

Heystek et al., *J Immunol* 168:102-7 (2002)). These scavenging receptors, which are highly concentrated in the liver, recognize glycoproteins bearing incompletely sialylated N-linked glycans and remove them from circulation (Tomana et al., *Gastroenterology* 94:762-70 (1988) and Daniels et al., *Hepatology* 9:229-34 (1989)).

Accordingly, there is a need in the art for IgA antibodies that have a longer half-life and for production methods to improve expression levels and polymeric IgA generation.

SUMMARY

The present disclosure relates to IgA antibodies and compositions comprising such antibodies, as well as methods of making and using such antibodies and compositions.

In certain examples, the present disclosure is directed to isolated IgA antibodies. For example, but not by way of limitation, an isolated IgA antibody, or a fragment thereof, of the present disclosure comprises a substitution at amino acid V458. In certain examples, amino acid V458 is substituted with an isoleucine (*i.e.*, V458I). In certain examples, the isolated IgA antibody is an IgA1, IgA2mn or IgA2m1 antibody.

In one aspect, provided herein is use of an isolated monomeric IgA antibody comprising a substitution at amino acid 458 of a heavy chain constant region according to EU numbering in the manufacture of a medicament for the treatment of a cancer, wherein the substitution at amino acid 458 is a valine to isoleucine (V458I) substitution or an isoleucine to valine (I458V) substitution.

In one example, the present disclosure provides an isolated IgA antibody, or a fragment thereof, of the present disclosure comprises a substitution at amino acid I458. In certain examples, amino acid I458 is substituted with a valine (*i.e.*, I458V). In certain examples, the isolated IgA antibody is an IgA2m2 antibody.

The present disclosure further provides an isolated IgA antibody that comprises a substitution at amino acid N459 and/or S461. In certain examples, amino acid N459 is substituted with a glutamine (*i.e.*, N459Q). In certain examples, amino acid S461 is substituted with an alanine (*i.e.*, S461A). In certain examples, IgA antibody is an IgA1 or IgA2m1 antibody.

In one example, the present disclosure further provides an isolated IgA antibody that comprises one or more substitutions at an amino acid selected from the group consisting of N166, T168, N211, S212, S213, N263, T265, N337, I338, T339, N459, S461 and a combination thereof. In certain examples, the IgA antibody has a substitution at

amino acid N459 and is an IgA1, IgA2m1 or an IgA2m2 antibody. In certain examples, the IgA antibody has a substitution at amino acid N166 and is an IgA2m1 or an IgA2m2 antibody. In certain examples, the IgA antibody has a substitution at amino acid S212 and is an

WHAT IS CLAIMED IS:

1. Use of an isolated monomeric IgA antibody comprising a substitution at amino acid 458 of a heavy chain constant region according to EU numbering in the manufacture of a medicament for the treatment of a cancer, wherein the substitution at amino acid 458 is a valine to isoleucine (V458I) substitution or an isoleucine to valine (I458V) substitution.
2. The use of claim 1, wherein the substitution at amino acid 458 is a valine to isoleucine (V458I) substitution.
3. The use of claim 1, wherein the substitution at amino acid 458 is an isoleucine to valine (I458V) substitution.
4. The use of any one of claims 1-3, wherein the cancer is breast cancer.
5. The use of any one of claims 1-4, wherein the IgA antibody is an IgA1, IgA2m1, IgA2m2 or IgA2mn antibody.
6. The use of claim 5, wherein the IgA antibody is an IgA1 antibody.
7. The use of claim 5, wherein the IgA antibody is an IgA2m1 antibody.
8. The use of claim 5, wherein the IgA antibody is an IgA2m2 antibody.
9. The use of claim 5, wherein the IgA antibody is an IgA2mn antibody.
10. The use of any one of claims 1-9, wherein the IgA antibody is a humanized, a chimeric antibody or a human antibody.