

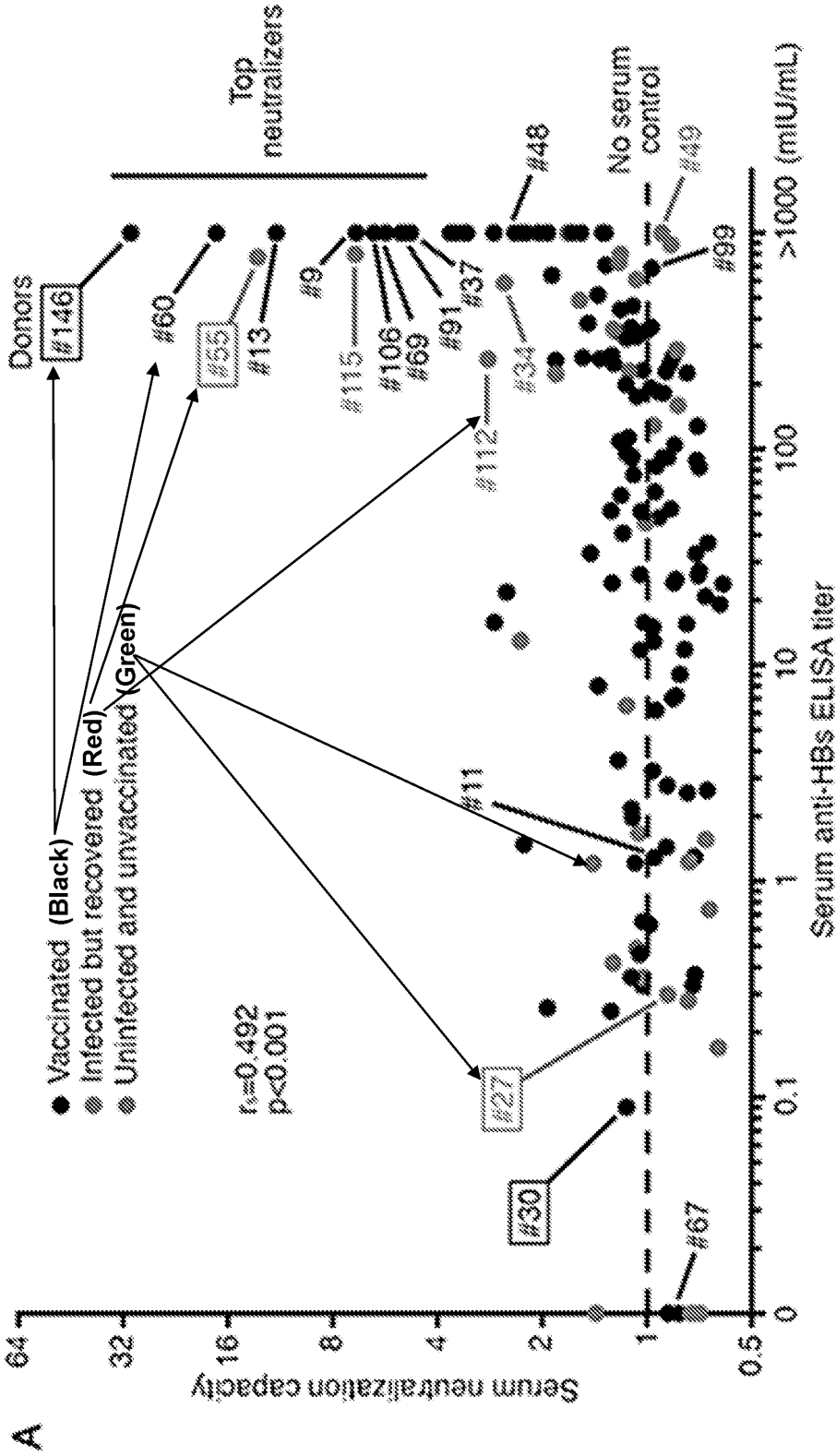


Fig. 1

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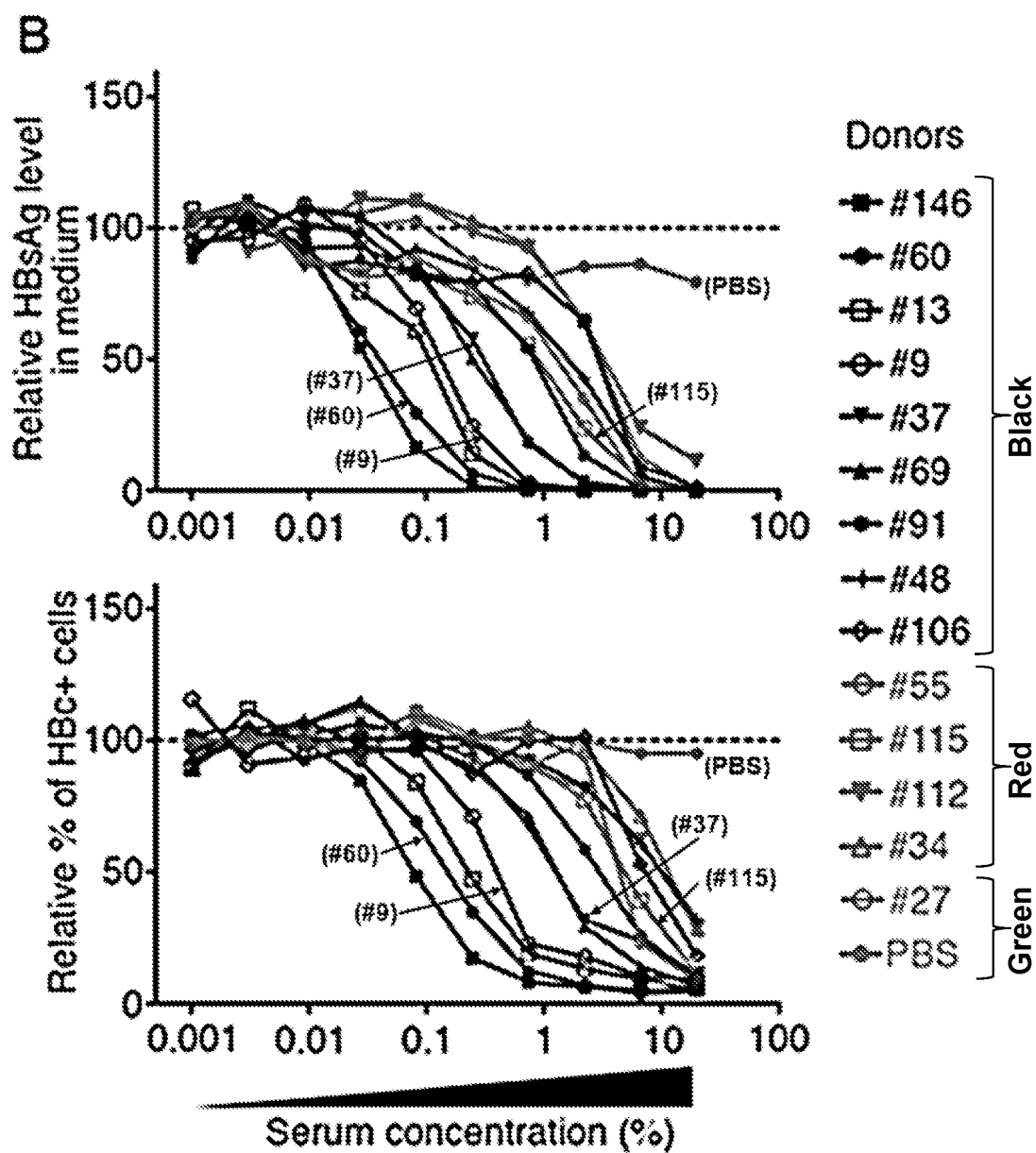


Fig. 1 (continued)

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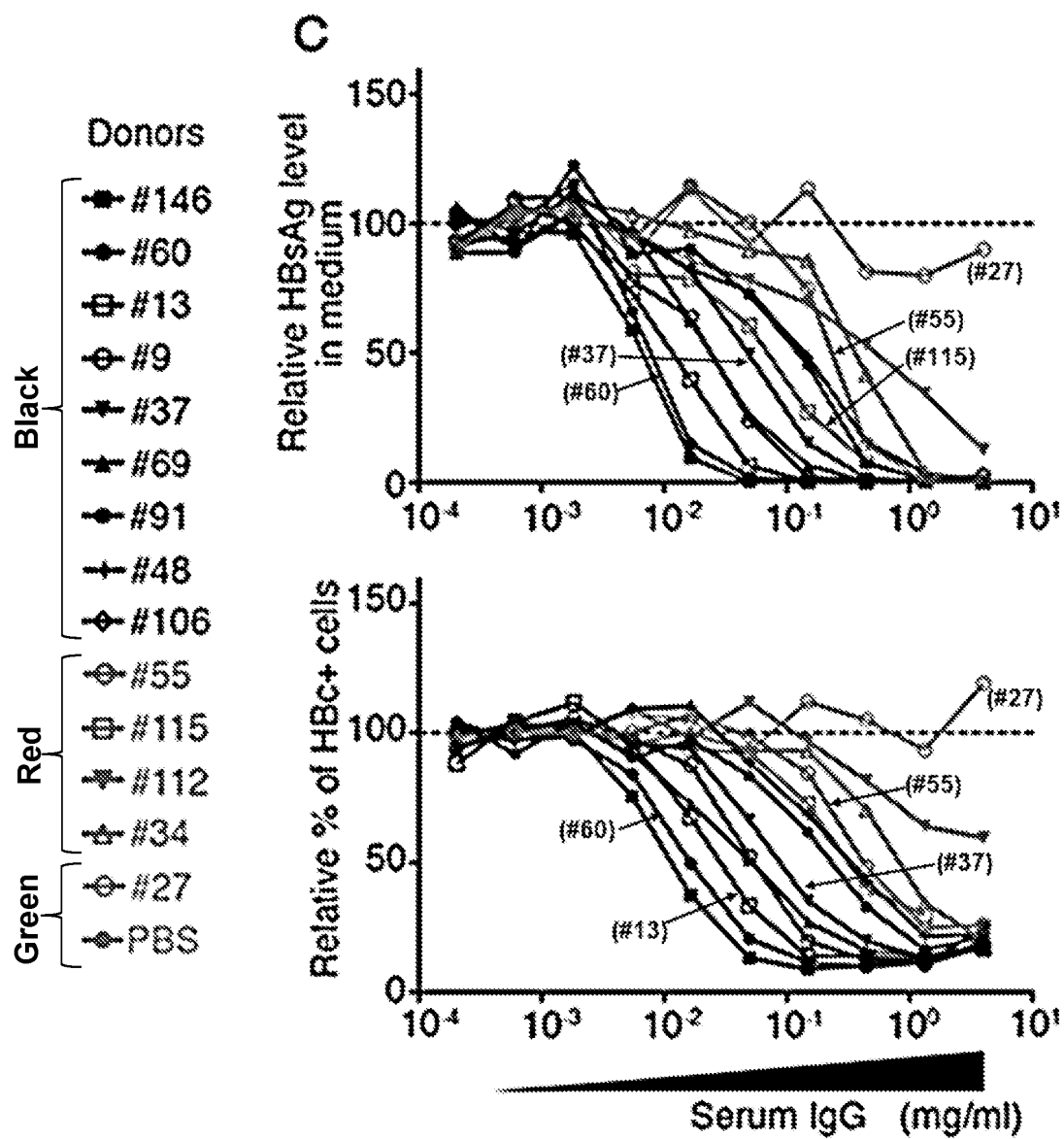


Fig. 1 (continued)

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D

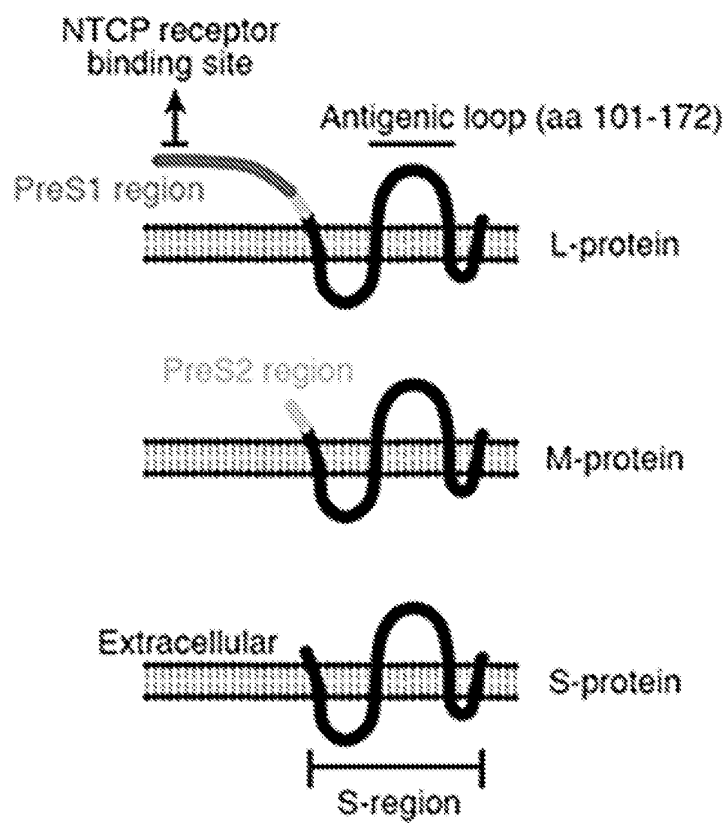


Fig. 1 (continued)

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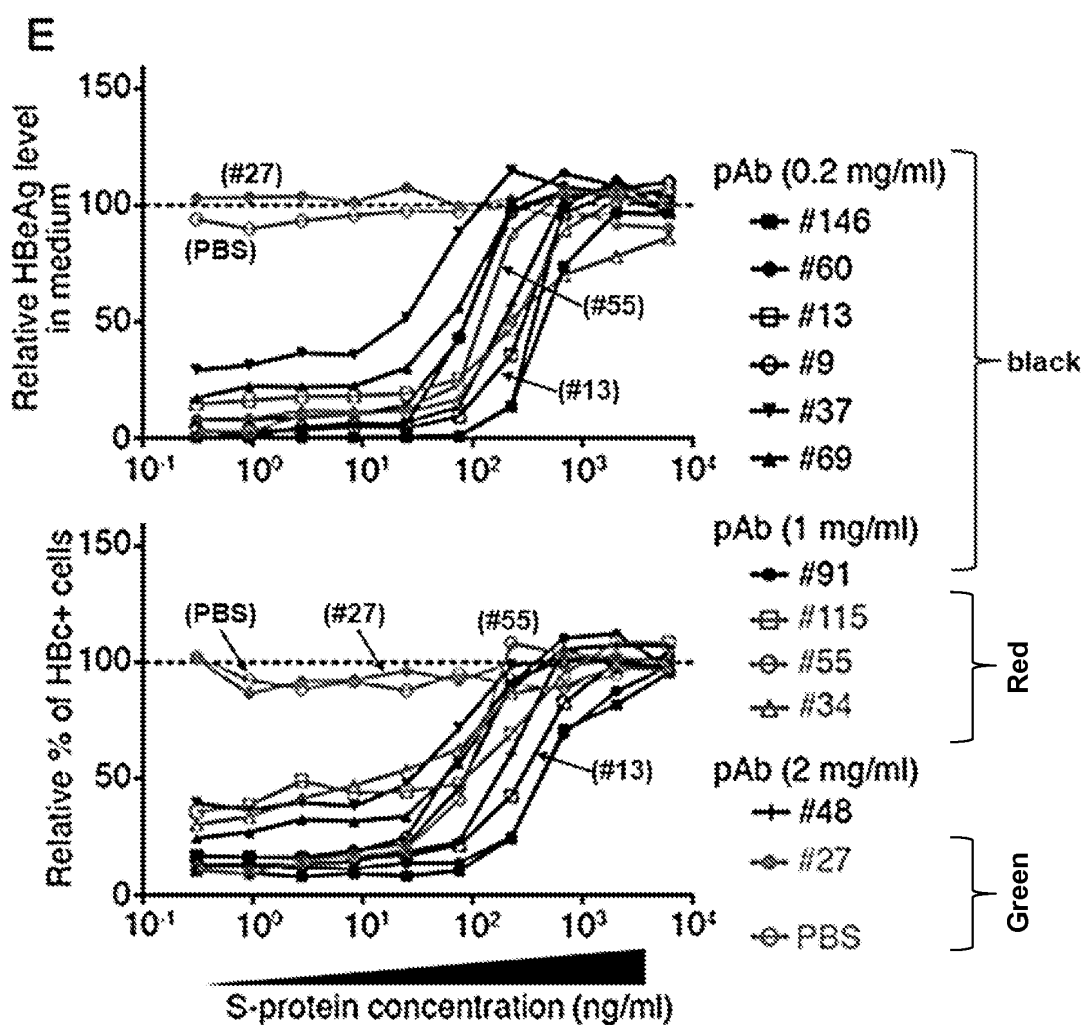


Fig. 1 (continued)

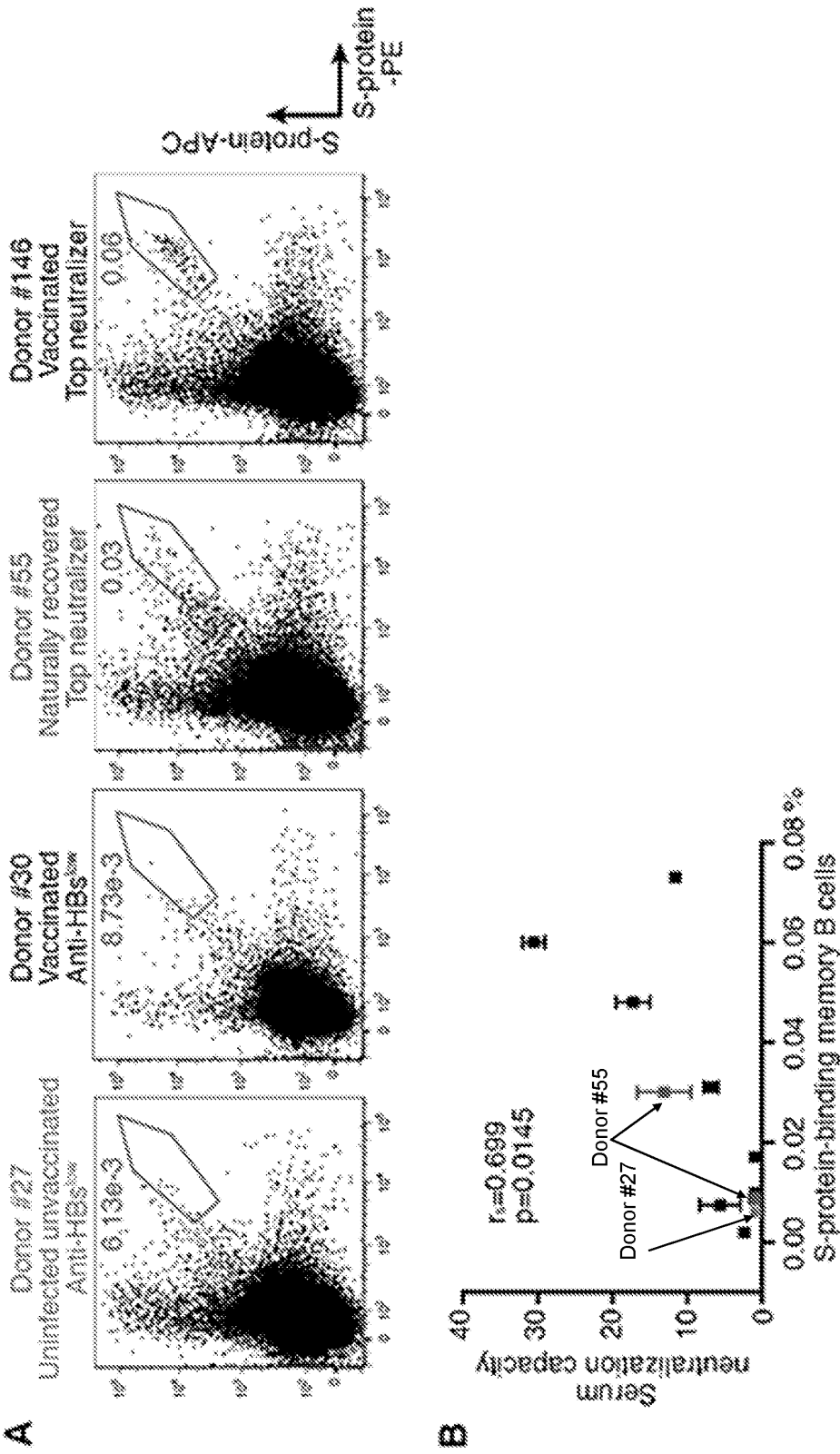


Fig. 2

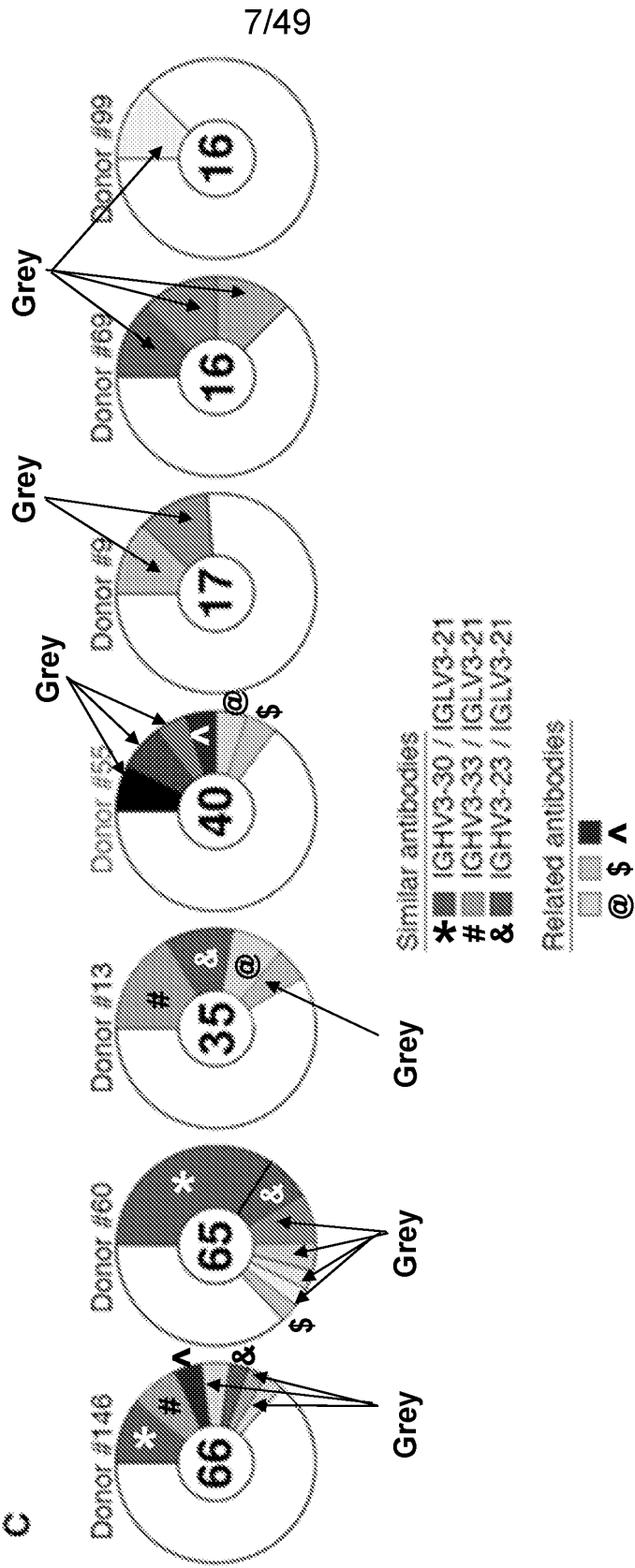


Fig. 2 (continued)

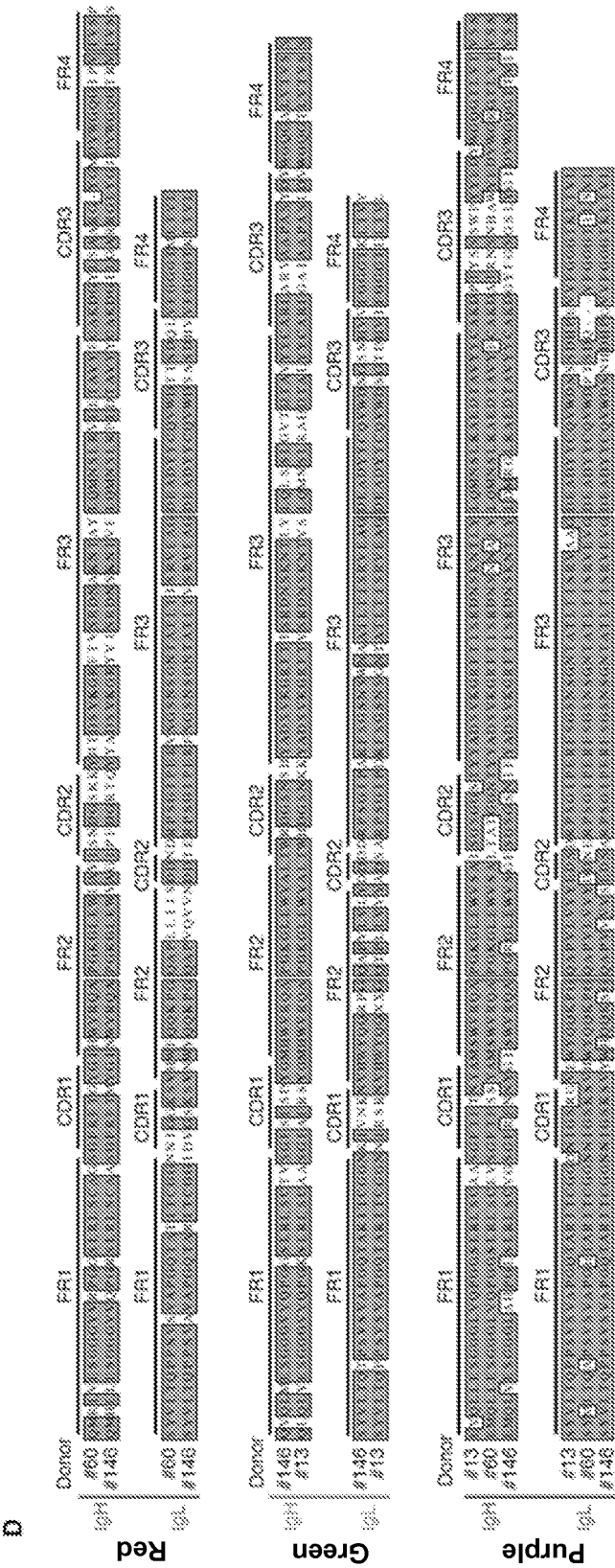


Fig. 2 (continued)

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**A**

| Antibody    | Donor ID           | Heavy chain V gene | Light chain V gene | adr CHO cell |
|-------------|--------------------|--------------------|--------------------|--------------|
| H001        | 146                | IGHV1-3*01         | IGKV1-39*01        | 27.1         |
| H002        | 146                | IGHV2-70D*04       | IGLV3-21*02        | 30.78        |
| H003        | 60                 | IGHV3-23*01        | IGLV3-21*02        | 33.76        |
| H004        | 146                | IGHV3-23*04        | IGLV3-21*02        | 24.65        |
| H005        | 60                 | IGHV3-30*18        | IGLV3-21*02        | 69.82        |
| H006        | 60                 | IGHV3-30*18        | IGLV3-21*02        | 49.56        |
| H007        | 146                | IGHV3-30*18        | IGKV3-20*01        | 46.77        |
| H008        | 146                | IGHV3-30*18        | IGLV3-21*02        | 48.27        |
| H009        | 60                 | IGHV3-30*18        | IGLV3-21*02        | 38.02        |
| H010        | 60                 | IGHV3-30*18        | IGLV3-21*03        | 35.17        |
| H011        | 13                 | IGHV3-33*01        | IGKV3-11*01        | 18.66        |
| H012        | 13                 | IGHV3-33*01        | IGLV3-21*02        | 170.9        |
| H013        | 146                | IGHV3-33*01        | IGLV3-21*02        | 351.2        |
| H014        | 146                | IGHV3-33*01        | IGLV3-21*02        | 111.1        |
| H015        | 60                 | IGHV3-33*01        | IGKV1-39*01        | 74.87        |
| H016        | 69                 | IGHV3-48*02        | IGKV3-15*01        | 33.58        |
| H017        | 55                 | IGHV3-74*01        | IGLV2-14*01        | 40.87        |
| H018        | 60                 | IGHV3-9*01         | IGLV1-51*01        | b.d.         |
| H019        | 69                 | IGHV4-30-4*01      | IGKV1-39*01        | 34.9         |
| H020        | 55                 | IGHV4-59*08        | IGKV1-12*01        | 29.58        |
| ilbivirumab | (positive control) |                    |                    | 105          |
| 10-1074     | (negative control) |                    |                    | not binding  |

Red

Orange

Red

Yellow

White

Fig. 3

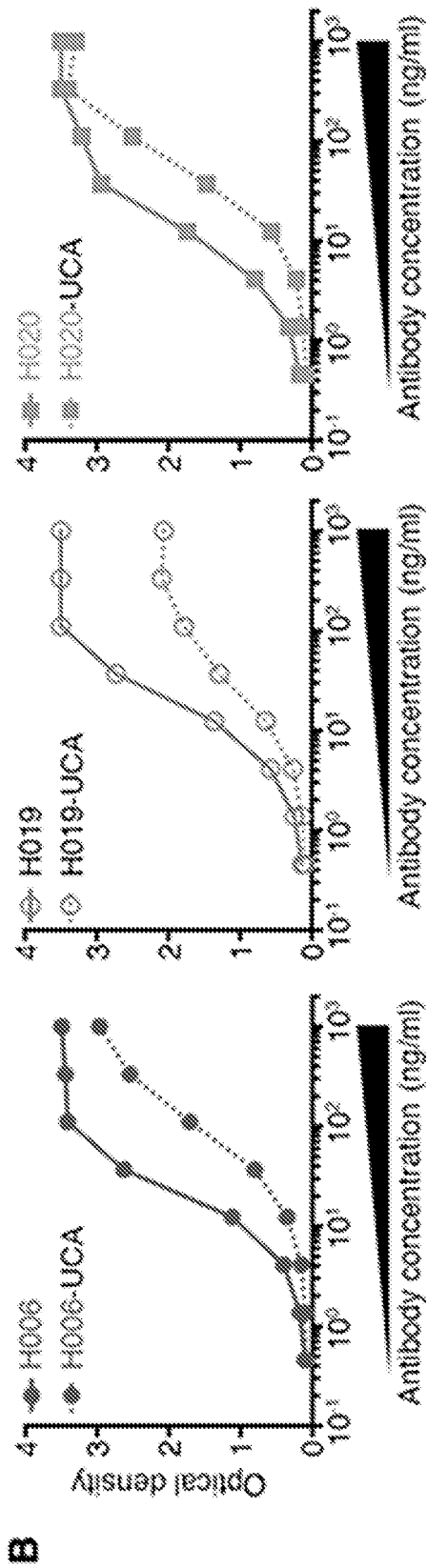


Fig. 3 (continued)

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**C**

|  | adr<br>Yeast | adw<br>Yeast | ad<br>Human blood | ayw<br>Yeast | ay<br>Human blood |
|--|--------------|--------------|-------------------|--------------|-------------------|
|  | 26.89        | 30.36        | 42.84             | 18.76        | 63.09             |
|  | 24.01        | 40.77        | 53.6              | b.d.         | 167.4             |
|  | 21.99        | 25.27        | 40.17             | 159.5        | 42.75             |
|  | 16.07        | 23           | 25.51             | 27.75        | 13.39             |
|  | 25           | 27.83        | 40.43             | 17.38        | 130.6             |
|  | 50.61        | 40.2         | 28.98             | 17.57        | 115.5             |
|  | 47.33        | 40.63        | 43.26             | 16.57        | 197.1             |
|  | 46.62        | 36.83        | 49.28             | 18.1         | 115.3             |
|  | 40.41        | 41.26        | 25.49             | 20.82        | 40.49             |
|  | 44.93        | 42.59        | 22.69             | 232          | 38.76             |
|  | 21.95        | 19.41        | 609.4             | 29.52        | b.d.              |
|  | 111.5        | 45.47        | 82.29             | 57.74        | 78.01             |
|  | 133.1        | 82.14        | 52.14             | 72.54        | 120.2             |
|  | 167.2        | 50           | 61.45             | 70.64        | b.d.              |
|  | 23.07        | b.d.         | 103.6             | 34.08        | 129.4             |
|  | 25.68        | 68.46        | 46.89             | 23.83        | 102.6             |
|  | 28.61        | 74.08        | 66.17             | 25.15        | 207.1             |
|  | b.d.         | b.d.         | 135.1             | b.d.         | b.d.              |
|  | 33.31        | 37.55        | 36.77             | 35.85        | 38.18             |
|  | 35.14        | 40.37        | 30.72             | 34.95        | 34.66             |
|  | 116.8        | 123.2        | 112.6             | 40.34        | 119.5             |
|  | not binding  | not binding  | not binding       | not binding  | not binding       |

Red  
 Orange  
 Yellow  
 White

Fig. 3 (continued)

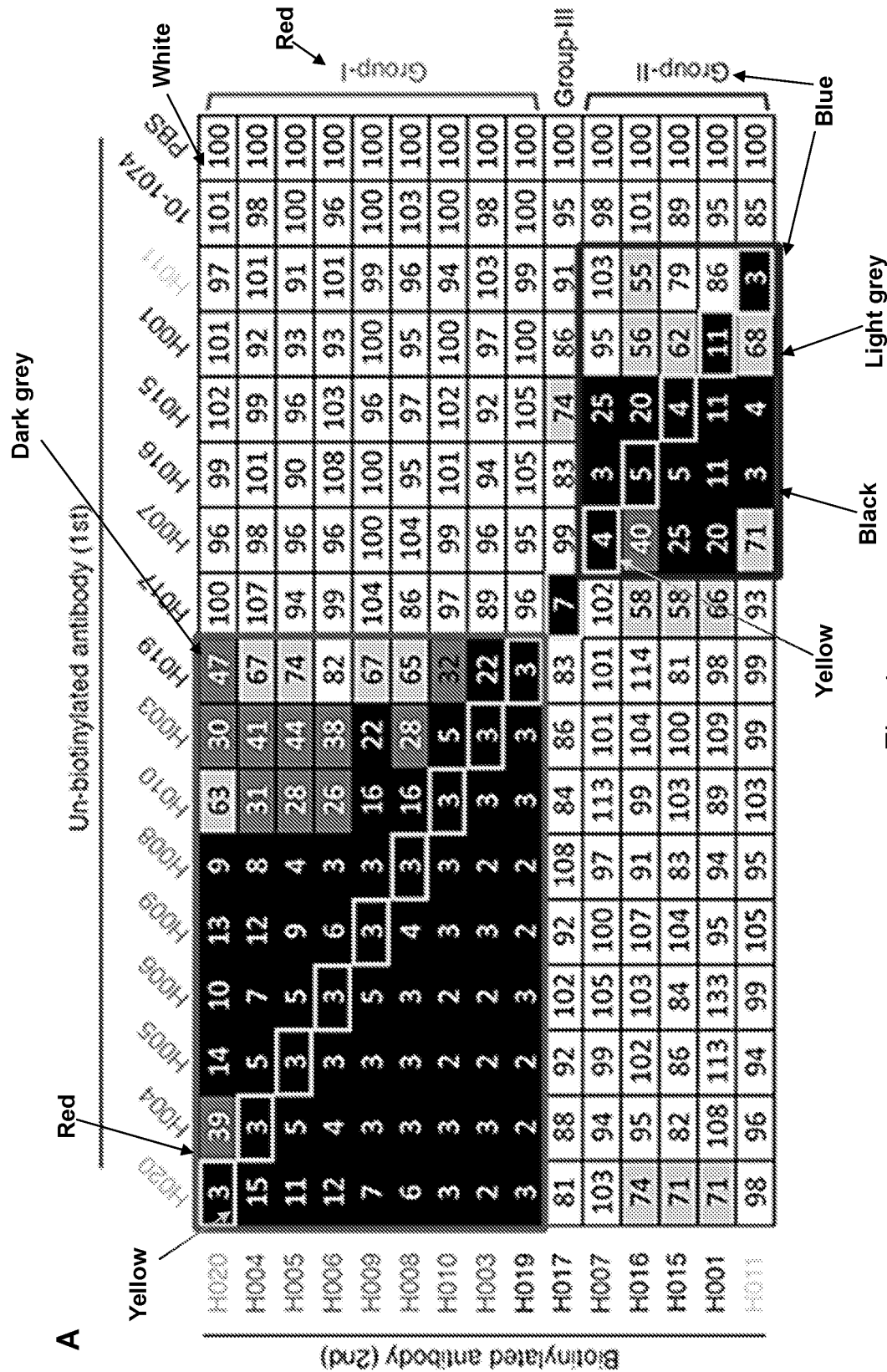


Fig. 4

B

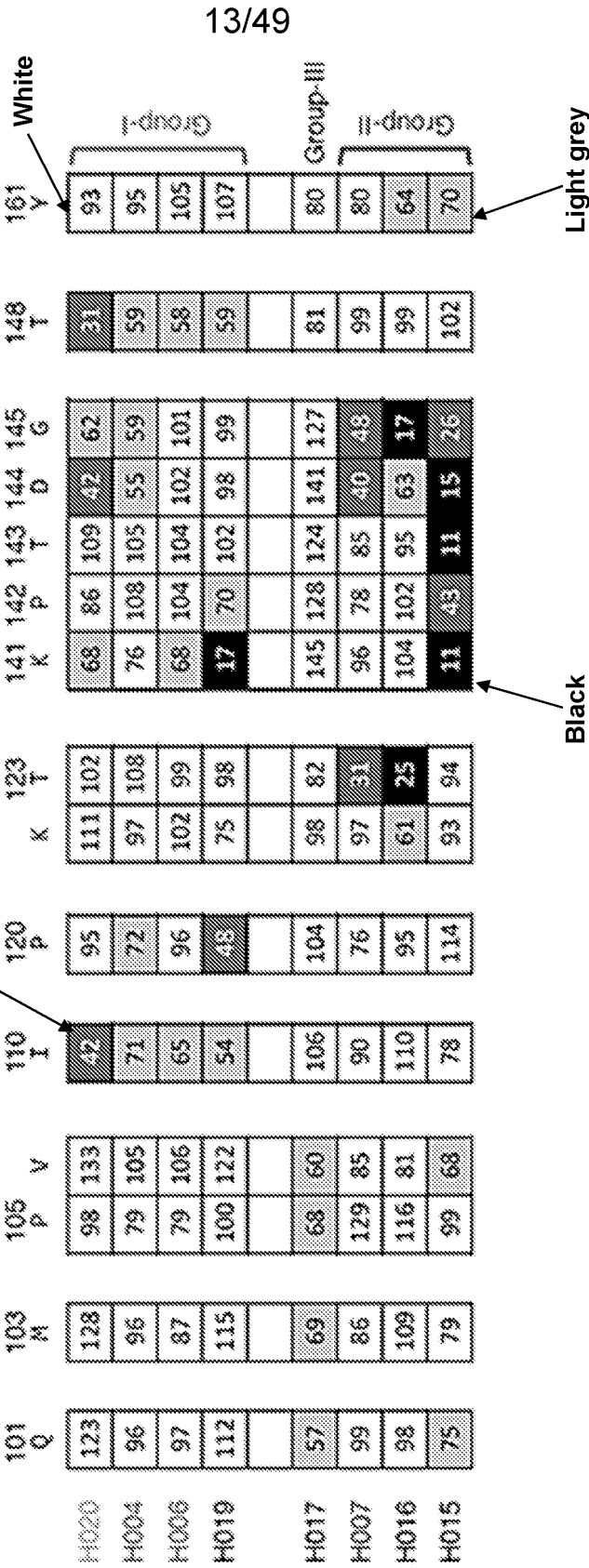
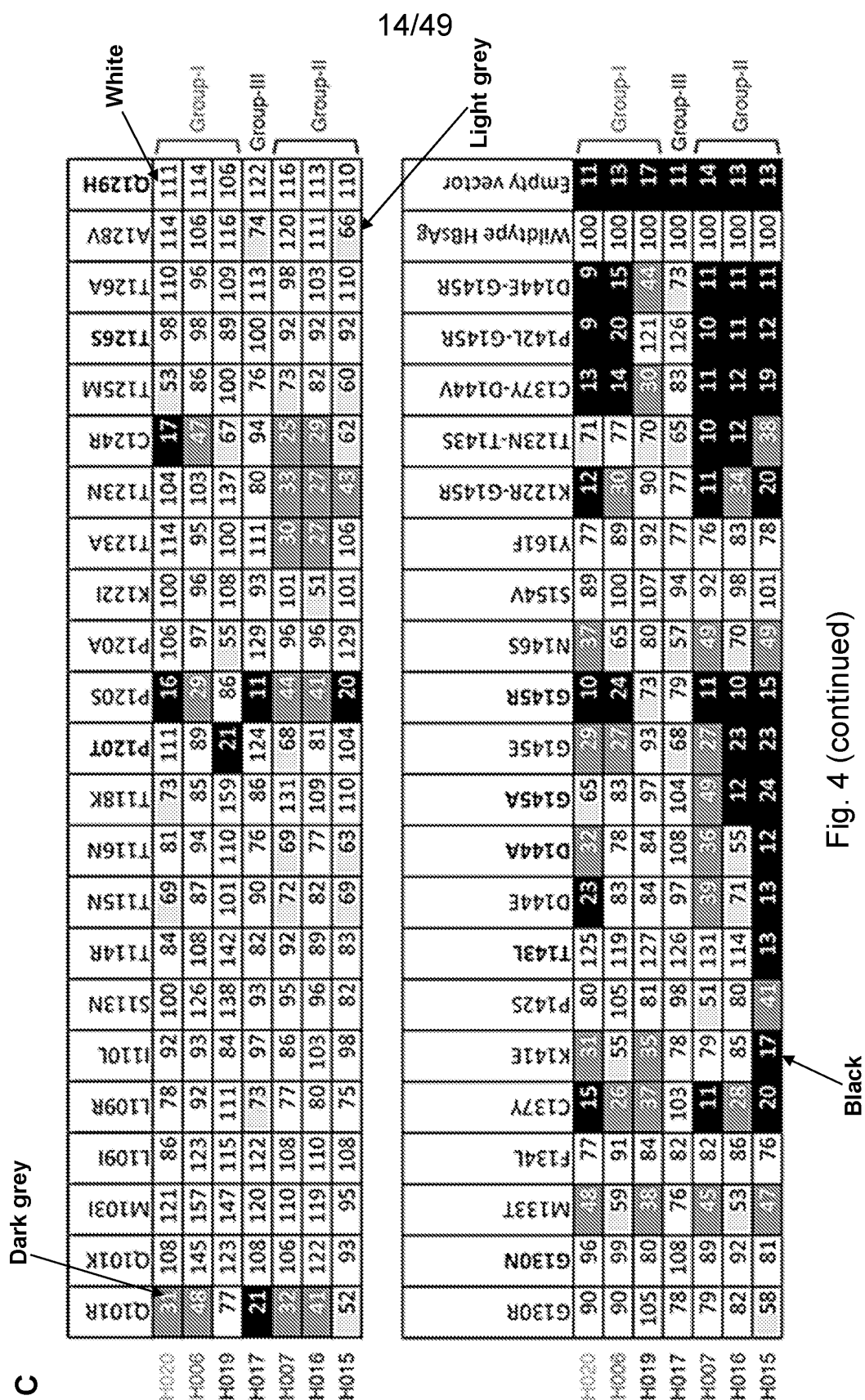


Fig. 4 (continued)



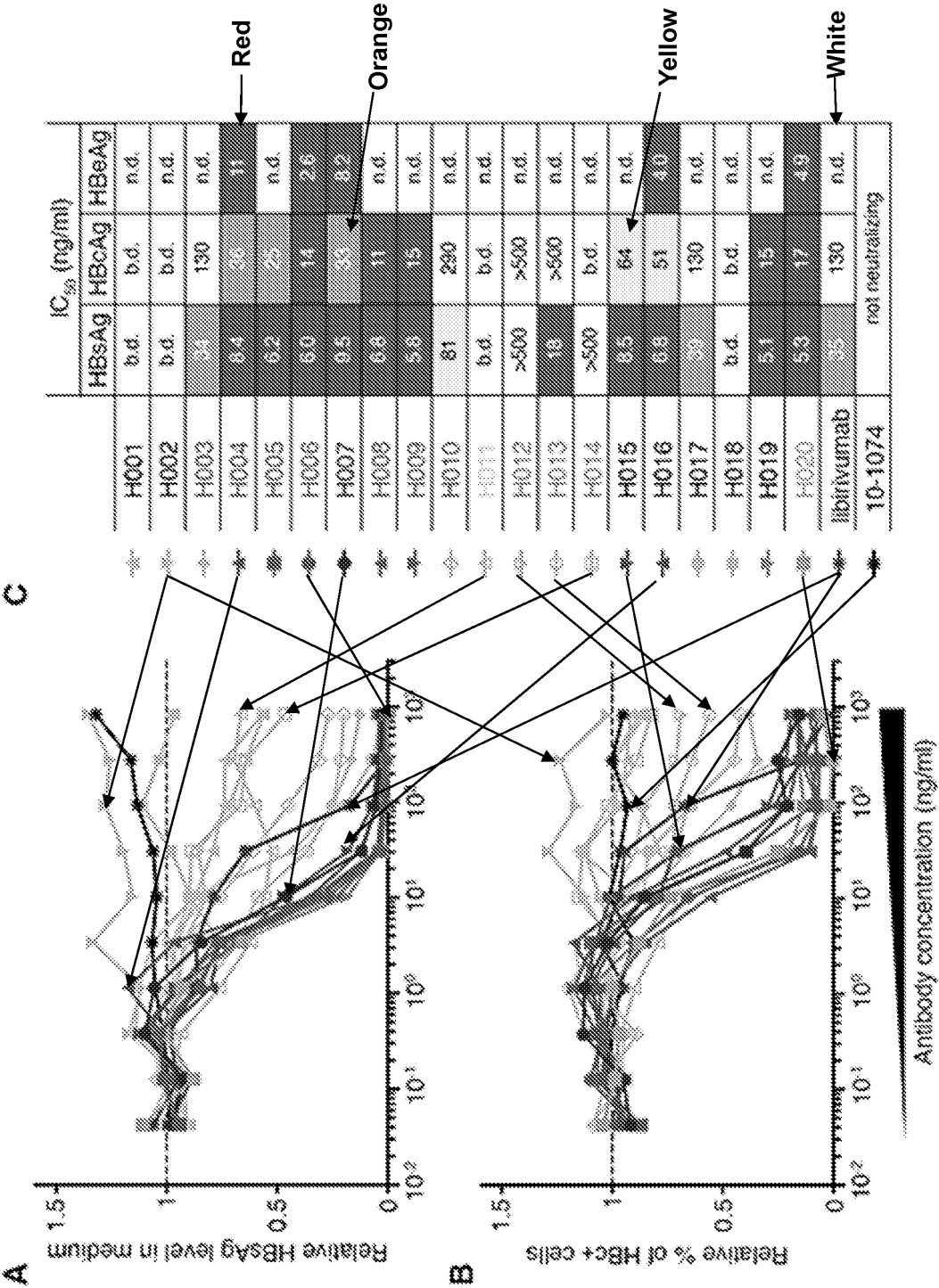


Fig. 5

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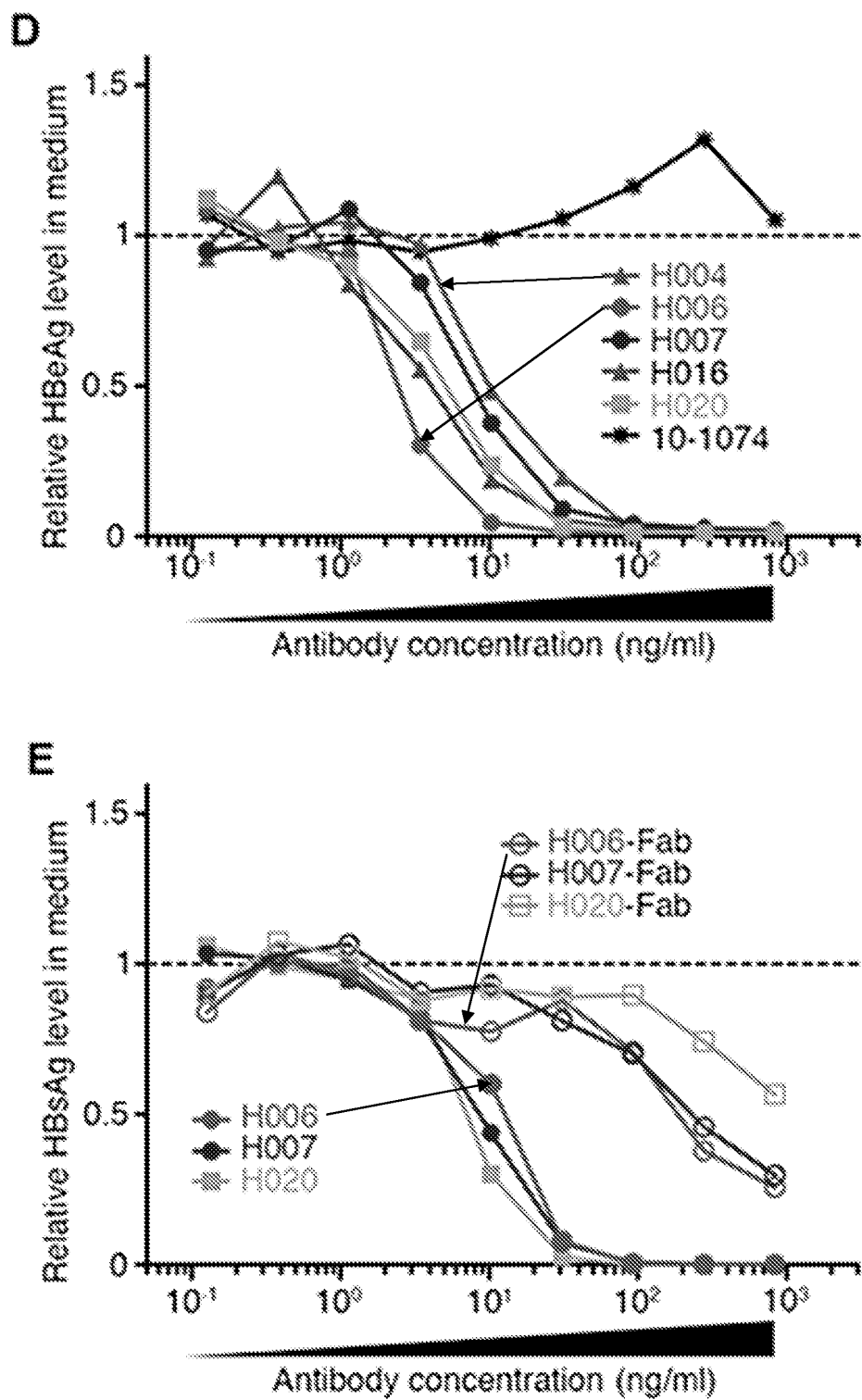


Fig. 5 (continued)

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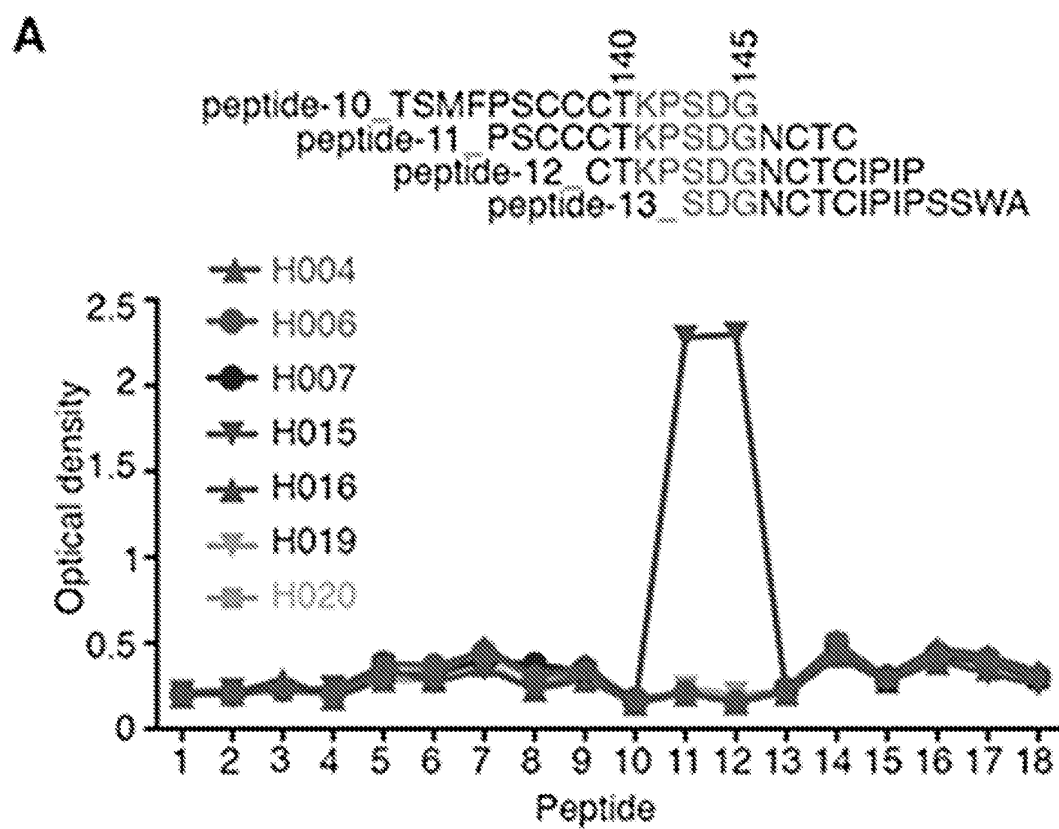


Fig. 6

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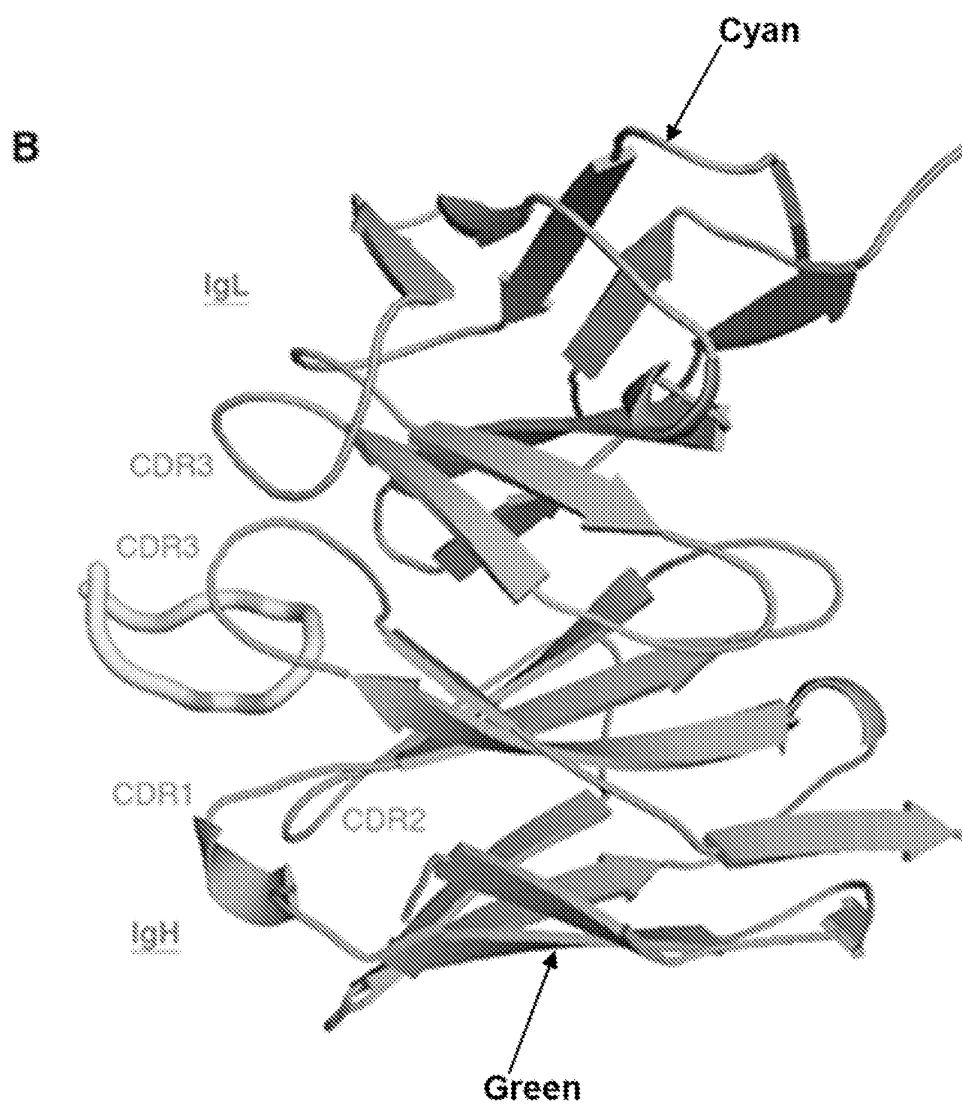


Fig. 6 (continued)

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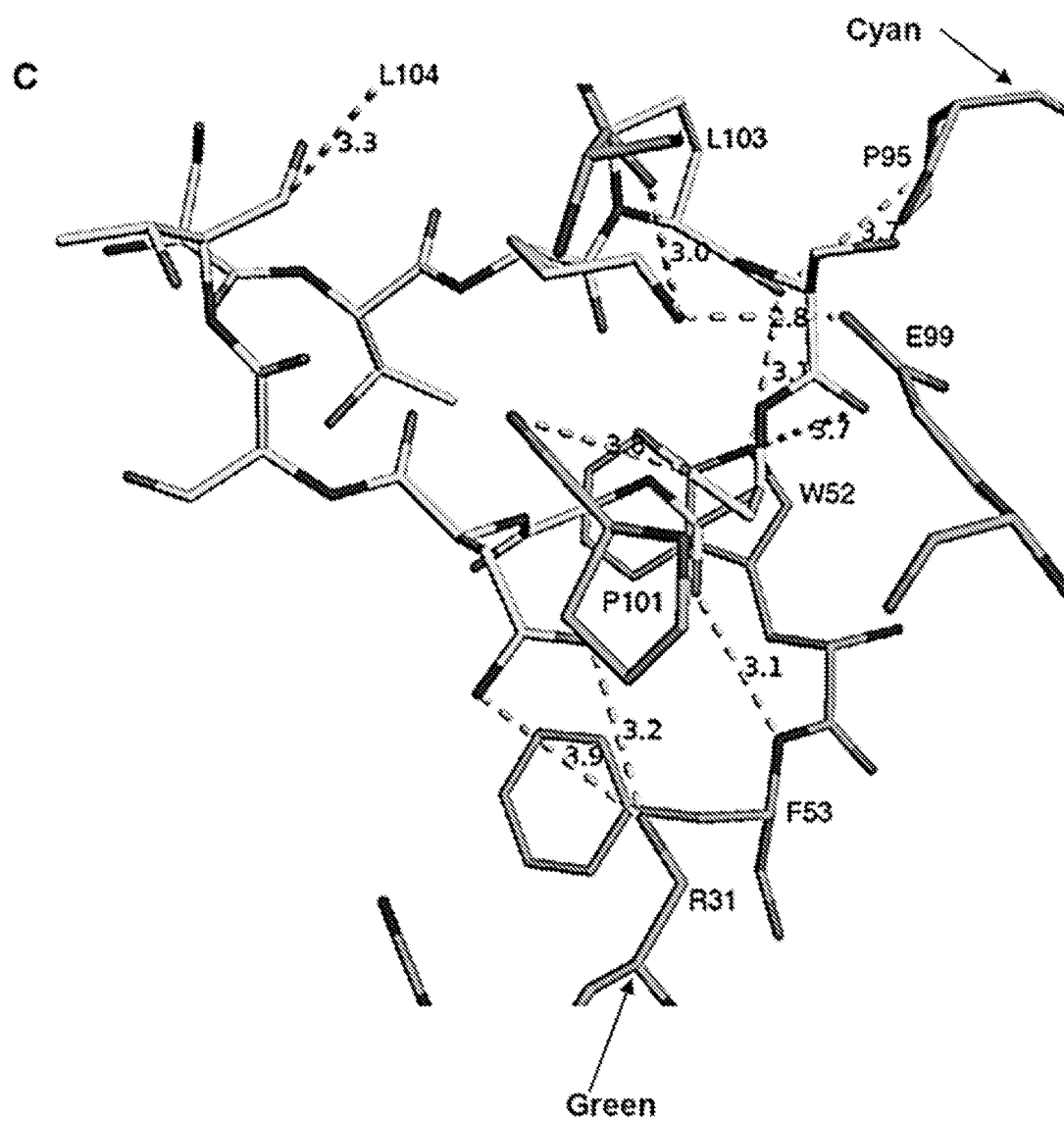


Fig. 6 (continued)

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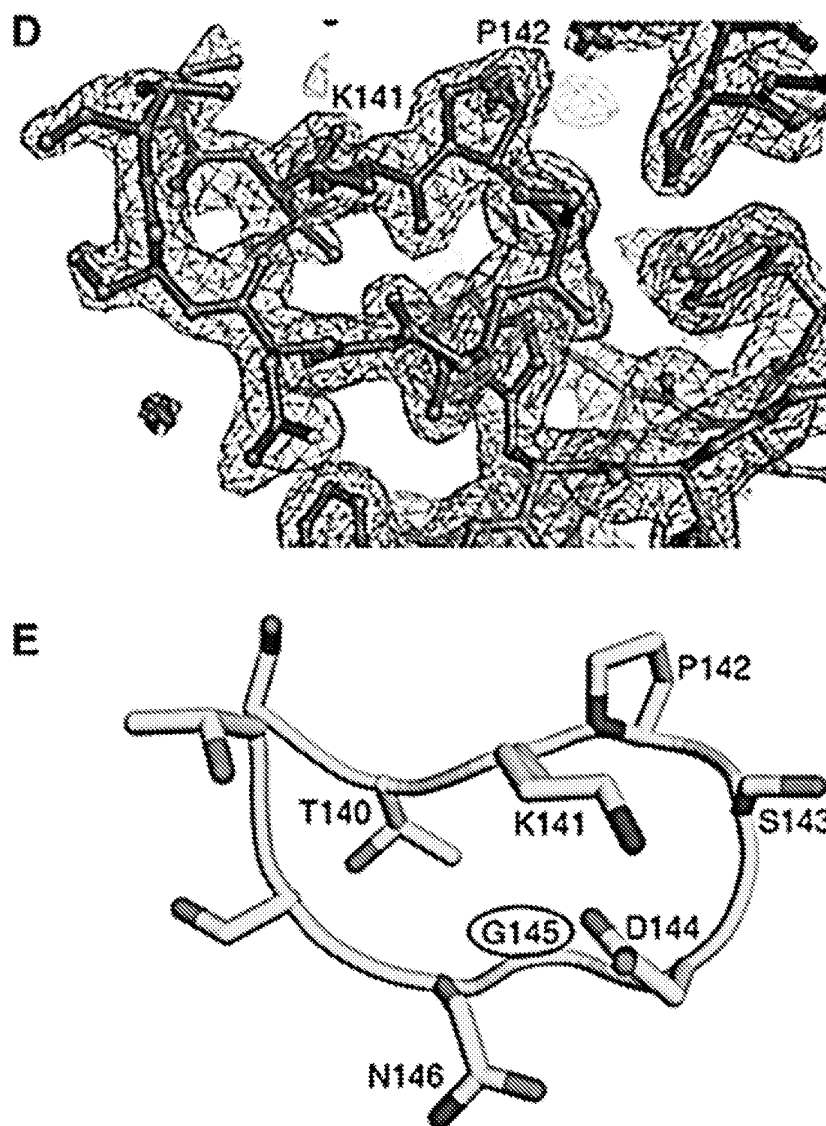


Fig. 6 (continued)

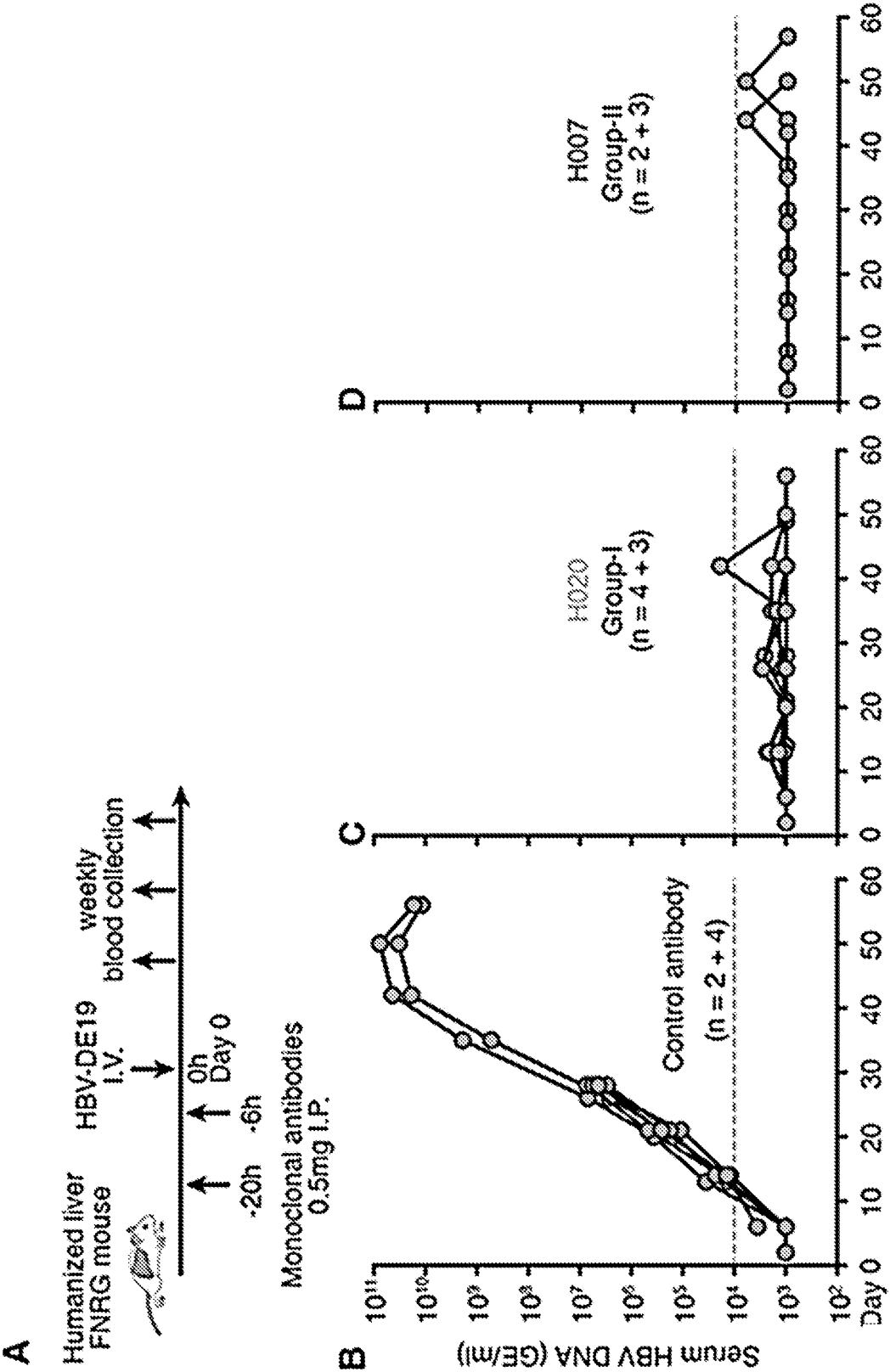
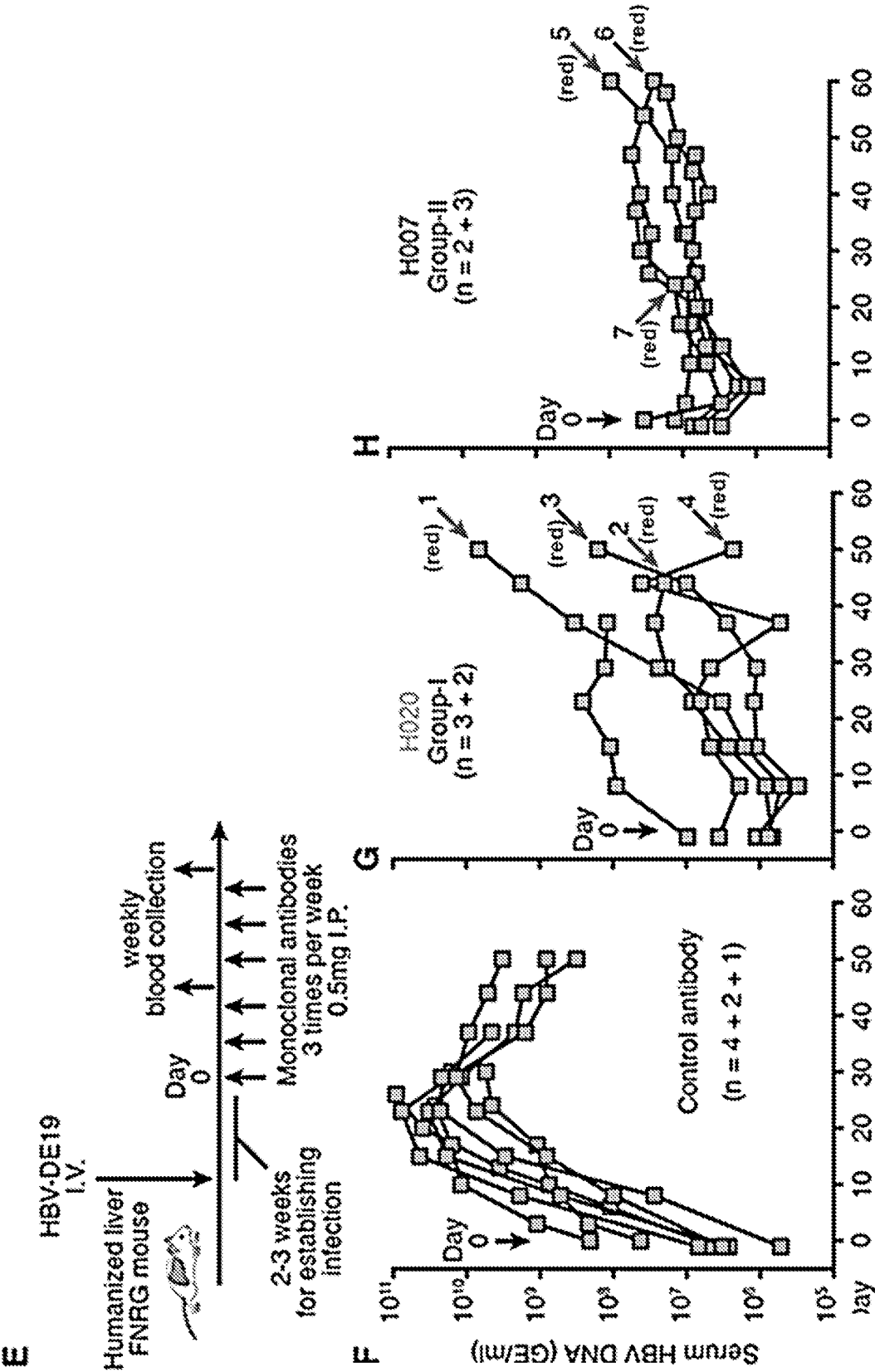


Fig. 7



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| I | Red arrow | Escape mutation |
|---|-----------|-----------------|
|   | 1         | G145R           |
|   | 2         | G145R           |
|   | 3         | G145R           |
|   | 4         | G145E           |
|   | 5         | G145R           |
|   | 6         | G145R           |
|   | 7         | G145R           |
|   | 8         | K122R / G145R   |
|   | 9         | C137Y           |
|   | 10        | C137Y / D144V   |

Fig. 7 (continued)

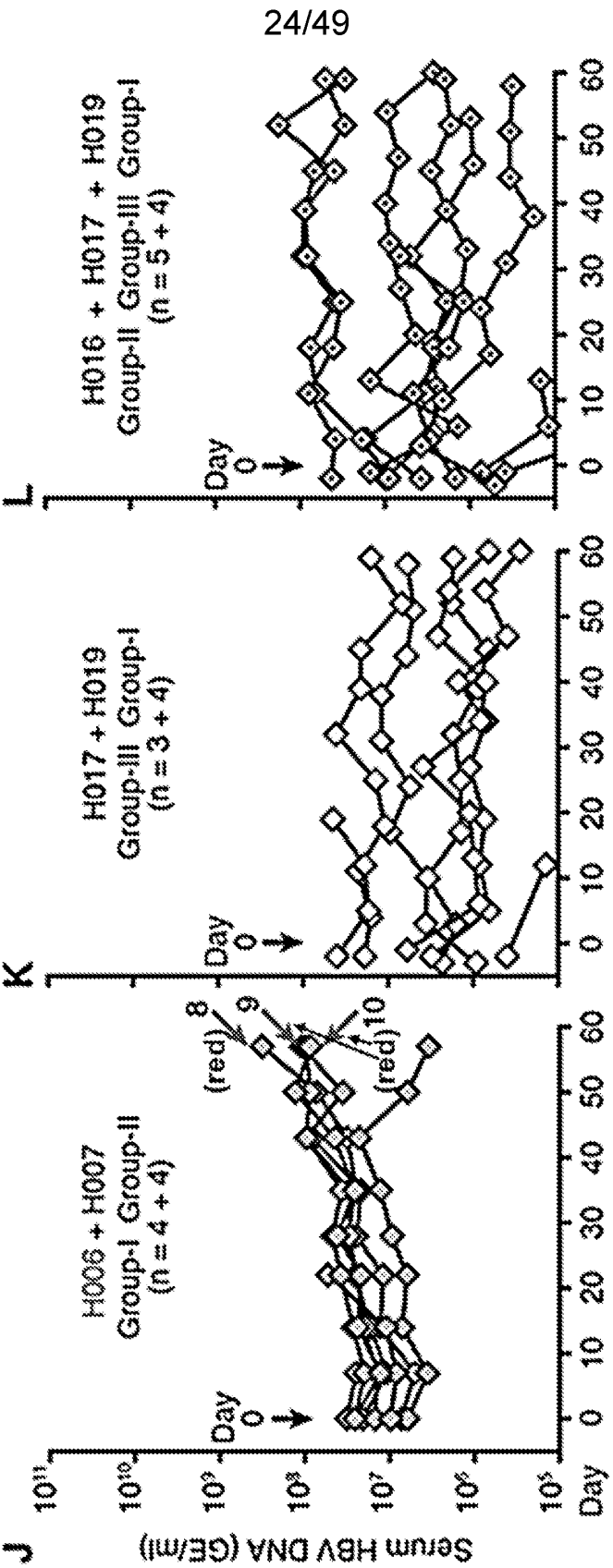


Fig. 7 (continued)

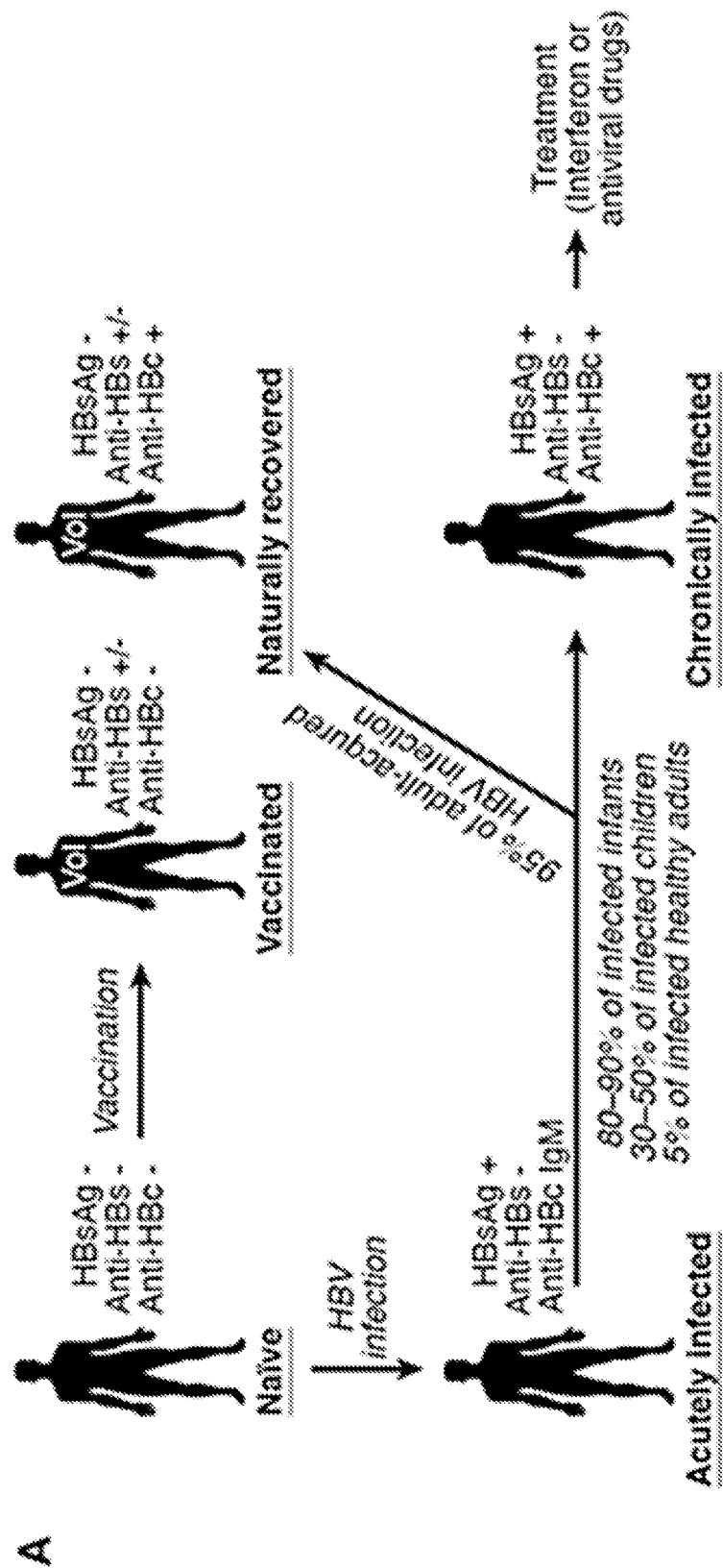


Fig. 8

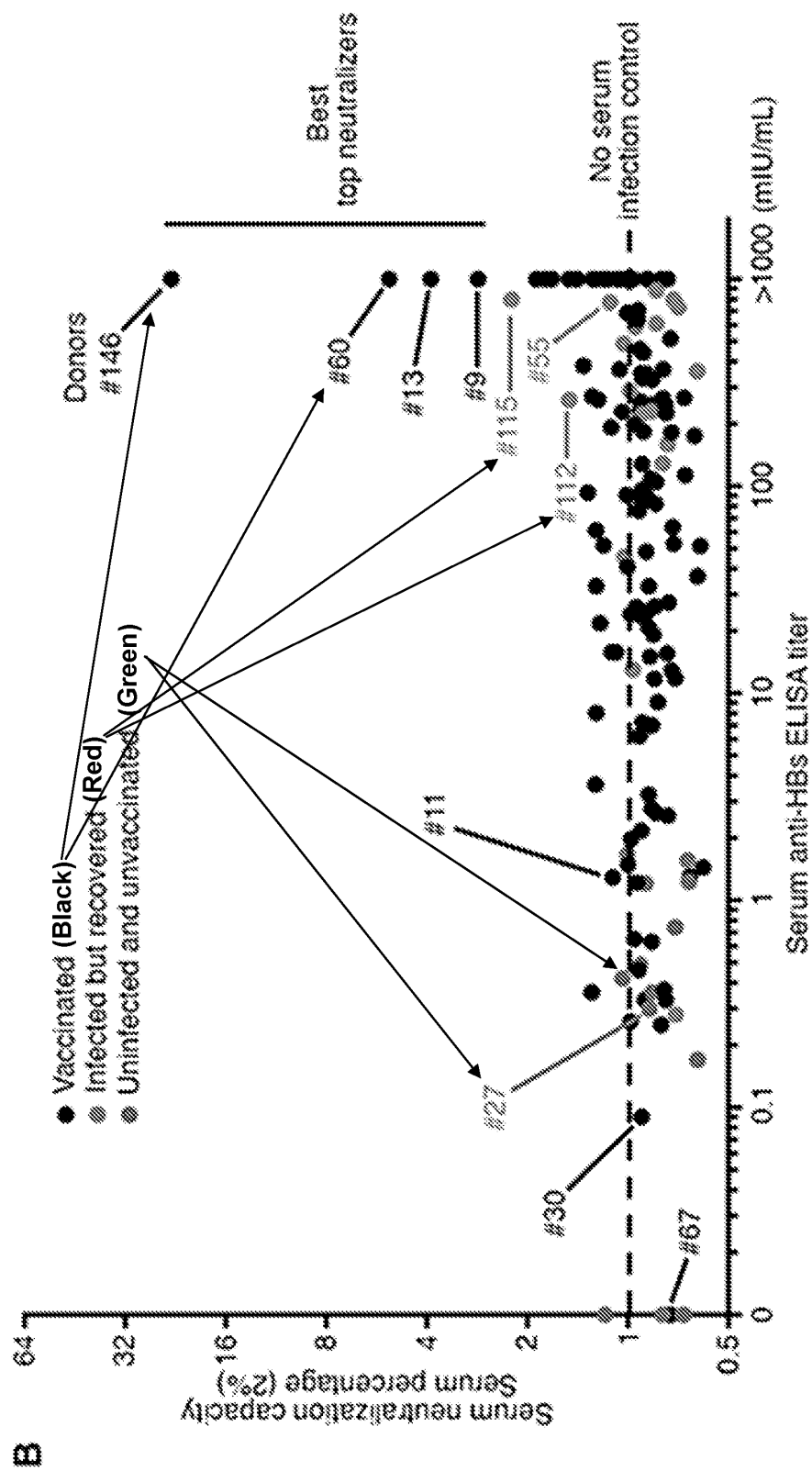


Fig. 8 (continued)

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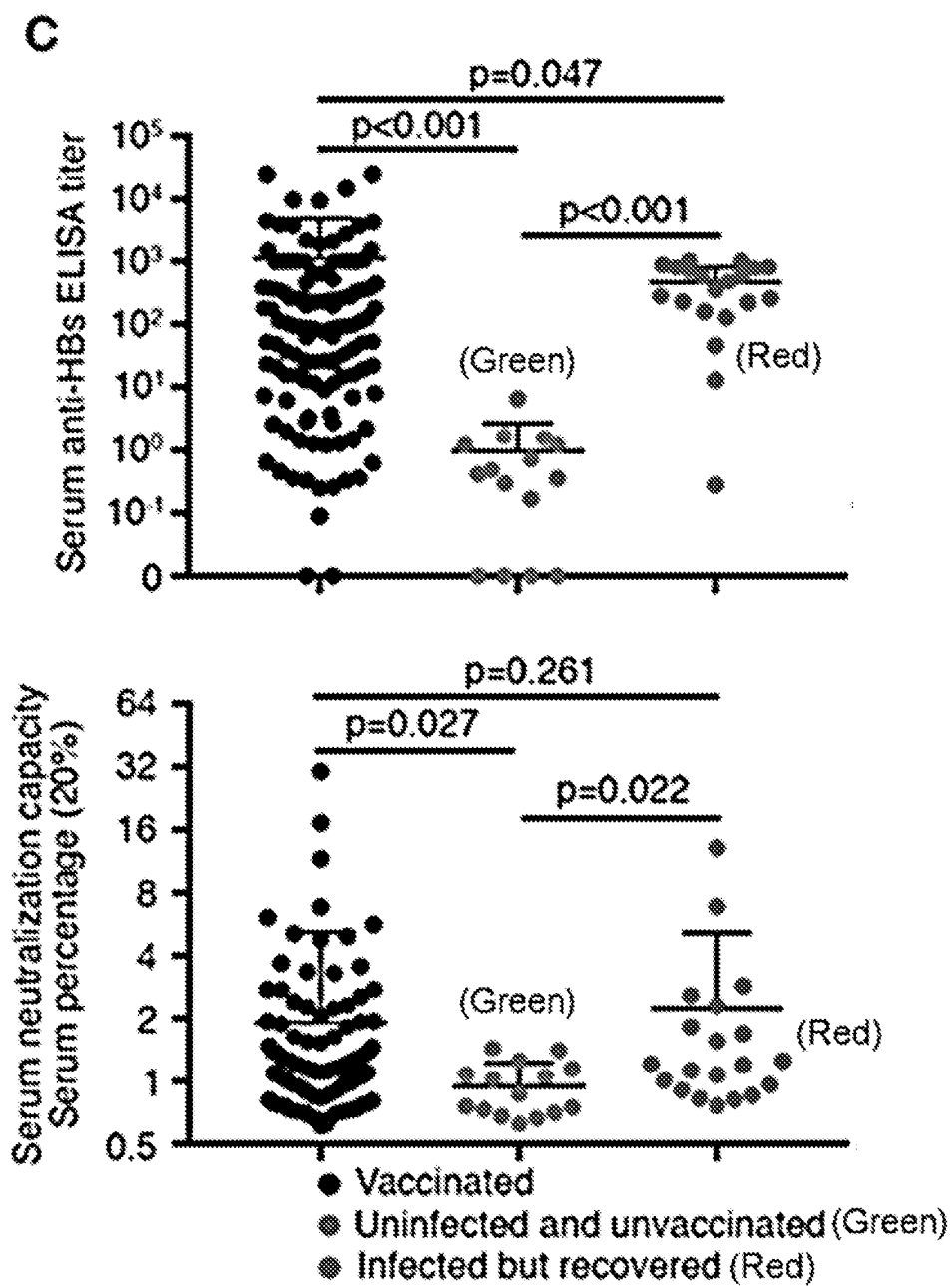


Fig. 8 (continued)

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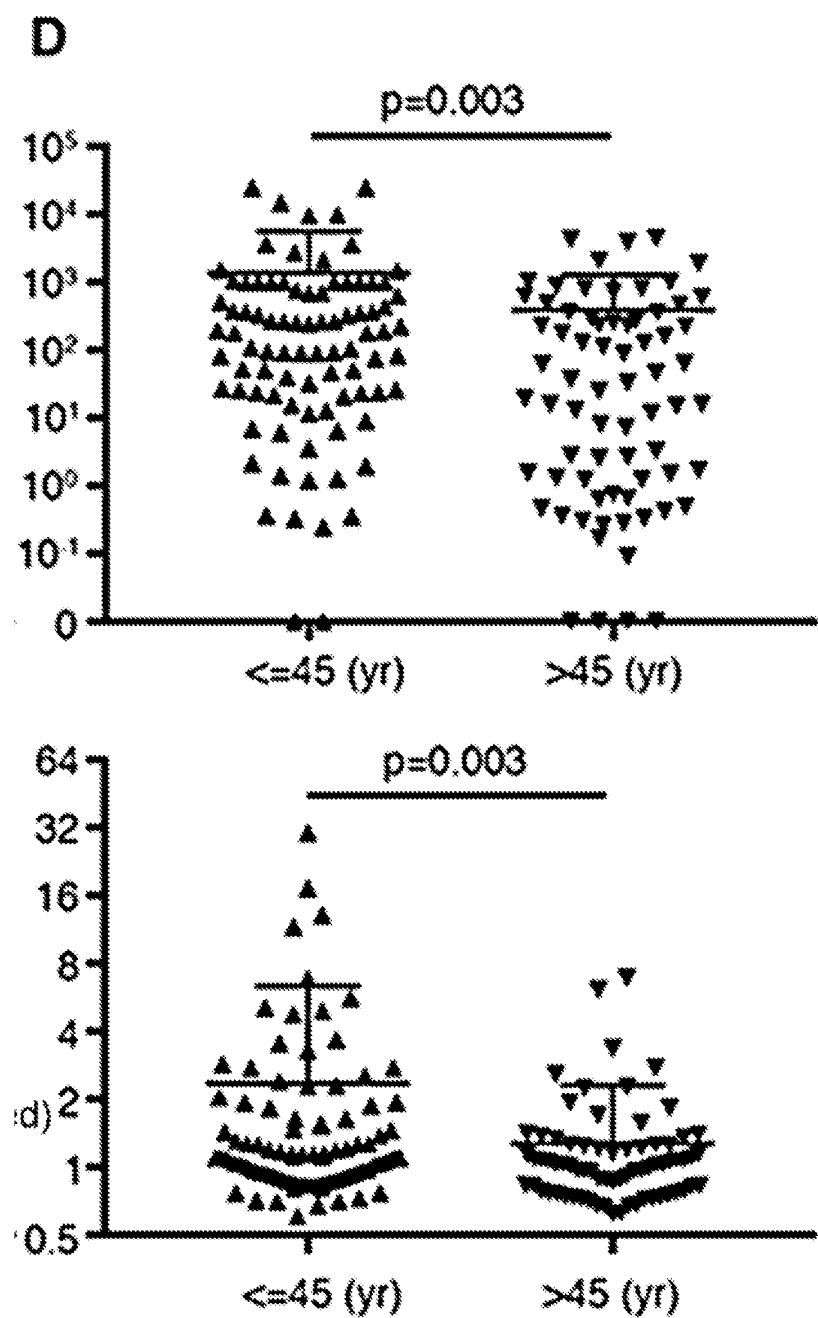


Fig. 8 (continued)

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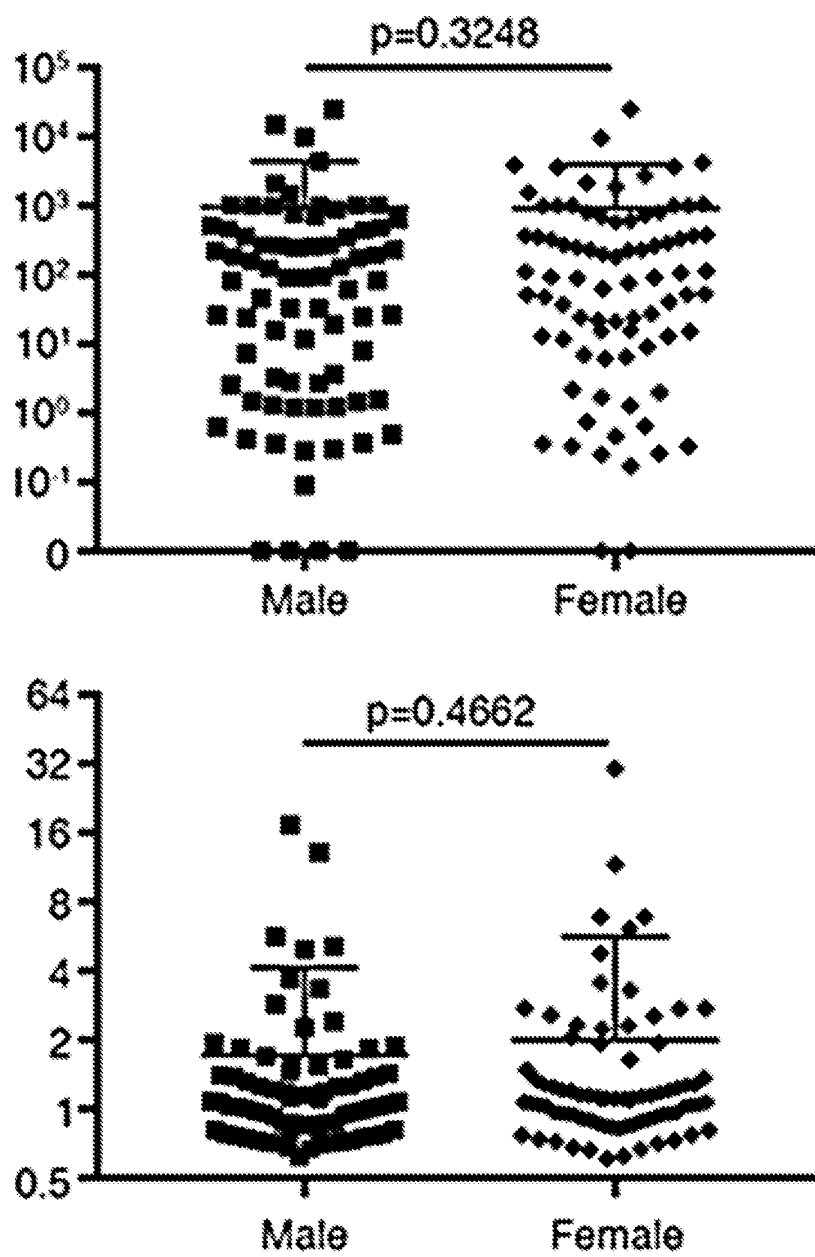
**E**

Fig. 8 (continued)

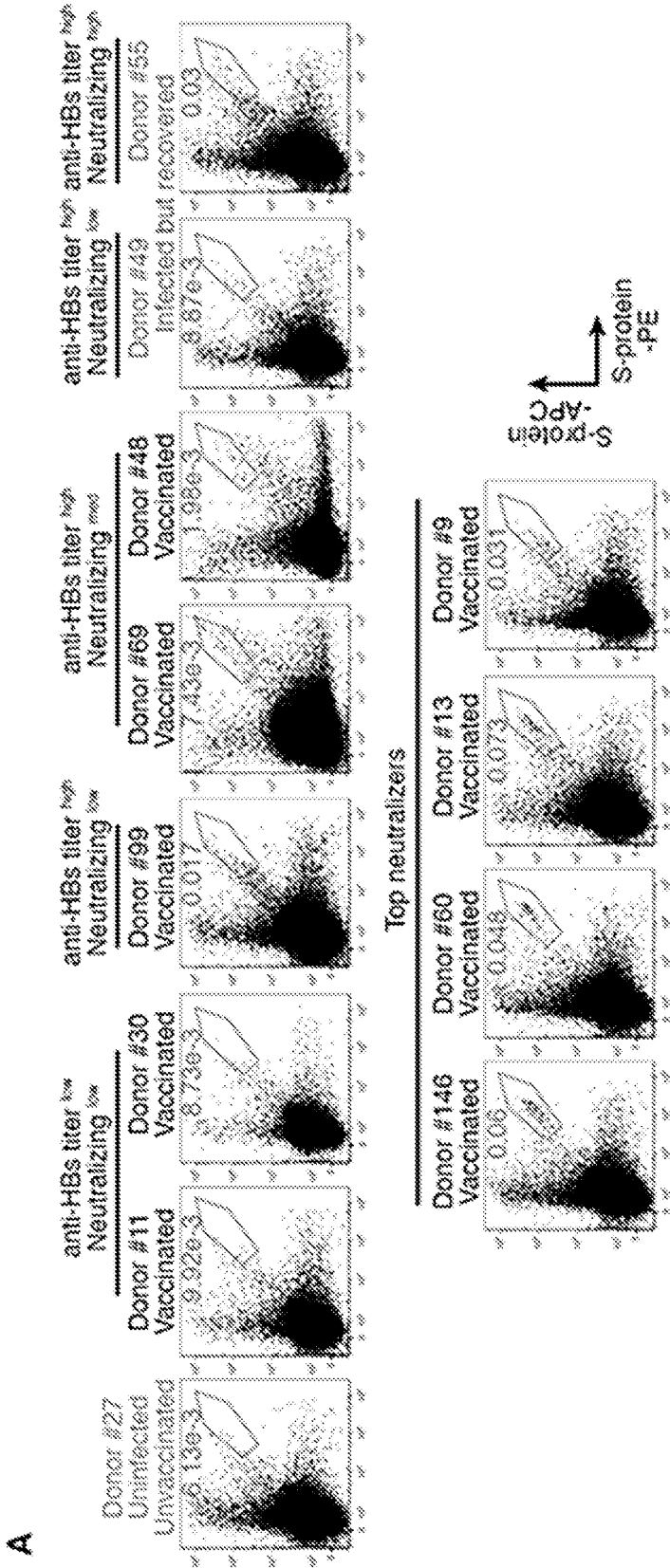


Fig. 9

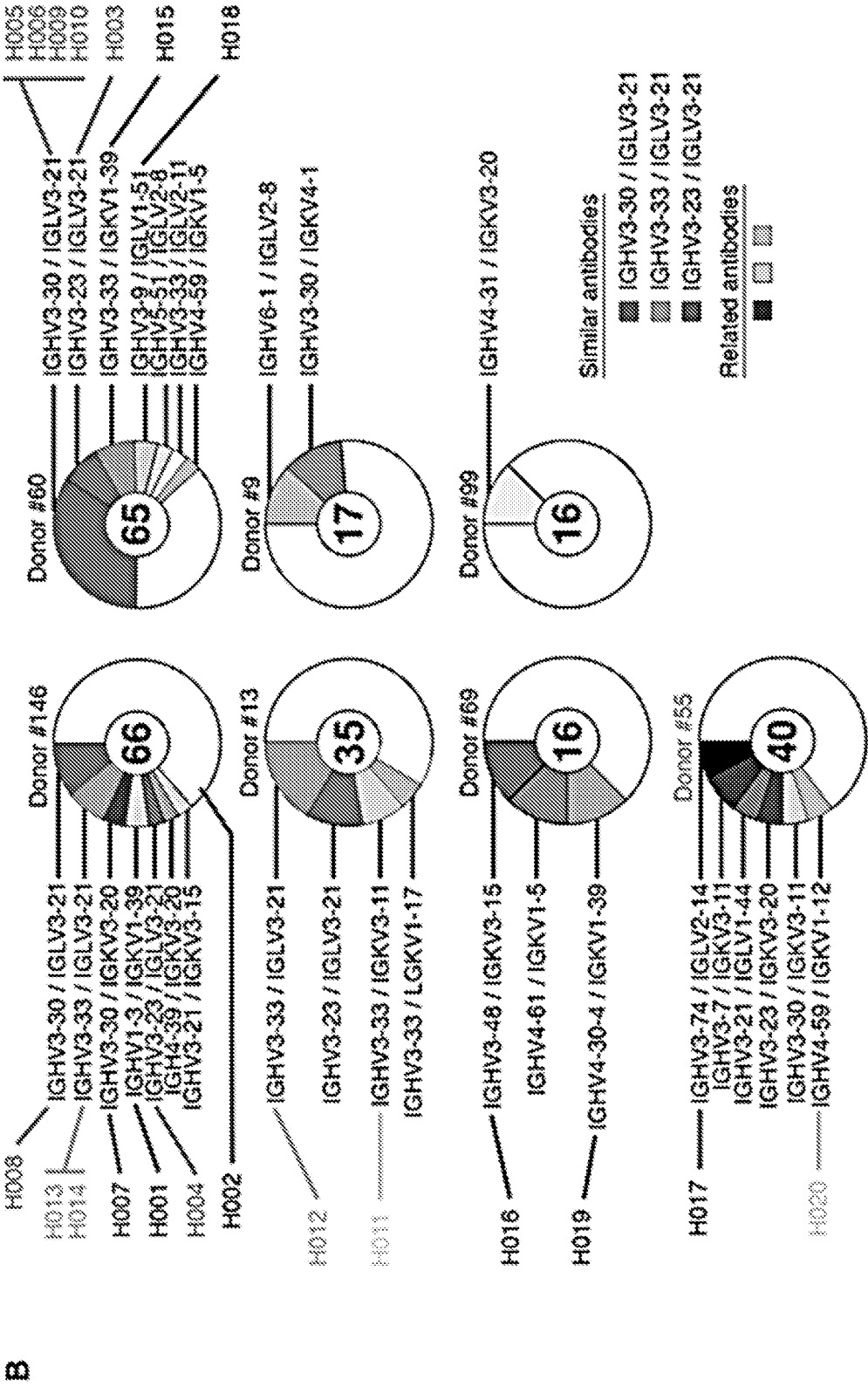


Fig. 9 (continued)

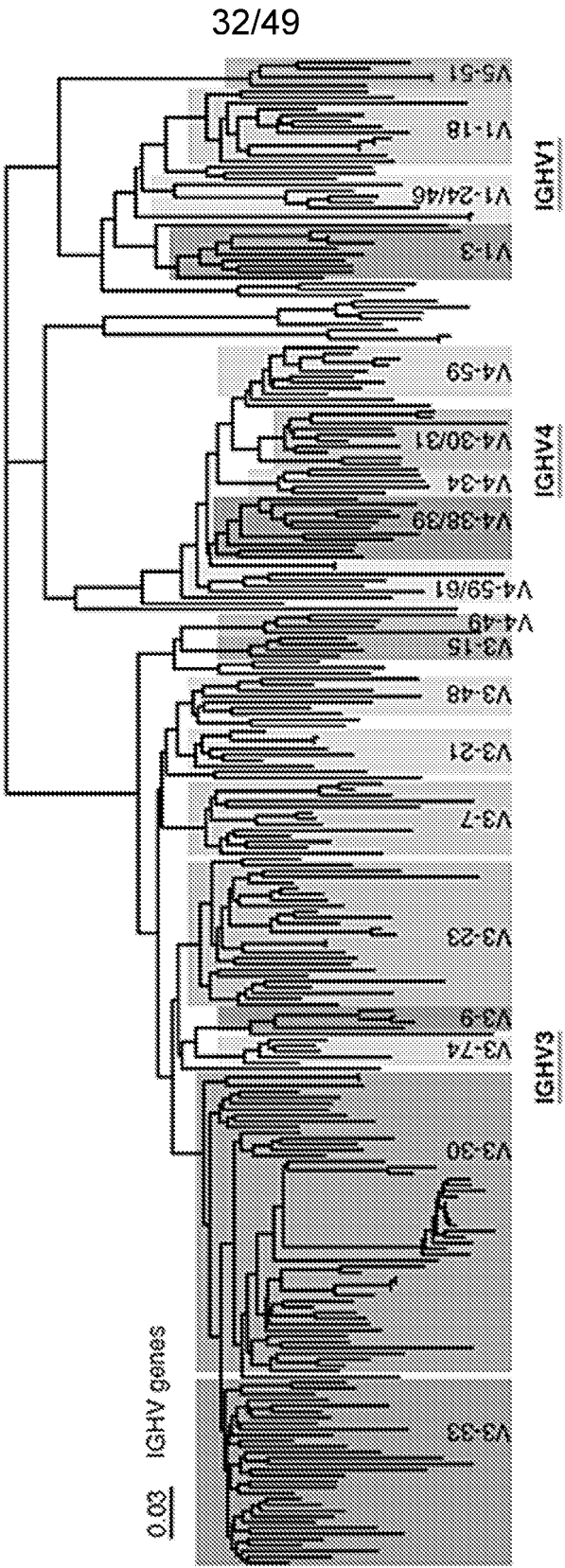
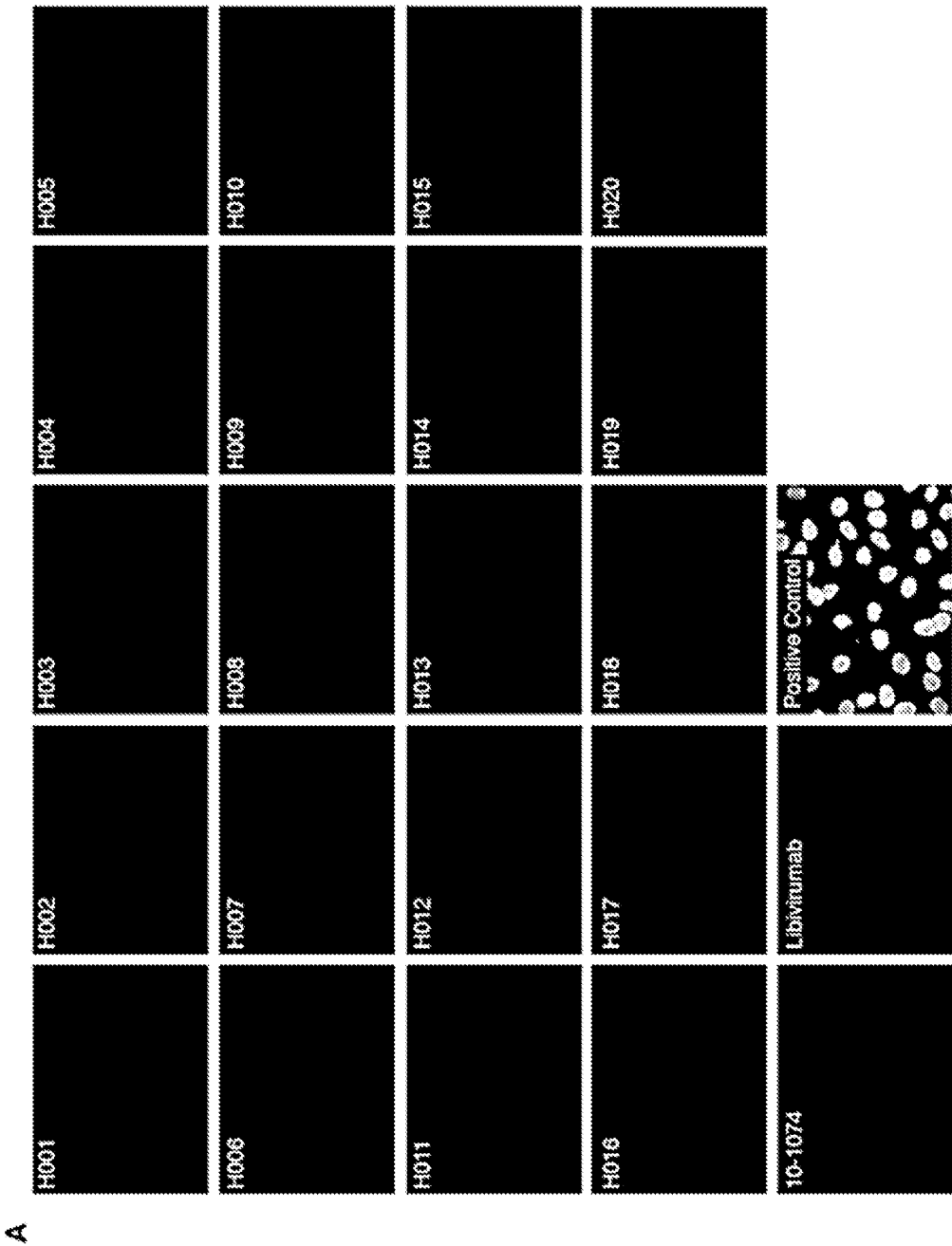


Fig. 9 (continued)



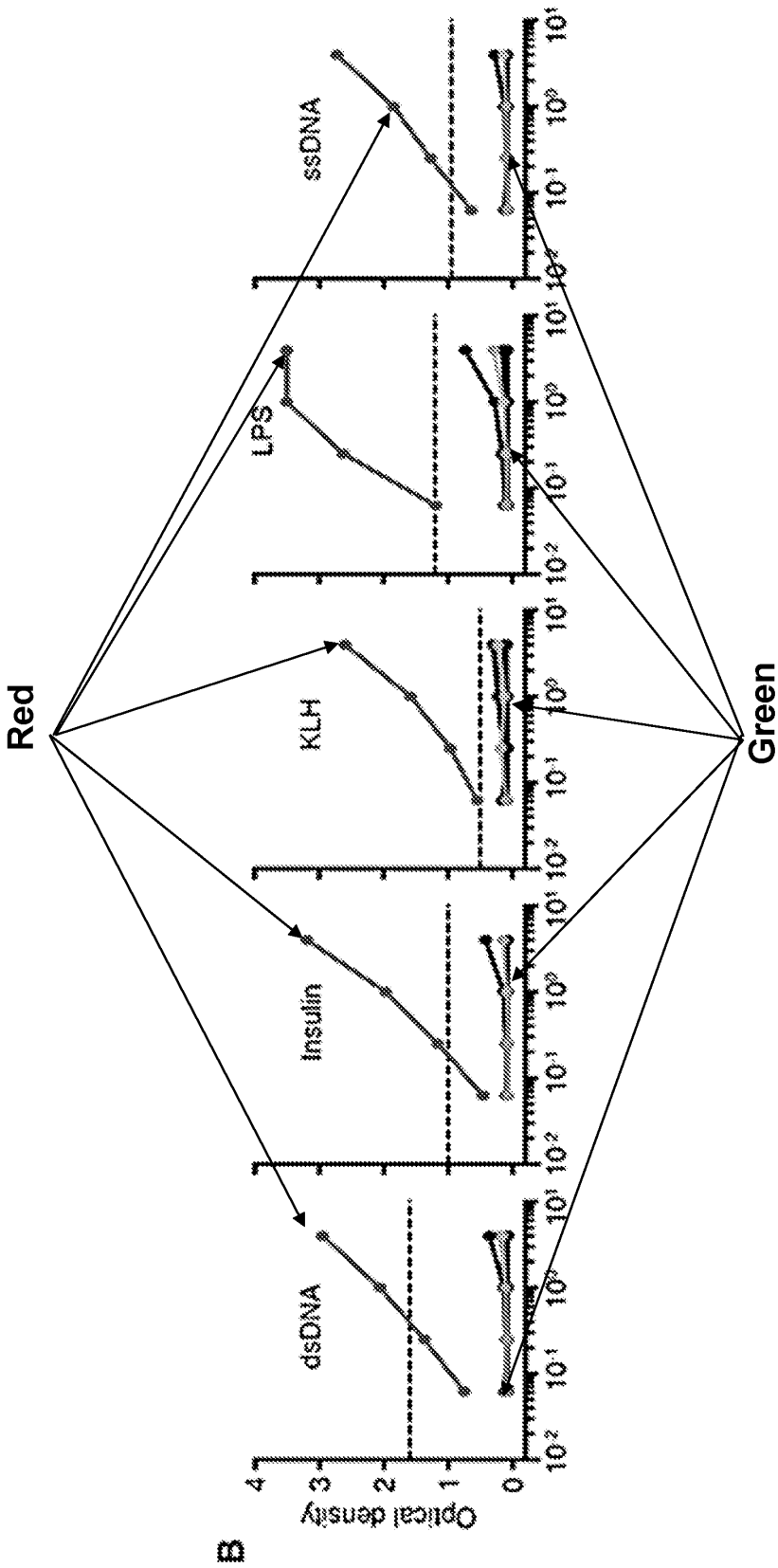


Fig. 10 (continued)

Fig. 11

A (continued)

|      | T   | P   | A   | Q   | G   | N   | S   | M   | F   | P   | S   | C   | C   | C   | T   | K   | P   | T   | D   | G   | N   | C   | T   | C   | I   |
|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|      | 131 | 141 | 144 | 145 | 148 | 149 | 150 | 151 | 152 | 153 | 154 | 155 | 156 | 157 | 158 | 159 | 160 | 161 | 162 | 163 | 164 | 165 | 166 | 167 | 168 |
| H020 | 96  | 94  |     | 96  | 106 | 89  | 91  | 95  | 97  | 94  | 101 |     |     |     | 102 | 68  | 86  | 109 | 77  | 62  | 93  |     |     | 31  | 95  |
| H004 | 110 | 107 |     | 101 | 102 | 95  | 99  | 102 | 108 | 101 | 100 |     |     |     | 109 | 76  | 108 | 105 | 55  | 59  | 92  |     |     | 59  | 112 |
| H006 | 101 | 108 |     | 100 | 101 | 93  | 97  | 101 | 103 | 101 | 98  |     |     |     | 100 | 68  | 104 | 104 | 102 | 101 | 92  |     |     | 58  | 108 |
| H019 | 102 | 91  |     | 94  | 88  | 81  | 91  | 89  | 84  | 89  | 103 |     |     |     | 101 | 17  | 70  | 102 | 98  | 99  | 102 |     |     | 59  | 86  |
| H017 | 99  | 101 |     | 92  | 102 | 103 | 94  | 99  | 95  | 108 | 120 |     |     |     | 133 | 145 | 128 | 124 | 141 | 127 | 105 |     |     | 81  | 91  |
| H007 | 98  | 104 |     | 103 | 102 | 111 | 104 | 107 | 105 | 104 | 98  |     |     |     | 97  | 96  | 78  | 85  | 40  | 45  | 106 |     |     | 99  | 99  |
| H016 | 95  | 97  |     | 102 | 100 | 120 | 110 | 99  | 95  | 109 | 98  |     |     |     | 86  | 104 | 102 | 95  | 63  | 17  | 108 |     |     | 99  | 106 |
| H015 | 97  | 99  |     | 105 | 101 | 111 | 108 | 106 | 109 | 103 | 101 |     |     |     | 105 | 11  | 43  | 11  | 15  | 25  | 107 |     |     | 102 | 94  |

Dark grey

Light grey

White

Black

Group-I

Group-II

Group-III

Fig. 11 (continued)

A (continued)

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White

Dark grey

|      | 151 |   |     |     |     |   |   |     |   | 161 |     |     |     |     |     |   |     |     |   |     | 171 |     |  | Emp WT |
|------|-----|---|-----|-----|-----|---|---|-----|---|-----|-----|-----|-----|-----|-----|---|-----|-----|---|-----|-----|-----|--|--------|
|      | P   | I | P   | S   | S   | W | A | F   | A | K   | Y   | L   | W   | E   | W   | A | S   | V   | R | F   | S   | W   |  |        |
| H020 | 103 |   | 104 | 98  | 115 |   |   | 99  |   | 99  | 93  | 110 | 107 | 100 | 99  |   | 104 | 105 |   | 96  | 93  | 100 |  | 19 100 |
| H004 | 103 |   | 108 | 97  | 108 |   |   | 103 |   | 99  | 95  | 102 | 96  | 91  | 99  |   | 97  | 96  |   | 94  | 100 | 99  |  | 27 100 |
| H006 | 100 |   | 108 | 102 | 111 |   |   | 109 |   | 106 | 105 | 102 | 94  | 93  | 99  |   | 98  | 102 |   | 106 | 101 | 105 |  | 17 100 |
| H019 | 98  |   | 100 | 93  | 101 |   |   | 99  |   | 94  | 107 | 110 | 100 | 105 | 104 |   | 99  | 96  |   | 99  | 103 | 89  |  | 23 100 |
| H017 | 109 |   | 145 | 113 | 117 |   |   | 117 |   | 106 | 80  | 94  | 101 | 99  | 92  |   | 110 | 104 |   | 106 | 102 | 96  |  | 16 100 |
| H007 | 99  |   | 100 | 108 | 93  |   |   | 98  |   | 107 | 80  | 97  | 101 | 102 | 101 |   | 99  | 100 |   | 100 | 99  | 101 |  | 21 100 |
| H016 | 98  |   | 90  | 99  | 85  |   |   | 95  |   | 97  | 64  | 94  | 102 | 104 | 103 |   | 104 | 101 |   | 107 | 106 | 105 |  | 20 100 |
| H015 | 99  |   | 91  | 103 | 87  |   |   | 97  |   | 97  | 70  | 85  | 100 | 105 | 95  |   | 99  | 99  |   | 97  | 97  | 100 |  | 17 100 |

Light grey

Black

Fig. 11 (continued)

**B**

Antibodies show reduced binding.

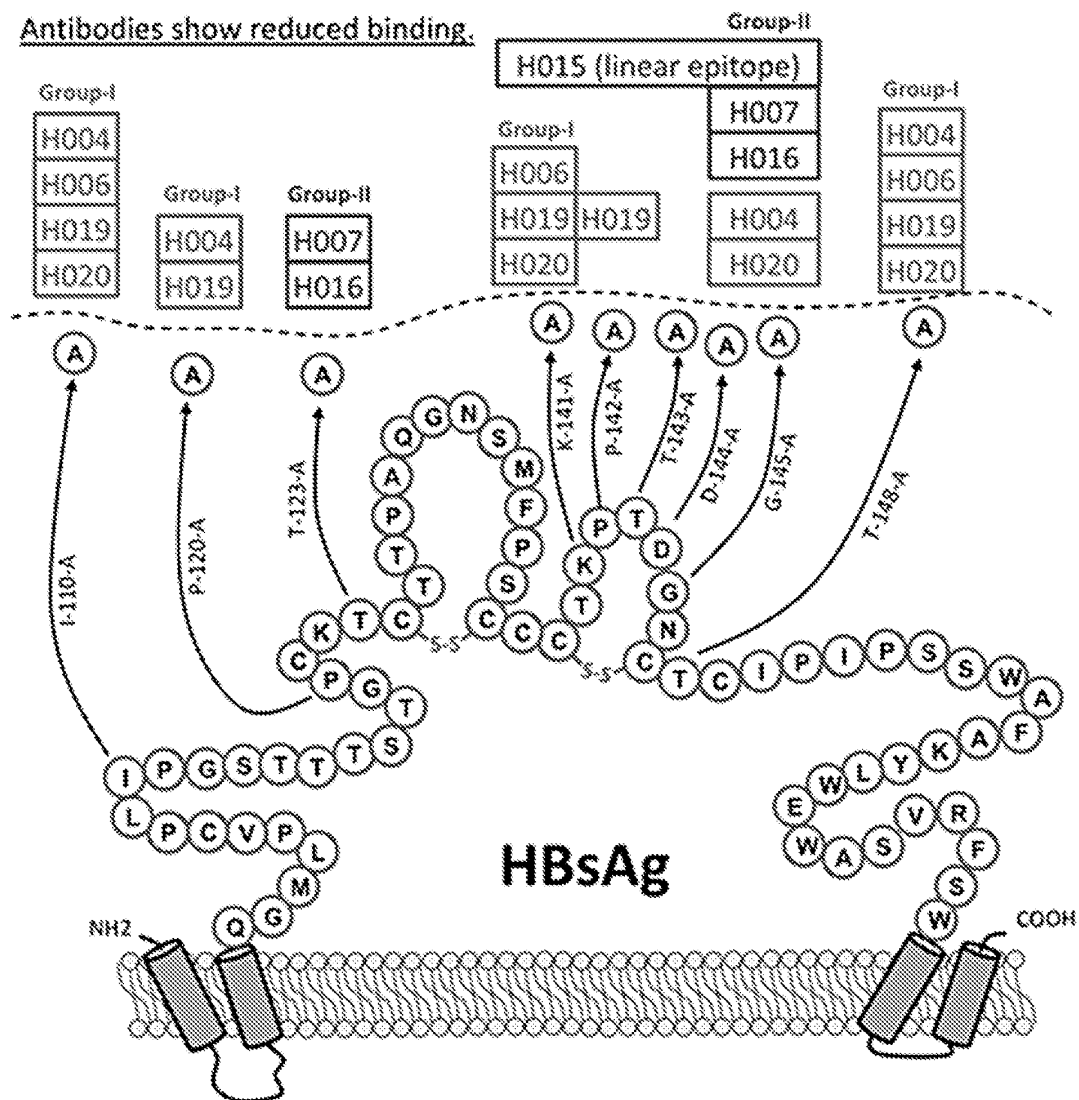


Fig. 11 (continued)

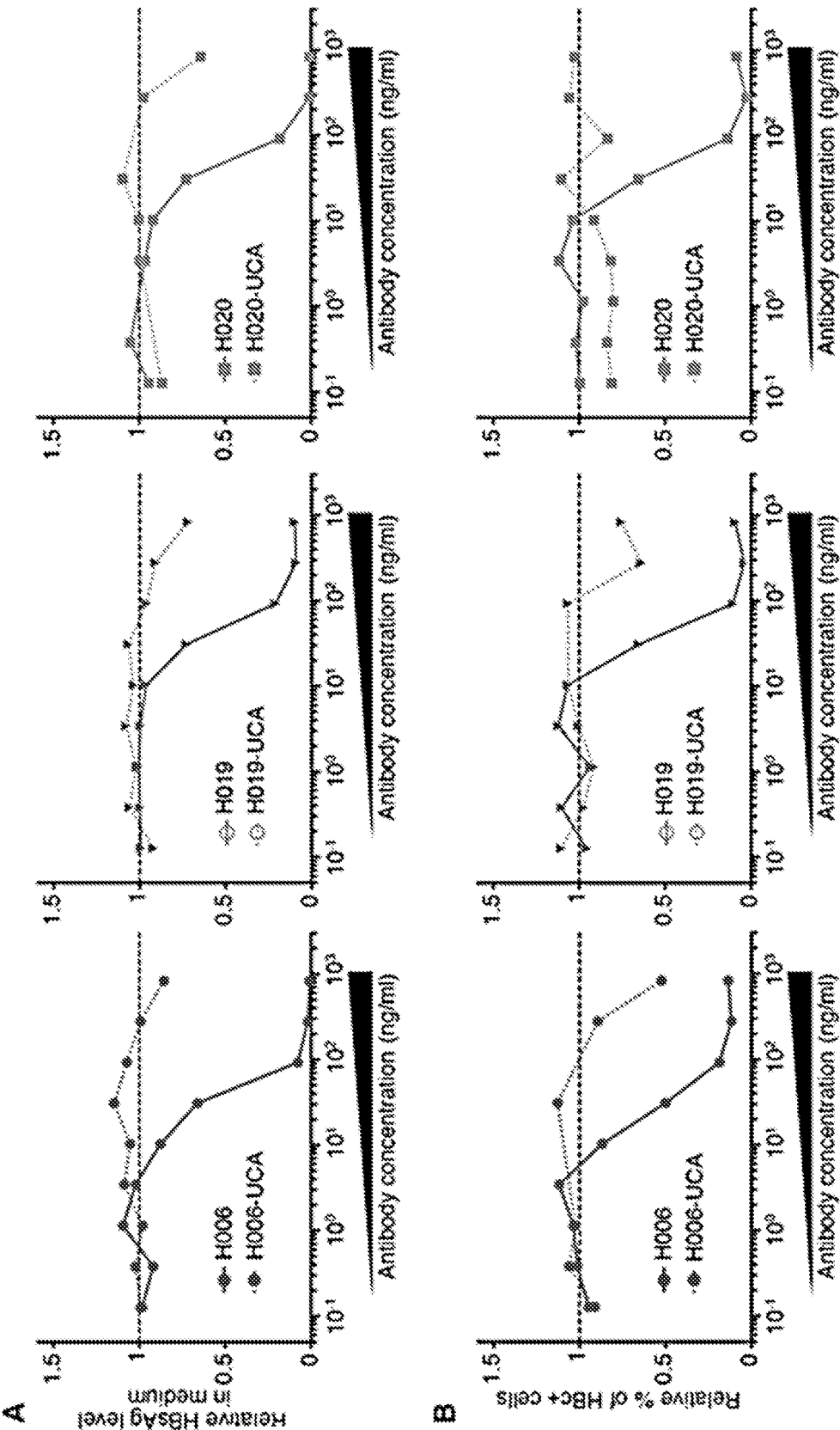


Fig. 12

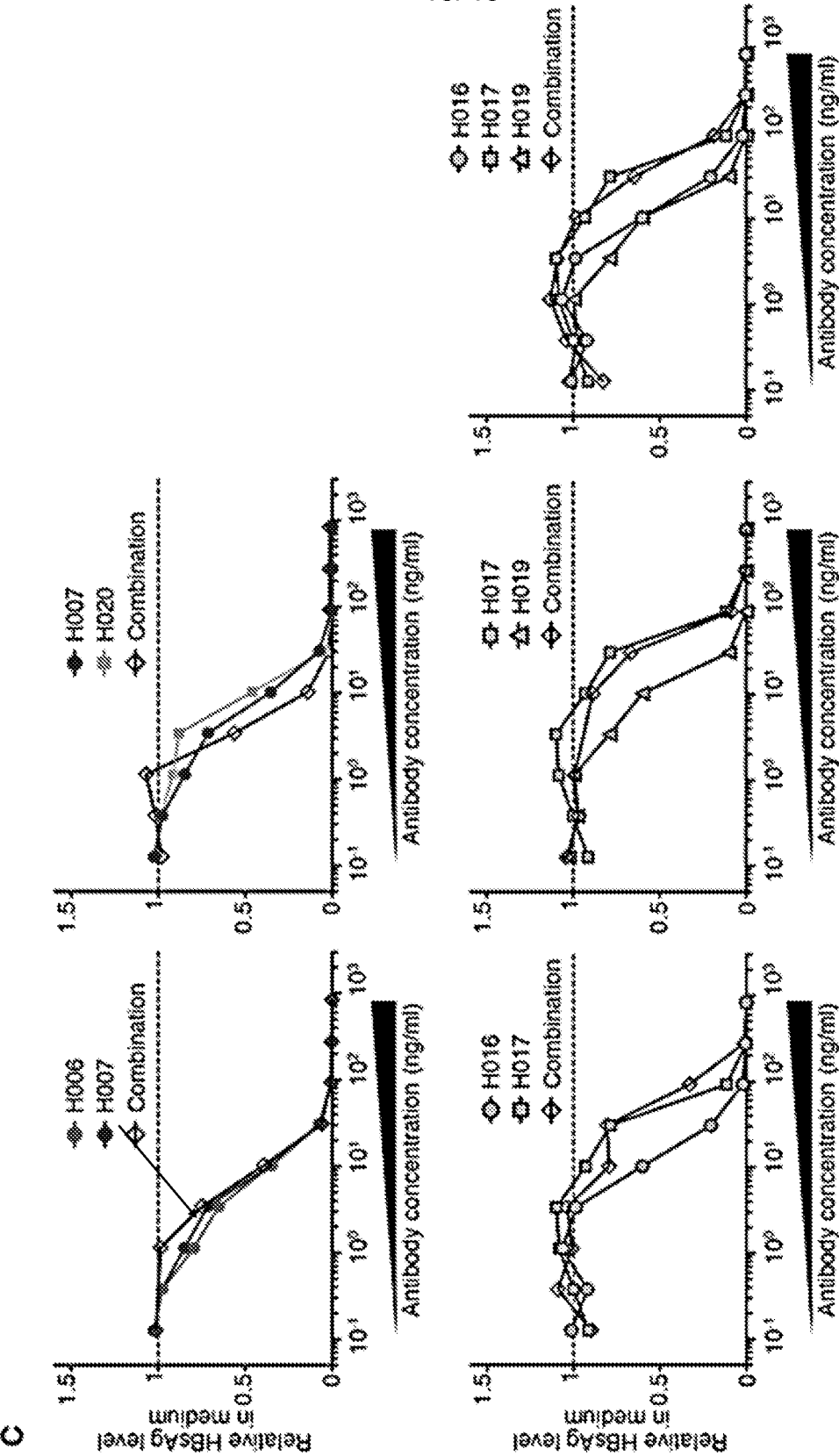


Fig. 12 (continued)

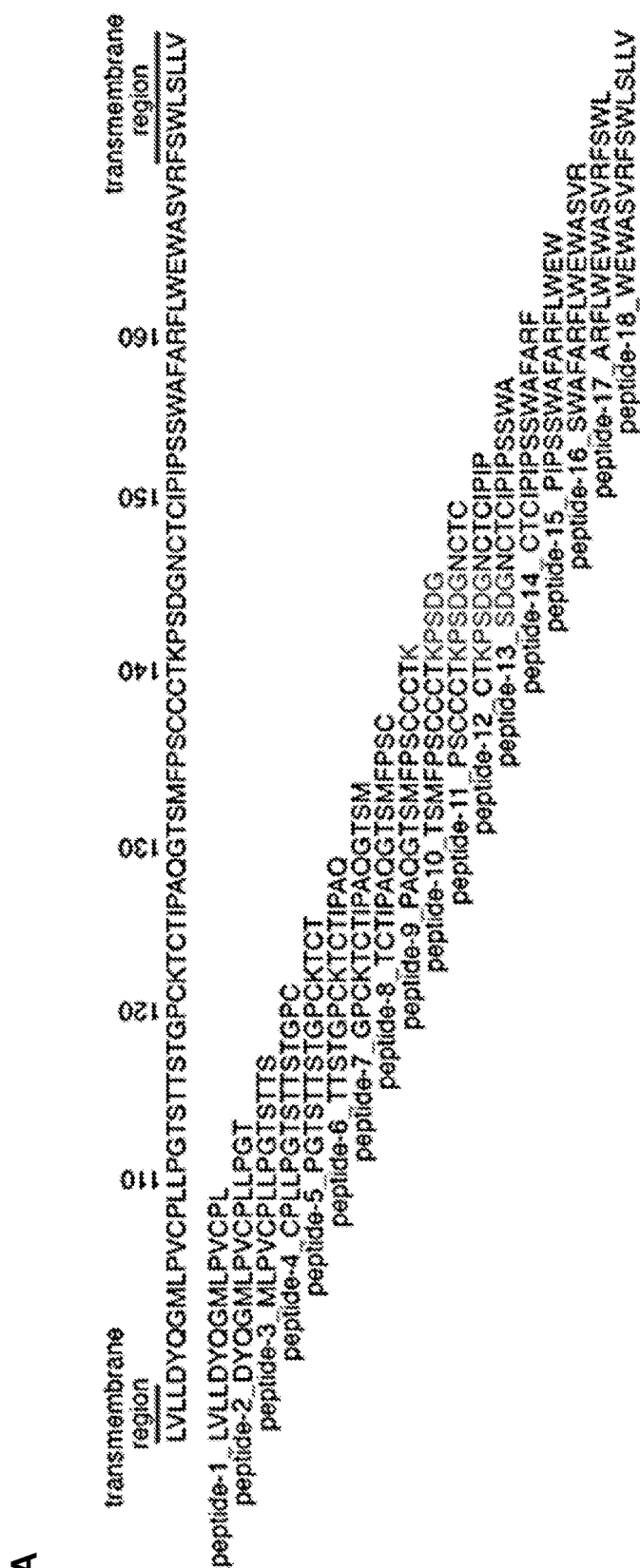


Fig. 13

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B

|                                |                                               |
|--------------------------------|-----------------------------------------------|
| Wavelength (Å)                 | 0.979                                         |
| Resolution range               | 67.35-1.78 (1.82-1.78)                        |
| Space group                    | P2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub> |
| Unit cell                      | 49.9 71.2 134.7                               |
| Total reflections              | 615,285 (56,022)                              |
| Unique reflections             | 46,432 (4,386)                                |
| Multiplicity                   | 12.9 (12.1)                                   |
| Completeness (%)               | 99.5 (91.0)                                   |
| Mean I/sigma (I)               | 17.2 (1.26)                                   |
| Wilson B-factor                | 33                                            |
| Anisotropy                     | 0.449                                         |
| R-merge                        | 0.084 (1.26)                                  |
| R-meas                         | 0.090 (1.309)                                 |
| R-pim                          | 0.034 (0.505)                                 |
| CC <sub>1/2</sub>              | 0.999 (0.793)                                 |
| Reflections used in refinement | 46432 (4380)                                  |
| Reflections used for R-free    | 1999 (188)                                    |
| R-work                         | 0.182 (0.276)                                 |
| R-free                         | 0.227 (0.293)                                 |

|                                                                                       |            |
|---------------------------------------------------------------------------------------|------------|
| Number of non-hydrogen atoms                                                          | 3752       |
| Macromolecules                                                                        | 3391       |
| Solvent                                                                               | 361        |
| Protein residues                                                                      | 451        |
| RMSZ (bonds)                                                                          | 0.37       |
| RMSZ (angles)                                                                         | 0.55       |
| Ramachandran favored (%)                                                              | 98         |
| Ramachandran allowed (%)                                                              | 2          |
| Ramachandran outliers (%)                                                             | 0.00       |
| Rotamer outliers (%)                                                                  | 0.00       |
| Clashscore                                                                            | 1.00       |
| Average B-factor                                                                      | 39         |
| Average B of H/L                                                                      | 39         |
| Average B of the peptide                                                              | 49         |
| Macromolecules                                                                        | 38         |
| Solvent                                                                               | 43         |
| Fo, Fc correlation                                                                    | 0.97       |
| Bulk solvent k <sub>iso</sub> (e/Å <sup>3</sup> ), B <sub>iso</sub> (Å <sup>2</sup> ) | 0.32, 42.8 |

Fig. 13 (continued)

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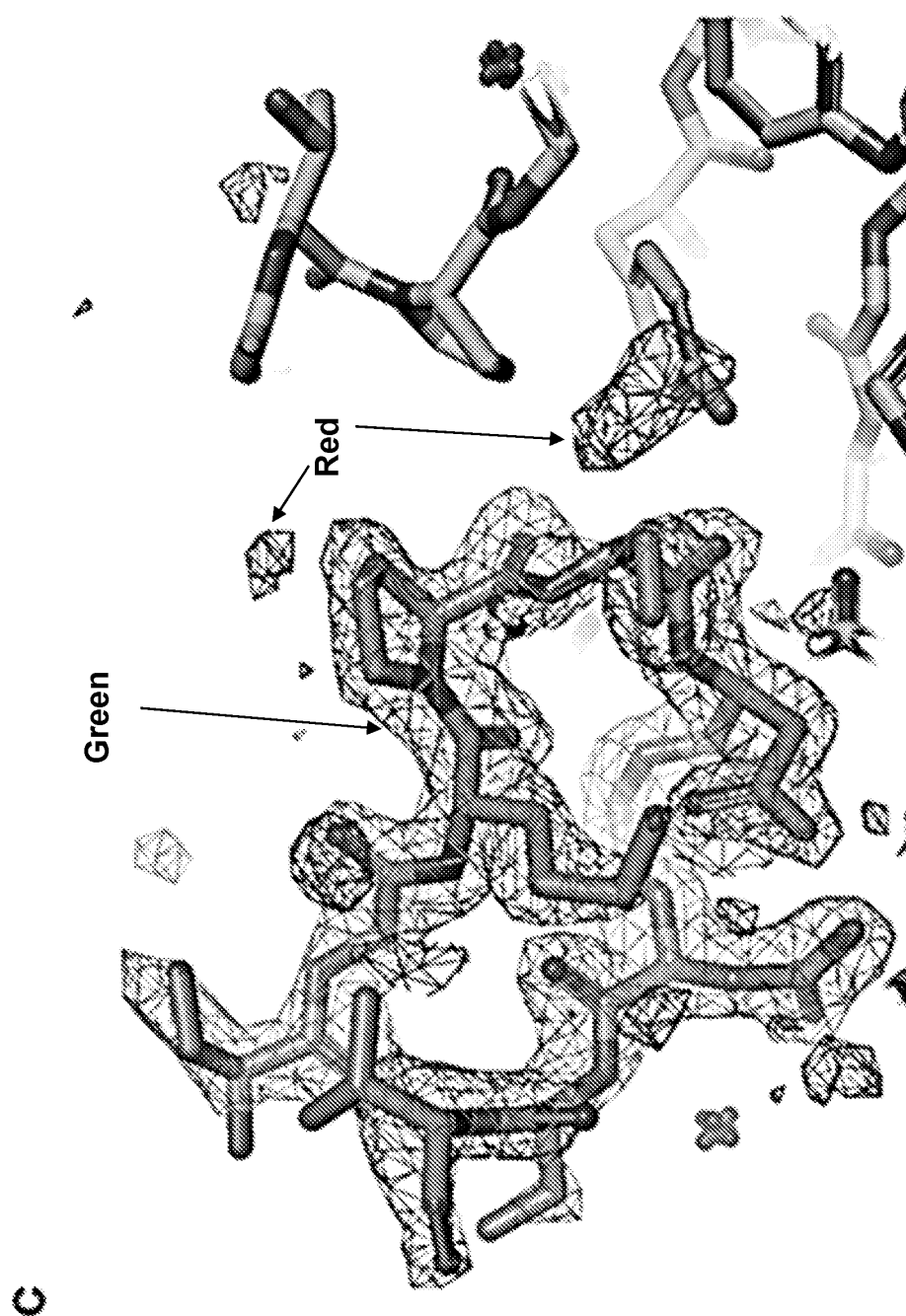


Fig. 13 (continued)

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**D**

|                                     |
|-------------------------------------|
| H-bonds within the peptide          |
| Ser139(O) – Thr 148(N, OG1)         |
| Lys141(N) – ASN146(O)               |
| Lys141(O) – Gly145(N)               |
| Asp144(OD2) – Asp146(N, ND2)        |
| Asp144(OD1) – Asp146(N)             |
|                                     |
| Salt bridge within the peptide      |
| Lys141(NZ) – Asp144(OD2)            |
|                                     |
| H-bonds between Fab and peptide     |
| Lys141(NZ) – Asp H100(O)            |
| Lys141(NZ) – Leu103(O)              |
| Pro142(O) – Trp H52(NE1)            |
| Ser143(O) – Tyr H59(OH)             |
| Ser143(OG) – Glu H99(OE2)           |
| Asp144(O) – Phe H53(N)              |
|                                     |
| Salt Bridge between Fab and peptide |
| Lys141(NZ) – Glu H99(OE2)           |
|                                     |
| Hydrophobic between Fab and peptide |
| Pro142 – Leu L29                    |
| Gly145 – Trp H52                    |

Fig. 13 (continued)

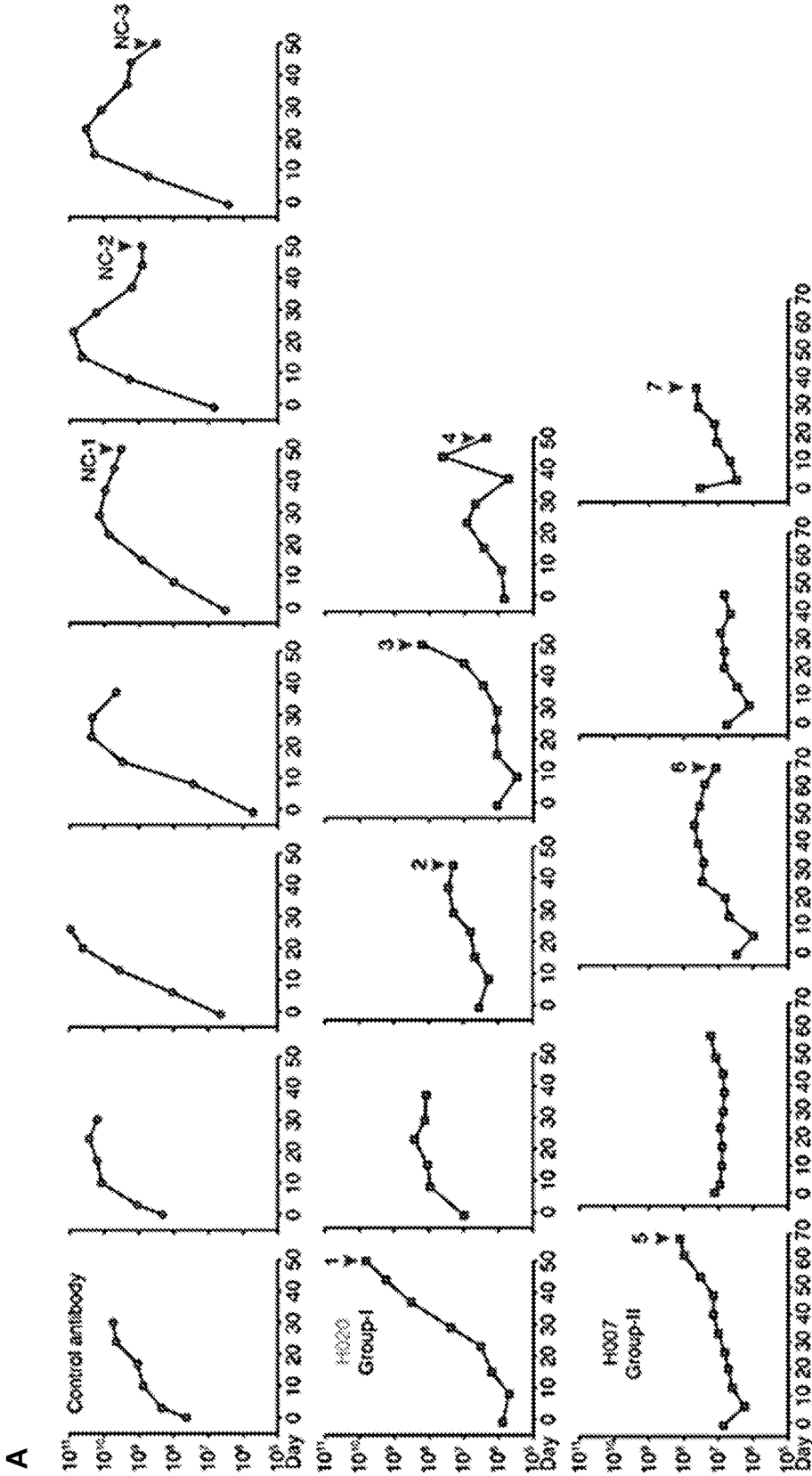


Fig. 14

A (continued)

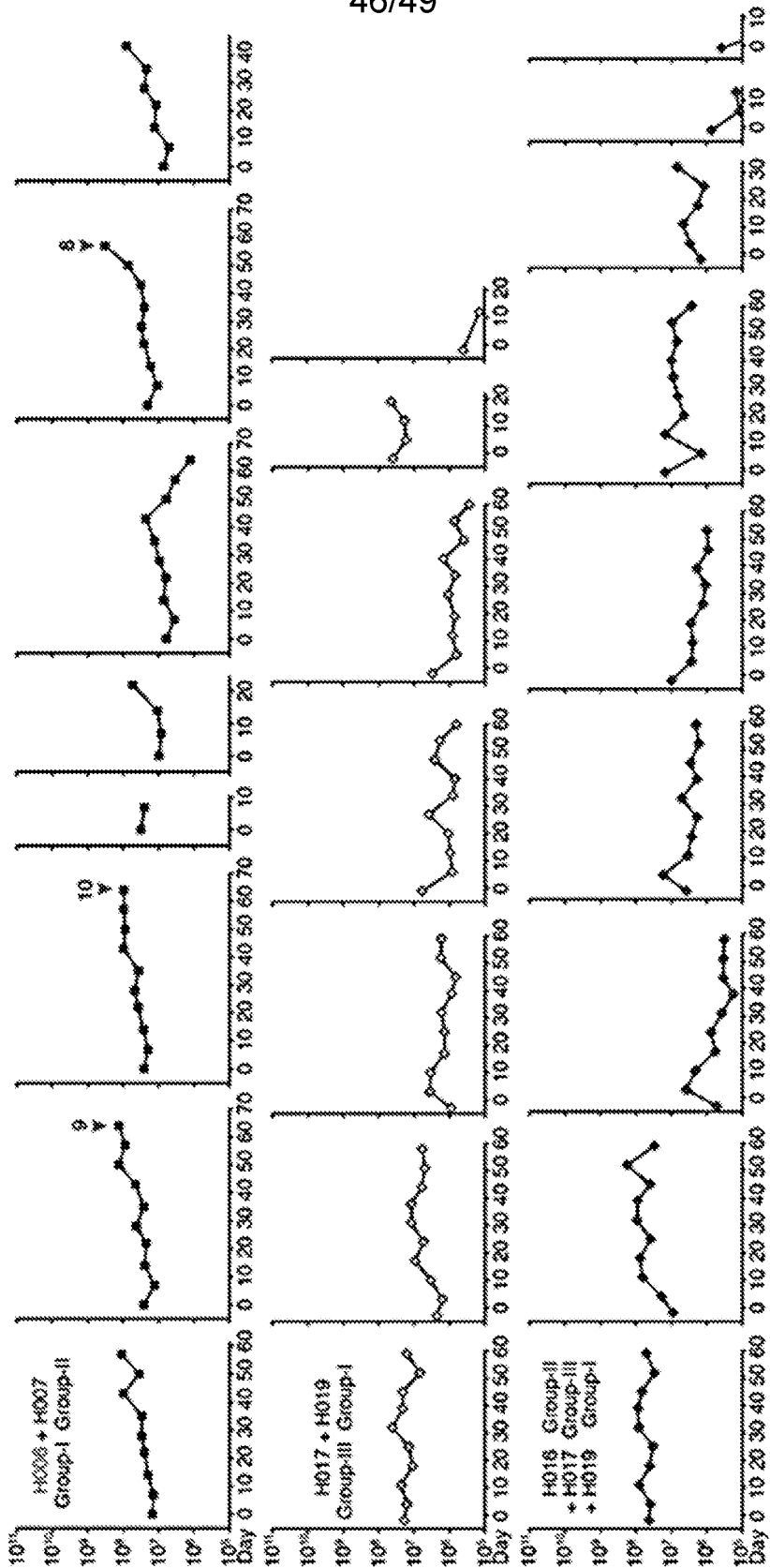


Fig. 14 (continued)

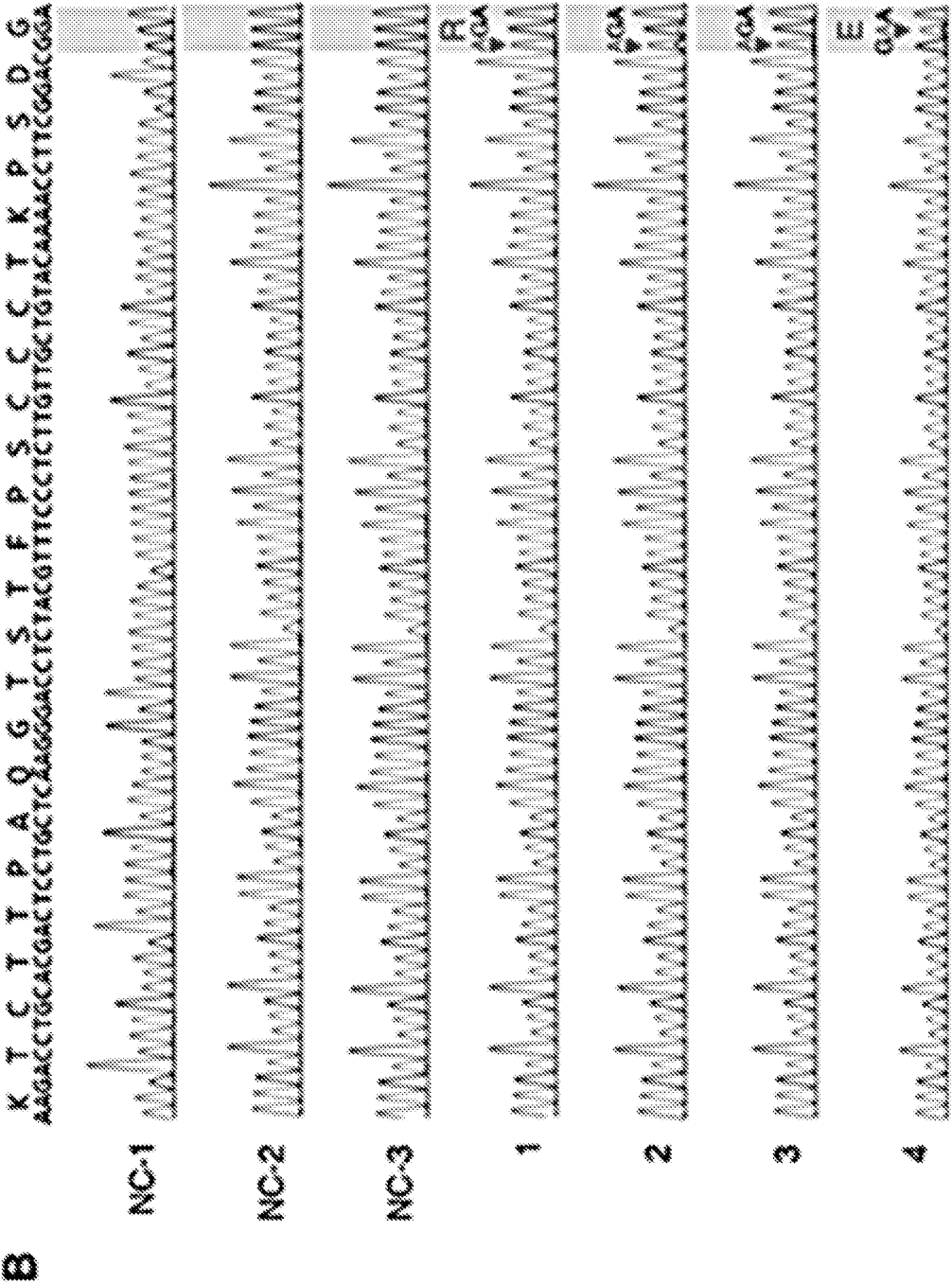


Fig. 14 (continued)

B (continued)

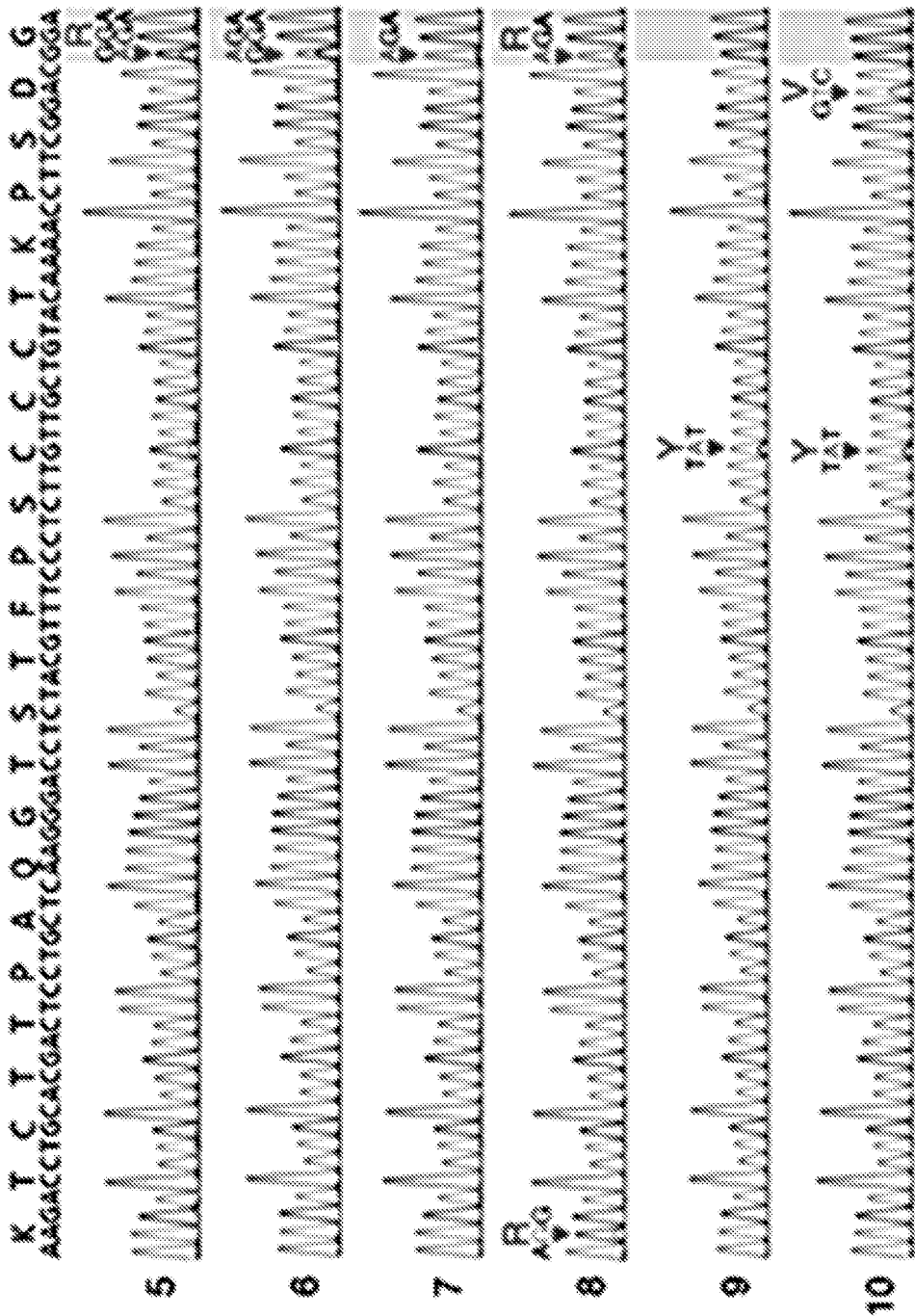


Fig. 14 (continued)

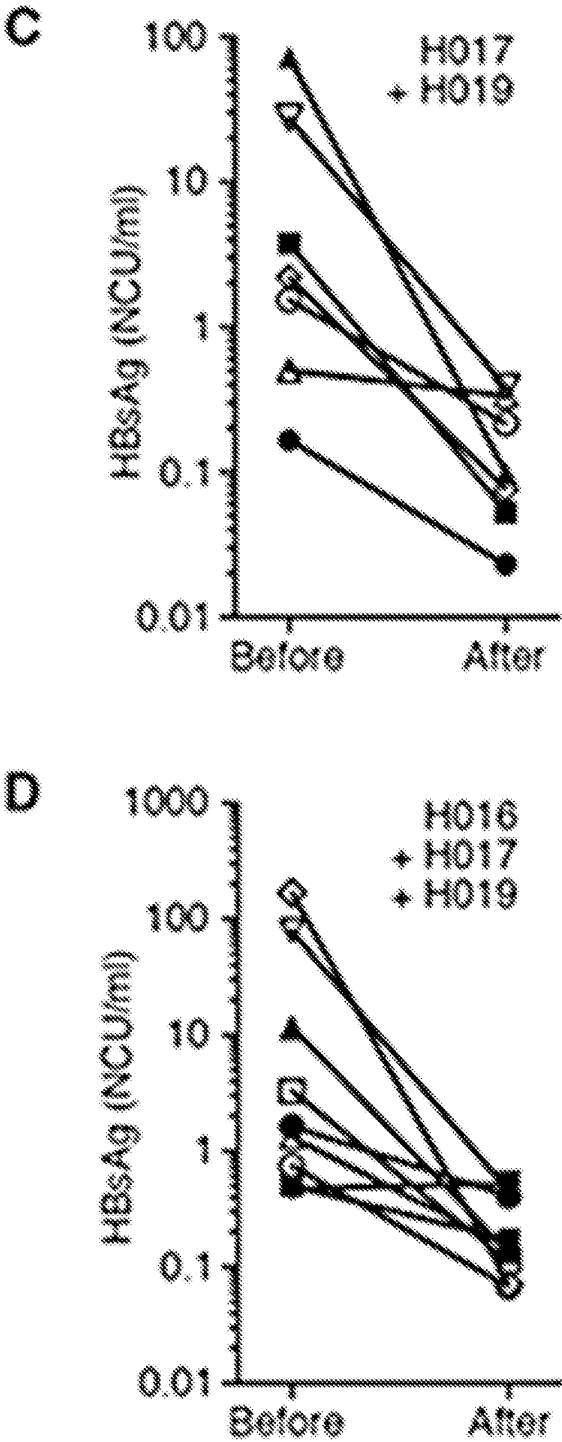


Fig. 14 (continued)  
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