

REPLACEMENT SHEETS**WHAT IS CLAIMED IS:**

1. A method for producing an antibody library, the method comprising:
 - (a) injecting one or more animals with an antigen;
 - (b) harvesting draining lymph nodes comprising B cells from each animal;
 - (c) forming a hybridoma between each B cell and a fusion partner; and
 - (d) screening the hybridomas for IgG having binding specificity to the antigen;
 wherein at least five of the following conditions apply:
 - (i) the animals are outbred animals;
 - (ii) the animals are injected at multiple sites;
 - (iii) the animals are injected every two weeks;
 - (iv) the animals are injected for between 6 weeks and 15 weeks;
 - (v) multiple adjuvants are used, such that different animals are injected with different adjuvants; and/or
 - (vi) B cells are enriched prior to step (c).
2. ~~_____ (Cancelled)~~
3. ~~_____ (Cancelled)~~
4. ~~_____ (Cancelled)~~
5. 2. The method of claim 1, wherein five of conditions (i)-(vii) apply.
6. 3. The method of claim 1, wherein six of conditions (i)-(vii) apply.
7. ~~_____ (Cancelled)~~
8. 4. The method of claim 1, wherein the fusion partner is engineered to express both surface and secreted IgG.
9. 5. The method of claim 1, wherein step (a) comprises injecting two or more animals with an antigen.

REPLACEMENT SHEETS

~~10.6.~~ 11.6. The method of claim 1, wherein step (a) comprises injecting three or more animals with an antigen.

~~11.7.~~ 12.7. The method of claim 1, wherein step (a) comprises injecting four or more animals with an antigen.

~~12.8.~~ 13.8. The method of claim 1, wherein step (a) comprises injecting five or more animals with an antigen.

~~13.9.~~ 14.9. The method of any one of the above claims, wherein the animals are rats.

~~14.10.~~ 15.10. The method of any one of claims ~~1, 5, 6, or 8 to 12~~ 1-8, wherein the multiple sites are sites near draining lymph nodes.

~~15.11.~~ 16.11. The method of any one of claims ~~1, 5, 6, or 8 to 12~~ 1-8, wherein the multiple sites comprise one or more of back, shoulder, intraperitoneal, base of tail, and hock.

~~16.12.~~ 17.12. The method of any one of claims ~~1, 5, 6, or 8 to 12~~ 1-8, wherein the animals are injected at multiple sites and the amount of antigen injected at each site is between 0.1 µg and 300 µg.

~~17.13.~~ 18.13. The method of any one of claims ~~1, 5, 6, or 8 to 12~~ 1-8, wherein the animals are injected at multiple sites and the amount of antigen injected at each site is between 0.5 µg and 200 µg.

~~18.14.~~ 19.14. The method of any one of claims ~~1, 5, 6, or 8 to 12~~ 1-8, wherein the animals are injected not more than once a week.

~~19.15.~~ 20.15. The method of any one of claims ~~1, 5, 6, or 8 to 12~~ 1-8, wherein the animals are injected not more than once every two weeks.

~~20.16.~~ 21.16. The method of any one of claims ~~1, 5, 6, or 8 to 12~~ 1-8, wherein the animals are injected for between 6 weeks and 15 weeks.

~~21.17.~~ 22.17. The method of any one of ~~1, 5, 6, or 8 to 12~~ claims 1-8, wherein the multiple adjuvants comprise complete Freund's adjuvant, Ribi, and/or TLR agonist cocktail.

REPLACEMENT SHEETS

~~22.18.~~ The method of any one of claims ~~1, 5, 6, or 8 to 12~~ 1-8, wherein the B cells are enriched by negative selection.

~~23.19.~~ The method of any one of claims ~~1, 5, 6, or 8 to 12~~ 1-8, wherein the fusion partner is a Sp2ab fusion partner.

~~24.20.~~ The method of any one of claims ~~1, 5, 6, or 8 to 12~~ 1-8, wherein screening the hybridomas comprises FACS sorting for expression of IgG antibodies that are specific to the antigen.

~~25.21.~~ A method for producing an antibody library, the method comprising:

- (a) injecting one or more outbred rats with an antigen at multiple sites of each rat;
- (b) repeating the injection every 2 weeks for at least 6 weeks;
- (c) harvesting immune cells from one or more draining lymph node of each rat;
- (d) depleting non-B cells from the immune cells by negative selection to form an enriched B cell sample;
- (e) contacting the enriched B cell sample with a plurality of fusion partners to form a hybridoma between each B cell and a fusion partner; and
- (f) screening the hybridomas for specificity to the antigen.

~~26.22.~~ The method of claim ~~25~~ 21, wherein the multiple sites are sites near draining lymph nodes.

~~27.23.~~ The method of claim ~~25~~ 21 or ~~26~~ 22, wherein the multiple sites comprise one or more of back, shoulder, intraperitoneal, base of tail, and hock.

~~28.24.~~ The method of claim ~~25~~ 21 or ~~26~~ 22, wherein the amount of antigen injected at each site is between 0.1 µg and 300 µg.

~~29.25.~~ The method of claim ~~28~~ 24, wherein the amount of antigen injected at each site is between 0.5 µg and 200 µg.

~~30.26.~~ The method of claim ~~25~~ 21 or ~~26~~ 22, wherein the animals are injected not more than once every two weeks.

REPLACEMENT SHEETS

- ~~31.27.~~ The method of claim ~~2521~~ or ~~2622~~, wherein the animals are injected for between 6 weeks and 10 weeks.
- ~~32.28.~~ The method of claim ~~2521~~ or ~~2622~~, wherein the fusion partner is a Sp2ab fusion partner.
- ~~33.29.~~ The method of claim ~~2521~~ or ~~2622~~, wherein screening the hybridomas comprises FACS sorting for expression of IgG antibodies that are specific to the antigen.
- ~~34.30.~~ The method of claim ~~2521~~ or ~~2622~~, wherein step (a) comprises injecting two or more animals with an antigen.
- ~~35.31.~~ The method of claim ~~2521~~ or ~~2622~~, wherein step (a) comprises injecting three or more animals with an antigen.
- ~~36.32.~~ The method of claim ~~2521~~ or ~~2622~~, wherein step (a) comprises injecting four or more animals with an antigen.
- ~~37.33.~~ The method of claim ~~2521~~ or ~~2622~~, wherein step (a) comprises injecting five or more animals with an antigen.
- ~~38.34.~~ An antibody library prepared using the method of any one of claims 1 to ~~3733~~.
- ~~39.35.~~ A hybridoma library prepared using the method of any one of claims 1 to ~~3733~~.
- ~~40.36.~~ The method of claim ~~3430~~, wherein multiple adjuvants are used, such that different animals are injected with different adjuvants.
- ~~41.37.~~ The method of any one of claims ~~1, 5, 6, or 8 to 12~~ ~~1-8~~, wherein the animals are injected at multiple sites every two weeks.
- ~~42.38.~~ The method of claim ~~4137~~, wherein the animals are injected in each of back, shoulder, intraperitoneal, base of tail, and hock every two weeks.