure refers to a recombinant host cell comprising an isolated nucleic acid as described herein operably linked to a promoter, or comprising an expression vector as described herein. In yet another aspect, the present disclosure refers to a method of making a CD27L antibody drug conjugate, said method comprising the steps of: (i) a) providing a CD27L antigen binding protein as described herein b) conjugating the CD27L antigen binding protein to a linker; and c) conjugating a drug to said linker; wherein the linker preferably comprises MCC; the drug preferably comprises DM1; or the linker preferably comprises MCC and the drug preferably comprises DM1; or (ii) a) providing a CD27L antigen binding protein as described herein; and b) conjugating a linker covalently bound to a drug to said CD27L antigen binding protein. In a further aspect, the present disclosure refers to use of the CD27L antigen binding protein as described herein conjugated to DM1 by an MCC linker, in the manufacture of a medicament for treating cancer.

In a first example, the CD27L antigen binding protein comprises a) a light chain variable domain having at least 90% identity, at least 95% identity, or is identical to the amino acid sequence set forth in SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, or SEQ ID NO:70; b) a heavy chain variable domain having at least 90% identity, at least 95% identity, or is identical to the amino acid sequence set forth in SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, or SEQ ID NO:24; or c) the light chain variable domain of a) and the heavy chain variable domain of b).

Preferred antigen binding proteins of the first example include those comprising a light chain variable domain having at least 90%, at least 95%, or is identical to the amino acid sequence set forth in SEQ ID NO:63 and a heavy chain variable domain having at

least 90%, at least 95%, or is identical to the amino acid sequence set forth in SEQ ID NO:17; those comprising a light chain variable domain having at least 90%, at least 95%, or is identical to the amino acid sequence set forth in SEQ ID NO:64 and a heavy chain variable domain having at least 90%, at least 95%, or is identical to the amino acid sequence set forth in SEQ ID NO:18; those comprising a light chain variable domain having at least 90%, at least 95%, or is identical to the amino acid sequence set forth in SEQ ID NO:65 and a heavy chain variable domain having at least 90%, at least 95%, or is identical to the amino acid sequence set forth in SEQ ID NO:19; those comprising a light chain variable domain having at least 90%, at least 95%, or is identical to the amino acid sequence set forth in SEQ ID NO:66 and a heavy chain variable domain having at least 90%, at least 95%, or is identical to the amino acid sequence set forth in SEQ ID NO:20; those comprising a light chain variable domain having at least 90%, at least 95%, or is identical to the amino acid sequence set forth in SEQ ID NO:67 and a heavy chain variable domain having at least 90%, at least 95%, or is identical to the amino acid sequence set forth in SEQ ID NO:21; those comprising a light chain variable domain having at least 90%, at least 95%, or is identical to the amino acid sequence set forth in SEQ ID NO:68 and a heavy chain variable domain having at least 90%, at least 95%, or is identical to the amino acid sequence set forth in SEQ ID NO:22; those comprising a light chain variable domain having at least 90%, at least 95%, or is identical to the amino acid sequence set forth in SEQ ID NO:69 and a heavy chain variable domain having at least 90%, at least 95%, or is identical to the amino acid sequence set forth in SEQ ID NO:23; and those comprising a light chain variable domain having at least 90%, at least 95%, or is identical to the amino acid sequence set forth in SEQ ID NO:70 and a heavy chain variable domain having at least 90%, at least 95%, or is identical to the amino acid sequence set forth in SEQ ID NO:24.

In a second example, the CD27L antigen binding protein comprises a) a light chain variable domain having no more than ten or no more than five amino acid additions, deletions or substitutions from the amino acid sequence set forth in SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, or SEQ ID NO:70; b) a heavy chain variable domain having no more than ten or no more than five amino acid additions, deletions or substitutions from

the amino acid sequence set forth in SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, or SEQ ID NO:24; or c) the light chain variable domain of a) and the heavy chain variable domain of b).

Preferred antigen binding proteins of the second example include those comprising a light chain variable domain having no more than ten or no more than five amino acid additions, deletions or substitutions from the amino acid sequence set forth in SEQ ID NO:63 and a heavy chain variable domain having no more than ten or no more than five amino acid additions, deletions or substitutions from the amino acid sequence set forth in SEQ ID NO:17; those comprising a light chain variable domain having no more than ten or no more than five amino acid additions, deletions or substitutions from the amino acid sequence set forth in SEQ ID NO:64 and a heavy chain variable domain having no more than ten or no more than five amino acid additions, deletions or substitutions from the amino acid sequence set forth in SEQ ID NO:18; those comprising a light chain variable domain having no more than ten or no more than five amino acid additions, deletions or substitutions from the amino acid sequence set forth in SEQ ID NO:65 and a heavy chain variable domain having no more than ten or no more than five amino acid additions, deletions or substitutions from the amino acid sequence set forth in SEQ ID NO:19; those comprising a light chain variable domain having no more than ten or no more than five amino acid additions, deletions or substitutions from the amino acid sequence set forth in SEQ ID NO:66 and a heavy chain variable domain having no more than ten or no more than five amino acid additions, deletions or substitutions from the amino acid sequence set forth in SEQ ID NO:20; those comprising a light chain variable domain having no more than ten or no more than five amino acid additions, deletions or substitutions from the amino acid sequence set forth in SEQ ID NO:67 and a heavy chain variable domain having no more than ten or no more than five amino acid additions, deletions or substitutions from the amino acid sequence set forth in SEQ ID NO:21; those comprising a light chain variable domain having no more than ten or no more than five amino acid additions, deletions or substitutions from the amino acid sequence set forth in SEQ ID NO:68 and a heavy chain variable domain having no more than ten or no more than five amino acid additions, deletions or substitutions from the amino acid sequence set forth in SEQ ID NO:22; those comprising a light chain variable domain having no

more than ten or no more than five amino acid additions, deletions or substitutions from the amino acid sequence set forth in SEQ ID NO:69 and a heavy chain variable domain having no more than ten or no more than five amino acid additions, deletions or substitutions from the amino acid sequence set forth in SEQ ID NO:23; and those comprising a light chain variable domain having no more than ten or no more than five amino acid additions, deletions or substitutions from the amino acid sequence set forth in SEQ ID NO:70 and a heavy chain variable domain having no more than ten or no more than five amino acid additions, deletions or substitutions from the amino acid sequence set forth in SEQ ID NO:24.

In a third example, the CD27L antigen binding protein contains a light chain variable domain comprising a) an LCDR1 having no more than three amino acid additions, deletions, or substitutions from the LCDR1 sequence set forth in SEQ ID NO:71; an LCDR2 having no more than three amino acid additions, deletions, or substitutions from the LCDR2 sequence set forth in SEQ ID NO:79; and an LCDR3 having no more than three amino acid additions, deletions, or substitutions from the LCDR3 sequence set forth in SEQ ID NO:87; b) an LCDR1 having no more than three amino acid additions, deletions, or substitutions from the LCDR1 sequence set forth in SEQ ID NO:72; an LCDR2 having no more than three amino acid additions, deletions, or substitutions from the LCDR2 sequence set forth in SEQ ID NO:80; and an LCDR3 having no more than three amino acid additions, deletions, or substitutions from the LCDR3 sequence set forth in SEQ ID NO:88; c) an LCDR1 having no more than three amino acid additions, deletions, or substitutions from the LCDR1 sequence set forth in SEQ ID NO:73; an LCDR2 having no more than three amino acid additions, deletions, or substitutions from the LCDR2 sequence set forth in SEQ ID NO:81; and an LCDR3 having no more than three amino acid additions, deletions, or substitutions from the LCDR3 sequence set forth in SEQ ID NO:89; d) an LCDR1 having no more than three amino acid additions, deletions, or substitutions from the LCDR1 sequence set forth in SEQ ID NO:74; an LCDR2 having no more than three amino acid additions, deletions, or substitutions from the LCDR2 sequence set forth in SEQ ID NO:82; and an LCDR3 having no more than three amino acid additions, deletions, or substitutions from the LCDR3 sequence set forth in SEQ ID NO:90; e) an LCDR1 having no more than three

amino acid additions, deletions, or substitutions from the LCDR1 sequence set forth in SEQ ID NO:75; an LCDR2 having no more than three amino acid additions, deletions, or substitutions from the LCDR2 sequence set forth in SEQ ID NO:83; and an LCDR3 having no more than three amino acid additions, deletions, or substitutions from the LCDR3 sequence set forth in SEQ ID NO:91; f) an LCDR1 having no more than three amino acid additions, deletions, or substitutions from the LCDR1 sequence set forth in SEQ ID NO:76; an LCDR2 having no more than three amino acid additions, deletions, or substitutions from the LCDR2 sequence set forth in SEQ ID NO:84; and an LCDR3 having no more than three amino acid additions, deletions, or substitutions from the LCDR3 sequence set forth in SEQ ID NO:92; g) an LCDR1 having no more than three amino acid additions, deletions, or substitutions from the LCDR1 sequence set forth in SEQ ID NO:77; an LCDR2 having no more than three amino acid additions, deletions, or substitutions from the LCDR2 sequence set forth in SEQ ID NO:85; and an LCDR3 having no more than three amino acid additions, deletions, or substitutions from the LCDR3 sequence set forth in SEQ ID NO:93; or h) an LCDR1 having no more than three amino acid additions, deletions, or substitutions from the LCDR1 sequence set forth in SEQ ID NO:78; an LCDR2 having no more than three amino acid additions, deletions, or substitutions from the LCDR2 sequence set forth in SEQ ID NO:86; and an LCDR3 having no more than three amino acid additions, deletions, or substitutions from the LCDR3 sequence set forth in SEQ ID NO:94; and a heavy chain variable domain comprising i) an HCDR1 having no more than three amino acid additions, deletions, or substitutions from the HCDR1 sequence set forth in SEQ ID NO:25; an HCDR2 having no more than three amino acid additions, deletions, or substitutions from the HCDR2 sequence set forth in SEQ ID NO:33; and an HCDR3 having no more than three amino acid additions, deletions, or substitutions from the HCDR3 sequence set forth in SEQ ID NO:41; j) an HCDR1 having no more than three amino acid additions, deletions, or substitutions from the HCDR1 sequence set forth in SEQ ID NO:26; an HCDR2 having no more than three amino acid additions, deletions, or substitutions from the HCDR2 sequence set forth in SEQ ID NO:34; and an HCDR3 having no more than three amino acid additions, deletions, or substitutions from the HCDR3 sequence set forth in SEQ ID NO:42; k) an HCDR1 having no more than three amino acid additions, deletions, or

substitutions from the HCDR1 sequence set forth in SEQ ID NO:27; an HCDR2 having no more than three amino acid additions, deletions, or substitutions from the HCDR2 sequence set forth in SEQ ID NO:35; and an HCDR3 having no more than three amino acid additions, deletions, or substitutions from the HCDR3 sequence set forth in SEQ ID NO:43; l) an HCDR1 having no more than three amino acid additions, deletions, or substitutions from the HCDR1 sequence set forth in SEQ ID NO:28; an HCDR2 having no more than three amino acid additions, deletions, or substitutions from the HCDR2 sequence set forth in SEQ ID NO:36; and an HCDR3 having no more than three amino acid additions, deletions, or substitutions from the HCDR3 sequence set forth in SEQ ID NO:44; m) an HCDR1 having no more than three amino acid additions, deletions, or substitutions from the HCDR1 sequence set forth in SEQ ID NO:29; an HCDR2 having no more than three amino acid additions, deletions, or substitutions from the HCDR2 sequence set forth in SEQ ID NO:37; and an HCDR3 having no more than three amino acid additions, deletions, or substitutions from the HCDR3 sequence set forth in SEQ ID NO:45; n) an HCDR1 having no more than three amino acid additions, deletions, or substitutions from the HCDR1 sequence set forth in SEQ ID NO:30; an HCDR2 having no more than three amino acid additions, deletions, or substitutions from the HCDR2 sequence set forth in SEQ ID NO:38; and an HCDR3 having no more than three amino acid additions, deletions, or substitutions from the HCDR3 sequence set forth in SEQ ID NO:46; o) an HCDR1 having no more than three amino acid additions, deletions, or substitutions from the HCDR1 sequence set forth in SEQ ID NO:31; an HCDR2 having no more than three amino acid additions, deletions, or substitutions from the HCDR2 sequence set forth in SEQ ID NO:39; and an HCDR3 having no more than three amino acid additions, deletions, or substitutions from the HCDR3 sequence set forth in SEQ ID NO:47; or p) an HCDR1 having no more than three amino acid additions, deletions, or substitutions from the HCDR1 sequence set forth in SEQ ID NO:32; an HCDR2 having no more than three amino acid additions, deletions, or substitutions from the HCDR2 sequence set forth in SEQ ID NO:40; and an HCDR3 having no more than three amino acid additions, deletions, or substitutions from the HCDR3 sequence set forth in SEQ ID NO:48.

Preferred CD27L antigen binding proteins of third example include those comprising the light chain variable domain of a) and the heavy chain variable domain of i); those comprising the light chain variable domain of b) and the heavy chain variable domain of j); those comprising the light chain variable domain of c) and the heavy chain variable domain of k); those comprising the light chain variable domain of d) and the heavy chain variable domain of l); those comprising the light chain variable domain of e) and the heavy chain variable domain of m); those comprising the light chain variable domain of f) and the heavy chain variable domain of n); those comprising the light chain variable domain of g) and the heavy chain variable domain of o); and those comprising the light chain variable domain of h) and the heavy chain variable domain of p).

In a fourth example of the disclosure, the CD27L antigen binding protein of the first, second, or third example binds to human CD27L with an affinity of less than or equal to 2×10^{-11} M.

In a fifth example of the disclosure, the CD27L antigen binding protein of the first, second, third, or fourth example inhibits binding of CD27L to CD27.

In a sixth example of the disclosure, the CD27L antigen binding protein of the first, second, third, fourth, or fifth example is an antibody, such as a human antibody. Preferred antibodies include those antibodies that comprise a light chain having the amino acid sequence set forth in SEQ ID:56 and a heavy chain having the amino acid sequence set forth in SEQ ID NO:10; those that comprise a light chain having the amino acid sequence set forth in SEQ ID:57 and a heavy chain having the amino acid sequence set forth in SEQ ID NO:11; those that comprise a light chain having the amino acid sequence set forth in SEQ ID:58 and a heavy chain having the amino acid sequence set forth in SEQ ID NO:12; those that comprise a light chain having the amino acid sequence set forth in SEQ ID:59 and a heavy chain having the amino acid sequence set forth in SEQ ID NO:13; those that comprise a light chain having the amino acid sequence set forth in SEQ ID:60 and a heavy chain having the amino acid sequence set forth in SEQ ID NO:14; those that comprise a light chain having the amino acid sequence set forth in SEQ ID:61 and a heavy chain having the amino acid sequence set forth in SEQ ID NO:15; and those that comprise a light chain having the amino acid sequence set forth in

SEQ ID:62 and a heavy chain having the amino acid sequence set forth in SEQ ID NO:16.

In a seventh example, a CD27L antigen binding protein of the first, second, third, fourth, fifth, or sixth example is conjugated to a drug or chemotherapeutic agent. In preferred examples, the drug or chemotherapeutic agent is conjugated to the antigen binding protein, e.g. antibody, using a linker. Preferred linkers include non-cleavable linkers such as MCC. A preferred chemotherapeutic agent is DM1. Thus, in particularly preferred examples, the seventh example provides a CD27L antigen binding protein of the first, second, third, fourth, fifth, or sixth example conjugated to DM1 by a MCC linker attached to one or more lysine residues.

The process of conjugating DM1 to a CD27L antigen binding protein, e.g. antibody, will produce a composition comprising a population of DM1-conjugated antibodies having a range of DM1 molecules per antibody. It is possible to measure an average number for the composition. In preferred examples, the average number of DM1 molecules per CD27L antigen binding protein, e.g. antibody, is between 1 and 10, between 3 and 7, or between 4 and 6. In preferred examples, the composition of CD27L antigen binding proteins of the first, second, third, fourth, fifth, sixth, or seventh example of this disclosure has an average number of DM1 molecules per CD27L antigen binding protein of about 4.0, about 4.1, about 4.2, about 4.3, about 4.4, about 4.5, about 4.6, about 4.7, about 4.8, about 4.9, about 5.0, about 5.1, about 5.2, about 5.3, about 5.4, about 5.5, about 5.6, about 5.7, about 5.8, about 5.9, or about 6.0. Such a composition may contain a therapeutically effective amount of the CD27L antigen binding protein and may be lyophilized.

In an eight example, the disclosure provides isolated nucleic acids encoding one or more polypeptide components of a CD27L antigen binding protein, e.g., an antibody light chain or antibody heavy chain. In preferred examples the nucleic acid encodes a polypeptide comprising:

a) a light chain variable domain having at least 95% identity to the amino acid sequence set forth in SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, or SEQ ID NO:70;

b) a heavy chain variable domain having at least 95% identity to the amino acid sequence set forth in SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, or SEQ ID NO:24;

c) a light chain variable domain having no more than five amino acid additions, deletions or substitutions from the amino acid sequence set forth in SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, or SEQ ID NO:70;

d) a heavy chain variable domain having no more than five amino acid additions, deletions or substitutions from the amino acid sequence set forth in SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, or SEQ ID NO:24;

e) a light chain variable domain comprising:

i) an LCDR1 having no more than three amino acid additions, deletions, or substitutions from the LCDR1 sequence set forth in SEQ ID NO:71; an LCDR2 having no more than three amino acid additions, deletions, or substitutions from the LCDR2 sequence set forth in SEQ ID NO:79; and an LCDR3 having no more than three amino acid additions, deletions, or substitutions from the LCDR3 sequence set forth in SEQ ID NO:87;

ii) an LCDR1 having no more than three amino acid additions, deletions, or substitutions from the LCDR1 sequence set forth in SEQ ID NO:72; an LCDR2 having no more than three amino acid additions, deletions, or substitutions from the LCDR2 sequence set forth in SEQ ID NO:80; and an LCDR3 having no more than three amino acid additions, deletions, or substitutions from the LCDR3 sequence set forth in SEQ ID NO:88;

iii) an LCDR1 having no more than three amino acid additions, deletions, or substitutions from the LCDR1 sequence set forth in SEQ ID NO:73; an LCDR2 having no more than three amino acid additions, deletions, or substitutions from the LCDR2 sequence set forth in SEQ ID NO:81; and an LCDR3 having no more than three amino acid additions, deletions, or substitutions from the LCDR3 sequence set forth in SEQ ID NO:89;

iv) an LCDR1 having no more than three amino acid additions, deletions, or substitutions from the LCDR1 sequence set forth in SEQ ID NO:74; an LCDR2 having no more than three amino acid additions, deletions, or substitutions from the LCDR2 sequence set forth in SEQ ID NO:82; and an LCDR3 having no more than three amino acid additions, deletions, or substitutions from the LCDR3 sequence set forth in SEQ ID NO:90;

v) an LCDR1 having no more than three amino acid additions, deletions, or substitutions from the LCDR1 sequence set forth in SEQ ID NO:75; an LCDR2 having no more than three amino acid additions, deletions, or substitutions from the LCDR2 sequence set forth in SEQ ID NO:83; and an LCDR3 having no more than three amino acid additions, deletions, or substitutions from the LCDR3 sequence set forth in SEQ ID NO:91;

vi) an LCDR1 having no more than three amino acid additions, deletions, or substitutions from the LCDR1 sequence set forth in SEQ ID NO:76; an LCDR2 having no more than three amino acid additions, deletions, or substitutions from the LCDR2 sequence set forth in SEQ ID NO:84; and an LCDR3 having no more than three amino acid additions, deletions, or substitutions from the LCDR3 sequence set forth in SEQ ID NO:92;

vii) an LCDR1 having no more than three amino acid additions, deletions, or substitutions from the LCDR1 sequence set forth in SEQ ID NO:77; an LCDR2 having no more than three amino acid additions, deletions, or substitutions from the LCDR2 sequence set forth in SEQ ID NO:85; and an LCDR3 having no more than three amino acid additions, deletions, or substitutions from the LCDR3 sequence set forth in SEQ ID NO:93; or

viii) an LCDR1 having no more than three amino acid additions, deletions, or substitutions from the LCDR1 sequence set forth in SEQ ID NO:78; an LCDR2 having no more than three amino acid additions, deletions, or substitutions from the LCDR2 sequence set forth in SEQ ID NO:86; and an LCDR3 having no more than three amino acid additions, deletions, or substitutions from the LCDR3 sequence set forth in SEQ ID NO:94; or

f) a heavy chain variable domain comprising:

i) an HCDR1 having no more than three amino acid additions, deletions, or substitutions from the HCDR1 sequence set forth in SEQ ID NO:25; an HCDR2 having no more than three amino acid additions, deletions, or substitutions from the HCDR2 sequence set forth in SEQ ID NO:33; and an HCDR3 having no more than three amino acid additions, deletions, or substitutions from the HCDR3 sequence set forth in SEQ ID NO:41;

ii) an HCDR1 having no more than three amino acid additions, deletions, or substitutions from the HCDR1 sequence set forth in SEQ ID NO:26; an HCDR2 having no more than three amino acid additions, deletions, or substitutions from the HCDR2 sequence set forth in SEQ ID NO:34; and an HCDR3 having no more than three amino acid additions, deletions, or substitutions from the HCDR3 sequence set forth in SEQ ID NO:42;

iii) an HCDR1 having no more than three amino acid additions, deletions, or substitutions from the HCDR1 sequence set forth in SEQ ID NO:27; an HCDR2 having no more than three amino acid additions, deletions, or substitutions from the HCDR2 sequence set forth in SEQ ID NO:35; and an HCDR3 having no more than three amino acid additions, deletions, or substitutions from the HCDR3 sequence set forth in SEQ ID NO:43;

iv) an HCDR1 having no more than three amino acid additions, deletions, or substitutions from the HCDR1 sequence set forth in SEQ ID NO:28; an HCDR2 having no more than three amino acid additions, deletions, or substitutions from the HCDR2 sequence set forth in SEQ ID NO:36; and an HCDR3 having no more than three amino acid additions, deletions, or substitutions from the HCDR3 sequence set forth in SEQ ID NO:44;

v) an HCDR1 having no more than three amino acid additions, deletions, or substitutions from the HCDR1 sequence set forth in SEQ ID NO:29; an HCDR2 having no more than three amino acid additions, deletions, or substitutions from the HCDR2 sequence set forth in SEQ ID NO:37; and an HCDR3 having no more than three amino acid additions, deletions, or substitutions from the HCDR3 sequence set forth in SEQ ID NO:45;

vi) an HCDR1 having no more than three amino acid additions, deletions, or substitutions from the HCDR1 sequence set forth in SEQ ID NO:30; an HCDR2 having no more than three amino acid additions, deletions, or substitutions from the HCDR2 sequence set forth in SEQ ID NO:38; and an HCDR3 having no more than three amino acid additions, deletions, or substitutions from the HCDR3 sequence set forth in SEQ ID NO:46;

vii) an HCDR1 having no more than three amino acid additions, deletions, or substitutions from the HCDR1 sequence set forth in SEQ ID NO:31; an HCDR2 having no more than three amino acid additions, deletions, or substitutions from the HCDR2 sequence set forth in SEQ ID NO:39; and an HCDR3 having no more than three amino acid additions, deletions, or substitutions from the HCDR3 sequence set forth in SEQ ID NO:47; or

viii) an HCDR1 having no more than three amino acid additions, deletions, or substitutions from the HCDR1 sequence set forth in SEQ ID NO:32; an HCDR2 having no more than three amino acid additions, deletions, or substitutions from the HCDR2 sequence set forth in SEQ ID NO:40; and an HCDR3 having no more than three amino acid additions, deletions, or substitutions from the HCDR3 sequence set forth in SEQ ID NO:48.

In certain examples, the polypeptide encodes an antibody light chain and is at least 80%, at least 90%, at least 95%, or is 100% identical to the nucleotide sequence set forth in SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, or SEQ ID NO:55. In other examples, the polypeptide encodes an antibody heavy chain and is at least 80%, at least 90%, at least 95%, or is 100% identical to the nucleotide sequence set forth in SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, or SEQ ID NO:9.

In a ninth example, the disclosure provides an expression vector comprising one or more isolated nucleic acids of the eighth example. In certain examples, the expression vector encodes an antibody light chain, an antibody heavy chain, or both an antibody light chain and a heavy chain.

In a tenth example, the disclosure provides a recombinant host cell comprising one or more isolated nucleic acids of the eighth example operably linked to a promoter,

including recombinant host cells comprising one or more expression vectors of the ninth example of the disclosure. In preferred examples, the recombinant host cell secretes an antibody that binds CD27L. Preferred host cells are mammalian host cells, including CHO cell lines.

In an eleventh example, the disclosure provides methods of making a CD27L antibody drug conjugate of the seventh example by conjugating a linker and drug, e.g., chemotherapeutic agent, to any of the CD27L antigen binding proteins of the first, second, third, fourth, fifth, or sixth examples. The linker and drug may be connect first and then conjugated to the CD27L antigen binding protein or the linker may be first conjugated to the CD27L antigen binding protein then connected to the drug. In preferred examples, the linker is MCC and the drug is DM1. In particularly preferred examples, the CD27L antigen binding protein is an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:63 and a heavy chain variable domain amino acid sequence as set forth in SEQ ID NO:17 (e.g., Ab1), an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:64 and a heavy chain variable domain amino acid sequence as set forth in SEQ ID NO:18 (e.g., Ab2), an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:65 and a heavy chain variable domain amino acid sequence as set forth in SEQ ID NO:19 (e.g., Ab3), an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:66 and a heavy chain variable domain amino acid sequence as set forth in SEQ ID NO:20 (e.g., Ab4), an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:67 and a heavy chain variable domain amino acid sequence as set forth in SEQ ID NO:21 (e.g., Ab5), an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:68 and a heavy chain variable domain amino acid sequence as set forth in SEQ ID NO:22 (e.g., Ab6), an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:69 and a heavy chain variable domain amino acid sequence as set forth in SEQ ID NO:23 (e.g., Ab7), or an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:70 and a heavy chain variable domain amino acid sequence as set forth in

SEQ ID NO:24 (e.g., Ab8) conjugated to DM1 by MCC by chemically reacting one or more lysine residues within the antibody with MCC or MCC-DM1.

In a twelfth example, the disclosure provides methods of treating cancer comprising administering to a patient a therapeutically effective amount of a composition comprising a therapeutically effective amount of a CD27L antigen binding protein of the first, second, third, fourth, fifth, or sixth example. In preferred examples, the CD27L antigen binding protein is an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:63 and a heavy chain variable domain amino acid sequence as set forth in SEQ ID NO:17 (e.g., Ab1), an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:64 and a heavy chain variable domain amino acid sequence as set forth in SEQ ID NO:18 (e.g., Ab2), an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:65 and a heavy chain variable domain amino acid sequence as set forth in SEQ ID NO:19 (e.g., Ab3), an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:66 and a heavy chain variable domain amino acid sequence as set forth in SEQ ID NO:20 (e.g., Ab4), an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:67 and a heavy chain variable domain amino acid sequence as set forth in SEQ ID NO:21 (e.g., Ab5), an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:68 and a heavy chain variable domain amino acid sequence as set forth in SEQ ID NO:22 (e.g., Ab6), an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:69 and a heavy chain variable domain amino acid sequence as set forth in SEQ ID NO:23 (e.g., Ab7), or an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:70 and a heavy chain variable domain amino acid sequence as set forth in SEQ ID NO:24 (e.g., Ab8). In particularly preferred examples, the CD27L antigen binding protein is conjugated to a chemotherapeutic agent (e.g., DM1) by a linker (MCC). In other preferred examples of the twelfth example, the antibody comprises enhanced effector function.

In some examples, the CD27L antigen binding protein is administered to a patient having renal cell carcinomas (RCC), clear cell RCC, head and neck cancer,

glioblastoma, breast cancer, brain tumor, nasopharangeal carcinoma, non-Hodgkin's lymphoma (NHL), acute lymphocytic leukemia (ALL), chronic lymphocytic leukemia (CLL), Burkitt's lymphoma, anaplastic large-cell lymphomas (ALCL), multiple myeloma, cutaneous T-cell lymphomas, nodular small cleaved-cell lymphomas, lymphocytic lymphomas, peripheral T-cell lymphomas, Lennert's lymphomas, immunoblastic lymphoma, T-cell leukemia/lymphomas (ATLL), adult T-cell leukemia (T-ALL), entroblastic/centrocytic (cb/cc) follicular lymphoma cancer, diffuse large cell lymphoma of B lineage, angioimmunoblastic lymphadenopathy (AILD)-like T cell lymphoma, HIV associated body cavity based lymphoma, embryonal carcinoma, undifferentiated carcinoma of the rhino-pharynx, Castleman's disease, Kaposi's Sarcoma, multiple myeloma, Waldenstrom's macroglobulinemia or other B-cell lymphoma.

In certain examples, a sample from a patient is tested for CD27L expression prior to administering the CD27L antigen binding protein. CD27L expression may be determined by testing for the presence of CD27L-encoding RNA or for the presence of CD27L protein in the sample. The sample may be a blood sample or biopsy.

In a thirteenth example, the disclosure provides methods of treating an autoimmune or inflammatory disorder said method comprising administering a therapeutically effective amount of a CD27L antigen binding protein of any one of the first, second, third, fourth, fifth, or sixth examples to a patient in need thereof. In preferred examples, the CD27L antigen binding protein is an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:63 and a heavy chain variable domain amino acid sequence as set forth in SEQ ID NO:17 (e.g., Ab1), an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:64 and a heavy chain variable domain amino acid sequence as set forth in SEQ ID NO:18 (e.g., Ab2), an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:65 and a heavy chain variable domain amino acid sequence as set forth in SEQ ID NO:19 (e.g., Ab3), an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:66 and a heavy chain variable domain amino acid sequence as set forth in SEQ ID NO:20 (e.g., Ab4), an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:67 and a heavy chain variable domain amino acid sequence as set

forth in SEQ ID NO:21 (e.g., Ab5), an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:68 and a heavy chain variable domain amino acid sequence as set forth in SEQ ID NO:22 (e.g., Ab6), an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:69 and a heavy chain variable domain amino acid sequence as set forth in SEQ ID NO:23 (e.g., Ab7), or an antibody comprising a light chain variable domain amino acid sequence as set forth in SEQ ID NO:70 and a heavy chain variable domain amino acid sequence as set forth in SEQ ID NO:24 (e.g., Ab8). In preferred examples, the CD27L antigen binding protein inhibits binding of CD27 to CD27L. In particularly preferred examples, the autoimmune or inflammatory disorder is systemic lupus erythematosus (SLE), insulin dependent diabetes mellitus (IDDM), inflammatory bowel disease (IBD), multiple sclerosis (MS), psoriasis, autoimmune thyroiditis, rheumatoid arthritis (RA), or glomerulonephritis. In other examples, treatment inhibits or prevents transplant rejection or graft versus host disease in the patient.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1. Summary of functional and physical characteristics of exemplary embodiments of CD27L antigen binding proteins.

FIG. 2. Measurement of the level and the rate of internalization of Ab4 (A4) and Ab8 (A8) and their conjugated counterparts into 786-0 cells over time (A).

FIG. 3. 786-0 cells were cultured for 4 days in the presence of increasing concentrations of anti streptavidin-MCC-DM1, Ab4-MCC-DM1 and Ab8-MCC-DM1. Effect on cell growth was measured using the CELL-TITER-GLO reagent that measures cell number using a luminescent read-out.

FIG. 4. Dose response of Ab4-MCC-DM1 and Ab8-MCC-DM1 in the 786-0 xenograft model. Intravenous dose on day 24 is denoted by arrow at the indicated doses.

CLAIMS

What is claimed is:

1. A CD27L antigen binding protein comprising

a light chain variable domain and a heavy chain variable domain, wherein

a) the light chain variable domain comprises an LCDR1 as set forth in SEQ ID NO: 74; an LCDR2 as set forth in SEQ ID NO: 82; and an LCDR3 as set forth in SEQ ID NO: 90; and the heavy chain variable domain comprises an HCDR1 as set forth in SEQ ID NO: 28; an HCDR2 as set forth in SEQ ID NO: 36; and an HCDR3 as set forth in SEQ ID NO: 44;

b) the light chain variable domain comprises the amino acid sequence SEQ ID NO: 66 but has an R24K-S26G mutation, and the heavy chain variable domain comprises the amino acid sequence SEQ ID NO: 20 but has an N31S-I34M mutation;

c) the light chain variable domain comprises the amino acid sequence SEQ ID NO: 66 but has an R24K-S26G mutation, and the heavy chain variable domain comprises the amino acid sequence SEQ ID NO: 20;

d) the light chain variable domain comprises the amino acid sequence SEQ ID NO: 66 but has an L55I-Y58F mutation, and the heavy chain variable domain comprises the amino acid sequence SEQ ID NO: 20;

e) the light chain variable domain comprises the amino acid sequence SEQ ID NO: 66 but has a Q95N-T96S mutation, and the heavy chain variable domain comprises the amino acid sequence SEQ ID NO: 20 but has an N31S-I34M mutation; or

f) the light chain variable domain comprises the amino acid sequence SEQ ID NO: 66 but has a Q95N-T96S mutation, and the heavy chain variable domain comprises the amino acid sequence SEQ ID NO: 20.

2. The CD27L antigen binding protein of claim 1, comprising

a) a light chain variable domain having at least 90% identity or at least 95% identity to the amino acid sequence set forth in SEQ ID NO: 66, or comprising the amino acid sequence SEQ ID NO: 66;

b) a heavy chain variable domain having at least 90% identity or at least 95% identity to the amino acid sequence set forth in SEQ ID NO: 20, or comprising the amino acid sequence SEQ ID NO: 20;

c) the light chain variable domain of a) and the heavy chain variable domain of b);

d) a light chain variable domain having no more than ten or no more than five amino acid additions, deletions or substitutions from the amino acid sequence set forth in SEQ ID NO: 66;

e) a heavy chain variable domain having no more than ten or no more than five amino acid additions, deletions or substitutions from the amino acid sequence set forth in SEQ ID NO: 20; or

f) the light chain variable domain of d) and the heavy chain variable domain of e).

3. The CD27L antigen binding protein of claim 1 or 2, wherein the antigen binding protein specifically binds human CD27L with an affinity of less than or equal to 2×10^{-11} M.

4. The CD27L antigen binding protein of any of claims 1 to 3, wherein the antigen binding protein inhibits binding of CD27L to CD27.

5. The CD27L antigen binding protein of any of claims 1 to 4, wherein the antigen binding protein is an antibody, preferably a human antibody.

6. The CD27L antigen binding protein of claim 5, comprising a light chain comprising the amino acid sequence set forth in SED ID NO: 58, and comprising a heavy chain comprising the amino acid sequence set forth in SED ID NO: 12.

7. The CD27L antigen binding protein of any of claims 1-6, wherein the CD27L antigen binding protein is a bispecific antibody.

8. The CD27L antigen binding protein of claim 7, wherein the bispecific antibody binds CD27L and a human effector cell antigen which is CD3.

9. The CD27L antigen binding protein of any one of claims 1-8, wherein the CD27L antigen binding protein is an antibody fragment.

10. The CD27L antigen binding protein of claim 9, wherein the antibody fragment is selected from the group consisting of F(ab), Fab fragments consisting of VL, VH, CL and CH1 domains, F(ab'), F(ab')2, Fv, Fv fragments consisting of the VL and VH domains of a single antibody, dAb fragments, single chain Fv molecules (scFv), bispecific single chain Fv dimers, diabodies and triabodies.

11. The CD27L antigen binding protein of any of claims 1-10, wherein the CD27L antigen binding protein is conjugated to a chemotherapeutic agent preferably via a linker, wherein the linker preferably is a non-cleavable linker, preferably comprising MCC.

12. The CD27L antigen binding protein of claim 11, wherein the chemotherapeutic agent is conjugated to one or more lysines contained with a polypeptide of the CD27L antigen binding protein.

13. The CD27L antigen binding protein of claim 11 or 12, wherein the chemotherapeutic agent is DM1.

14. A composition comprising a CD27L antigen binding protein of claim 13, wherein the average number of DM1 molecules per CD27L antigen binding protein is between 1 and 10, preferably between 3 and 7, preferably between 4 and 6, or 4.0, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, or 6.0.

15. The composition of claim 14, wherein the composition is a pharmaceutical composition comprising a therapeutically effective amount of the CD27L

antigen binding protein, preferably wherein the pharmaceutical composition is lyophilized.

16. An isolated nucleic acid encoding a polypeptide, said polypeptide comprising:

a) a light chain variable domain comprising an LCDR1 having the amino acid sequence set forth in SEQ ID NO: 74; an LCDR2 having the amino acid sequence set forth in SEQ ID NO: 82; and an LCDR3 having the amino acid sequence set forth in SEQ ID NO: 90; and a heavy chain variable domain comprising an HCDR1 having the amino acid sequence set forth in SEQ ID NO: 28; an HCDR2 having the amino acid sequence set forth in SEQ ID NO: 36; and an HCDR3 having the amino acid sequence set forth in SEQ ID NO: 44;

b) a light chain variable domain comprising the amino acid sequence SEQ ID NO: 66 but having an R24K-S26G mutation or a Q95N-T96S mutation; and a heavy chain variable domain comprising the amino acid sequence SEQ ID NO: 20 but having an N31S-I34M mutation; or

c) a light chain variable domain comprising the amino acid sequence SEQ ID NO: 66 but having an L55I-Y58F mutation; and a heavy chain variable domain comprising the amino acid sequence SEQ ID NO: 20.

17. The isolated nucleic acid of claim 16, wherein

a) the isolated nucleic acid comprises a nucleotide sequence which is at least 80% identical, preferably at least 90% identical, preferably at least 95% identical to the nucleotide sequence set forth in SEQ ID NO:51, or comprises the nucleotide sequence set forth in SEQ ID NO:51;

b) the isolated nucleic acid comprises a nucleotide sequence which is at least 80% identical, preferably at least 90% identical, preferably at least 95% identical to the nucleotide sequence set forth in SEQ ID NO:5; or comprises the nucleotide sequence set forth in SEQ ID NO:5;

c) the polypeptide comprises a light chain variable domain having

i) at least 95% identity to the amino acid sequence set forth in SEQ ID NO: 66;

ii) no more than five amino acid additions, deletions or substitutions from the amino acid sequence set forth in SEQ ID NO: 66; or

iii) the amino acid sequence set forth in SEQ ID NO: 66; or

d) the polypeptide comprises a heavy chain variable domain having

i) at least 95% identity to the amino acid sequence set forth in SEQ ID NO: 20;

ii) no more than five amino acid additions, deletions or substitutions from the amino acid sequence set forth in SEQ ID NO: 20; or

iii) the amino acid sequence set forth in SEQ ID NO: 20.

18. An expression vector comprising the isolated nucleic acid of claim 16 or 17.

19. A recombinant host cell comprising an isolated nucleic acid of claim 16 or 17 operably linked to a promoter, or comprising an expression vector of claim 18.

20. A method of making a CD27L antibody drug conjugate, said method comprising the steps of:

(i) a) providing a CD27L antigen binding protein of any one of claims 1-10

b) conjugating the CD27L antigen binding protein to a linker; and

c) conjugating a drug to said linker;

wherein the linker preferably comprises MCC; the drug preferably comprises DM1; or the linker preferably comprises MCC and the drug preferably comprises DM1; or

(ii) a) providing a CD27L antigen binding protein of any one of claims 1-10; and

b) conjugating a linker covalently bound to a drug to said CD27L antigen binding protein.

21. Use of the CD27L antigen binding protein of any one of claims 1-10 conjugated to DM1 by an MCC linker, in the manufacture of a medicament for treating cancer.

22. The use as in claim 21, wherein the CD27L antigen binding protein is comprised in a pharmaceutical composition.

23. The use as in claim 22, wherein the antibody comprises enhanced effector function.

24. The use as in claim 23, wherein
the average number of DM1 molecules per antibody is between 1 and 10, preferably between 3 and 7, preferably between 4 and 6, or is 4.0, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, or 6.0.

25. The use as in any of claims 22-24, wherein a sample from the patient, preferably a blood sample or a biopsy, is to be tested for CD27L expression, preferably for CD27L mRNA expression or for CD27L protein expression.

26. The use as in any one of claims 22-25, wherein the cancer is renal cell carcinomas (RCC), clear cell RCC, head and neck cancer, glioblastoma, breast cancer, brain tumor, nasopharangeal carcinoma, non-Hodgkin's lymphoma (NHL), acute lymphocytic leukemia (ALL), chronic lymphocytic leukemia (CLL), Burkitt's lymphoma, anaplastic large-cell lymphomas (ALCL), multiple myeloma, cutaneous T-cell lymphomas, nodular small cleaved-cell lymphomas, lymphocytic lymphomas, peripheral T-cell lymphomas, Lennert's lymphomas, immunoblastic lymphoma, T-cell leukemia/lymphomas (ATLL), adult T-cell leukemia (T-ALL), entroblastic/centrocytic (cb/cc) follicular lymphoma cancer, diffuse large cell lymphoma of B lineage, angioimmunoblastic lymphadenopathy (AILD)-like T cell lymphoma, HIV associated body cavity based lymphoma, embryonal carcinoma, undifferentiated carcinoma of the rhino-pharynx, Castleman's disease, Kaposi's Sarcoma, multiple myeloma, Waldenstrom's macroglobulinemia or other B-cell lymphoma.