

CLAIMS

1. A method of generating an anti-CTLA-4 antibody with reduced binding to CTLA-4 at acidic pH, comprising replacing tyrosine with histidine within or near one or more CDR1-3 regions of at least one of a light chain and heavy chain variable region of the antibody.

2. An anti-CTLA-4 antibody variant with reduced binding to CTLA-4 at acidic pH, wherein the anti-CTLA-4 antibody comprises the amino acid sequence of Tremelimumab or Ipilimumab in which one or more tyrosine residues in at least one of a light chain and heavy chain variable region is replaced with histidine.

3. An anti-CTLA-4 antibody comprising a heavy chain comprising the sequence set forth in SEQ ID NO: 1, 3, 5, 6 or 8, and a light chain comprising the sequence set forth in SEQ ID NO: 2 or 4.

4. The anti-CTLA-4 antibody of claim 3, comprising a heavy chain comprising the sequence set forth in SEQ ID NO: 6, and a light chain comprising the sequence set forth in SEQ ID NO: 2.

5. An anti-CTLA-4 antibody comprising a heavy chain comprising the sequence set forth in one of SEQ ID NOS: 14-18, and a light chain comprising the sequence set forth in one of SEQ ID NOS: 10-12.

6. A method of cancer immunotherapy in a subject in need thereof, comprising administering to the subject an anti-CTLA-4 antibody of any one of the preceding claims, either alone or in combination with one or more other therapies.

7. The method of claim 6, wherein the other therapy is an antibody that binds to PD-1 or PD-L1.

8. The method of claim 7, wherein the anti-PD-1 antibody is Nivolumab or Pembrolizumab.

9. An anti-CTLA-4 antibody of any one of the preceding claims for use in treating cancer in a subject.

10. Use of an anti-CTLA-4 antibody of any one of the preceding claims in the manufacture of a medicament for treating cancer in a subject.