

Supplemental table 1: Contact analysis between anti-A $\beta$  antibodies V-DOMAIN and A $\beta$ <sub>2-8</sub> (AEFRHDS) using IMGT/3Dstructure-DB (Ehrenmann et al., 2010).

|          |              | A $\beta$ <sub>2-8</sub> ligand residues |                                |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |              |
|----------|--------------|--|--------------------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|--------------|
|          |              | A  |                                | E                 |                   | F                 |                   | R                 |                   | H                 |                   | D                 |                   | S                 |                   |              |
|          |              | Antibody position <sup>a</sup>           | Number of contact <sup>b</sup> | Antibody position | Number of contact | Antibody position | Number of contact | Antibody position | Number of contact | Antibody position | Number of contact | Antibody position | Number of contact | Antibody position | Number of contact |              |
| VH PFA-1 | Not observed | Not observed                             | Not observed                   | Not observed      | FR2-W52           | 6 (0;0;6)         | CDR2-W57          | 38 (2;0;36)       | CDR3-R107         | 5 (2;0;3)         | CDR3-H109         | 30 (7;2;23)       | CDR3-H110         | 11 (0;0;11)       | Not observed      | Not observed |
|          |              |  |                                |                   | FR2-H55           | 9 (0;0;9)         | CDR2-W58          | 13 (3;0;10)       | CDR3-H109         | 14 (2;0;12)       |                   |                   |                   |                   |                   |              |
|          |              |  |                                |                   | CDR2-W57          | 13 (0;0;13)       | CDR2-D59          | 15 (6;2;7)        | CDR3-D113         | 16 (3;1;12)       |                   |                   |                   |                   |                   |              |
|          |              |  |                                |                   | FR3-S66           | 7 (0;0;7)         | CDR2-D64          | 12 (2;0;10)       |                   |                   |                   |                   |                   |                   |                   |              |
|          |              |  |                                |                   | CDR3-R107         | 6 (0;0;6)         | CDR3-H109         | 42 (6;0;36)       |                   |                   |                   |                   |                   |                   |                   |              |
|          |              |  |                                |                   |                   | CDR3-D113         | 1 (1;0;0)         |                   |                   |                   |                   |                   |                   |                   |                   |              |
| VH PFA-2 | Not observed | Not observed                             | Not observed                   | Not observed      | FR2-W52           | 1 (0;0;1)         | CDR2-W57          | 23 (1;0;22)       | CDR3-R107         | 6 (3;0;3)         | CDR3-H109         | 31 (8;1;23)       | CDR3-N110         | 16 (4;0;12)       | Not observed      | Not observed |
|          |              |  |                                |                   | FR2-H55           | 8 (0;0;8)         | CDR2-W58          | 5 (1;0;4)         | CDR3-A108         | 1 (1;0;0)         | CDR3-N110         | 16 (4;0;12)       |                   |                   |                   |              |
|          |              |  |                                |                   | CDR2-W57          | 12 (0;0;12)       | CDR2-D59          | 13 (6;1;6)        | CDR3-N109         | 21 (3;0;18)       | CDR3-D113         | 1 (1;0;0)         |                   |                   |                   |              |
|          |              |  |                                |                   | FR3-N66           | 7 (0;0;7)         | CDR2-D64          | 8 (2;0;6)         | CDR3-D113         | 18 (3;1;14)       |                   |                   |                   |                   |                   |              |
|          |              |  |                                |                   | CDR3-R107         | 2 (0;0;2)         | CDR3-N109         | 32 (6;0;26)       |                   |                   |                   |                   |                   |                   |                   |              |
|          |              |  |                                |                   |                   | CDR3-D113         | 1 (1;0;0)         |                   |                   |                   |                   |                   |                   |                   |                   |              |
| VH 12A11 | Not observed | Not observed                             |                                | FR3-Y66           | 2 (2;0;0)         | FR2-W52           | 2 (0;0;2)         | CDR2-W57          | 57 (1;0;56)       | CDR2-W57          | 4 (4;0;0)         | CDR2-W57          | 4 (0;0;4)         | Not observed      | Not observed      |              |
|          |              |  |                                |                   |                   | FR2-H55           | 17 (0;0;17)       | CDR2-W58          | 6 (2;0;4)         | CDR3-R107         | 4 (1;0;3)         | CDR3-T109         | 7 (0;0;7)         |                   |                   |              |
|          |              |  |                                |                   |                   | CDR2-W57          | 10 (0;0;10)       | CDR2-D59          | 15 (5;3;7)        | CDR3-T109         | 3 (0;0;3)         |                   |                   |                   |                   |              |
|          |              |  |                                |                   |                   | FR3-Y66           | 16 (0;0;16)       | CDR2-D64          | 15 (4;1;10)       | CDR3-D113         | 18 (4;1;13)       |                   |                   |                   |                   |              |
|          |              |  |                                |                   |                   | CDR3-R107         | 2 (0;0;2)         | FR3-Y66           | 17 (3;0;14)       |                   |                   |                   |                   |                   |                   |              |
|          |              |  |                                |                   |                   | CDR3-D113         | 1 (1;0;0)         |                   |                   |                   |                   |                   |                   |                   |                   |              |
| VH 12B4  | FR3-R66      | 9 (3;0;6)                                | FR3-R66                        | 9 (4;1;5)         | FR2-W52           | 5 (0;0;5)         | CDR2-Y57          | 32 (2;1;29)       | CDR2-W57          | 4 (4;0;0)         | CDR3-H109         | 6 (0;0;6)         | Not observed      | Not observed      |                   |              |
|          |              |  |                                |                   | FR2-H55           | 13 (0;0;13)       | CDR2-W58          | 7 (0;0;7)         | CDR3-R107         | 5 (2;0;3)         | CDR3-I110         | 17 (2;0;15)       |                   |                   |                   |              |
|          |              |  |                                |                   | CDR2-Y57          | 14 (0;0;14)       | CDR2-D59          | 13 (5;2;6)        | CDR3-I109         | 10 (0;0;10)       |                   |                   |                   |                   |                   |              |
|          |              |  |                                |                   | FR3-R66           | 16 (0;0;16)       | CDR2-D64          | 14 (3;1;10)       | CDR3-D113         | 19 (5;1;13)       |                   |                   |                   |                   |                   |              |
|          |              |  |                                |                   | CDR3-R107         | 7 (1;0;6)         | CDR3-I109         | 10 (0;0;10)       |                   |                   |                   |                   |                   |                   |                   |              |
|          |              |  |                                |                   |                   | CDR3-I109         | 1 (1;0;0)         |                   |                   |                   |                   |                   |                   |                   |                   |              |
| VH 10D5  | Not observed | Not observed                             |                                | FR3-R66           | 2 (2;0;0)         | FR2-S40           | 1 (0;0;1)         | CDR2-Y57          | 43 (2;1;41)       | CDR2-Y57          | 1 (1;0;0)         | CDR2-W58          | 4 (0;0;4)         | Not observed      | Not observed      |              |
|          |              |  |                                |                   |                   | FR2-W52           | 5 (0;0;5)         | CDR2-W58          | 11 (0;0;11)       | CDR3-R107         | 6 (3;0;3)         | CDR3-H109         | 7 (0;0;7)         |                   |                   |              |
|          |              |  |                                |                   |                   | FR2-H55           | 15 (0;0;15)       | CDR2-D59          | 12 (5;2;5)        | CDR3-I109         | 22 (0;0;22)       | CDR3-T110         | 19 (6;1;13)       |                   |                   |              |
|          |              |  |                                |                   |                   | CDR2-Y57          | 18 (0;0;18)       | CDR2-D64          | 13 (2;1;10)       | CDR3-T110         | 10 (3;1;6)        |                   |                   |                   |                   |              |
|          |              |  |                                |                   |                   | FR3-R66           | 4 (0;0;4)         | FR3-R66           | 14 (2;0;12)       | CDR3-D113         | 18 (5;1;12)       |                   |                   |                   |                   |              |
|          |              |  |                                |                   |                   | CDR3-I109         | 10 (0;0;10)       |                   |                   |                   |                   |                   |                   |                   |                   |              |
| VH WO-2  | Not observed | Not observed                             |                                | FR3-R66           | 2 (2;0;0)         | FR2-W52           | 2 (0;0;2)         | CDR2-Y57          | 56 (2;1;54)       | CDR2-Y57          | 2 (1;0;1)         | CDR2-W58          | 4 (1;0;3)         | CDR3-R111.1       | 1 (1;0;0)         |              |
|          |              |  |                                |                   |                   | FR2-H55           | 17 (0;0;17)       | CDR2-W58          | 4 (1;0;3)         | CDR3-R107         | 5 (2;0;3)         | CDR3-Y112.2       | 15 (3;0;12)       | CDR3-Y112.2       | 13 (1;0;12)       |              |
|          |              |  |                                |                   |                   | CDR2-Y57          | 21 (1;0;20)       | CDR2-D59          | 16 (6;3;7)        | CDR3-E112.1       | 4 (0;0;4)         | CDR3-E112.1       | 10 (2;0;8)        | CDR3-E112.1       | 9 (2;0;7)         |              |
|          |              |  |                                |                   |                   | FR3-R66           | 4 (0;0;4)         | CDR2-D64          | 15 (4;1;10)       | CDR3-N113         | 12 (2;0;10)       |                   |                   |                   |                   |              |
|          |              |  |                                |                   |                   | CDR3-R107         | 2 (0;0;2)         | FR3-R66           | 10 (2;0;8)        |                   |                   |                   |                   |                   |                   |              |

Aβ<sub>2-8</sub> ligand residues

|                  | A                 |                   | E                 |                   | F                 |                   | R                 |                   | H                 |                   | D                 |                   | S                 |                   |
|------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
|                  | Antibody position | Number of contact | Antibody position | Number of contact | Antibody position | Number of contact | Antibody position | Number of contact | Antibody position | Number of contact | Antibody position | Number of contact | Antibody position | Number of contact |
| V-Kappa<br>PFA-1 | CDR3-S108         | 1 (1;0;0)         | CDR1-V30          | 1 (1;0;0)         | CDR1-H31          | 8 (2;1;5)         | CDR1-H31          | 1 (1;0;0)         | CDR1-H31          | 24 (3;0;21)       | CDR1-N34          | 9 (2;1;6)         | CDR1-N34          | 18 (3;0;15)       |
|                  | CDR3-H109         | 7 (2;0;5)         | CDR1-H31          | 7 (2;0;5)         | CDR3-G107         | 9 (1;0;8)         |                   |                   | CDR1-N34          | 6 (1;0;5)         | CDR1-Y38          | 1 (1;0;0)         |                   |                   |
|                  | CDR3-V114         | 15 (4;1;10)       | CDR1-S32          | 15 (4;1;10)       | CDR3-S108         | 12 (2;1;9)        |                   |                   | CDR1-Y38          | 43 (2;0;41)       |                   |                   |                   |                   |
|                  |                   |                   | CDR3-S108         | 1 (1;0;0)         | CDR3-H109         | 9 (1;0;8)         |                   |                   | CDR3-G107         | 9 (2;1;6)         |                   |                   |                   |                   |
|                  |                   |                   | CDR3-H109         | 7 (2;0;5)         | CDR3-V114         | 7 (2;0;5)         |                   |                   | CDR3-S108         | 6 (2;0;4)         |                   |                   |                   |                   |
|                  |                   |                   | CDR3-V114         | 15 (4;1;10)       | CDR3-L116         | 20 (0;0; 20)      |                   |                   |                   |                   |                   |                   |                   |                   |
| V-Kappa<br>PFA-2 | CDR3-S108         | 3 (1;0;2)         | CDR1-V30          | 1 (1;0;0)         | CDR1-H31          | 10 (3;1;7)        | CDR1-H31          | 3 (1;0;2)         | CDR1-H31          | 25 (4;0;21)       | CDR1-N34          | 9 (2;1;6)         | CDR1-N34          | 14 (2;0;12)       |
|                  | CDR3-H109         | 11 (3;0;8)        | CDR1-H31          | 29 (4;0;25)       | CDR3-G107         | 9 (1;0;8)         |                   |                   | CDR1-N34          | 6 (1;0;5)         | CDR1-N36          | 1 (1;0;0)         |                   |                   |
|                  | CDR3-V114         | 20 (2;1;17)       | CDR1-S32          | 16 (4;3;9)        | CDR3-S108         | 13 (2;1;10)       |                   |                   | CDR1-Y38          | 43 (2;0;41)       | CDR1-Y38          | 1 (1;0;0)         |                   |                   |
|                  |                   |                   | CDR3-S108         | 9 (2;0;7)         | CDR3-H109         | 5 (1;0;4)         |                   |                   | CDR3-G107         | 9 (2;1;6)         |                   |                   |                   |                   |
|                  |                   |                   | CDR3-H109         | 8 (1;0;7)         | CDR3-V114         | 12 (1;0;11)       |                   |                   | CDR3-S108         | 3 (1;0;2)         |                   |                   |                   |                   |
|                  |                   |                   | CDR3-V114         | 9 (1;0;8)         | CDR3-L116         | 17 (0;0;17)       |                   |                   |                   |                   |                   |                   |                   |                   |
| V-Kappa<br>12A11 | CDR3-S108         | 1 (1;0;0)         | CDR1-V30          | 1 (1;0;0)         | CDR1-H31          | 8 (2;1;5)         |                   |                   | CDR1-H31          | 15 (2;0;13)       |                   |                   |                   |                   |
|                  | CDR3-H109         | 9 (3;0;6)         | CDR1-H31          | 30 (6;0;24)       | CDR3-S107         | 11 (1;0;10)       |                   |                   | CDR1-N34          | 6 (1;0;5)         |                   |                   |                   |                   |
|                  | CDR3-V114         | 19 (3;1;15)       | CDR1-S32          | 16 (4;2;10)       | CDR3-S108         | 11 (2;1;9)        |                   |                   | CDR1-Y38          | 45 (2;0;43)       |                   |                   |                   |                   |
|                  |                   |                   | CDR3-S108         | 10 (3;0;7)        | CDR3-H109         | 7 (1;0;6)         | Not observed      | Not observed      | CDR3-S107         | 15 (4;1;10)       | Not observed      | Not observed      | Not observed      | Not observed      |
|                  |                   |                   | CDR3-H109         | 7 (0;0;7)         | CDR3-V114         | 9 (1;0;8)         |                   |                   | CDR3-S108         | 7 (2;0;5)         |                   |                   |                   |                   |
|                  |                   |                   | CDR3-V114         | 8 (1;0;7)         | CDR3-L116         | 18 (0;0;18)       |                   |                   |                   |                   |                   |                   |                   |                   |
| V-Kappa<br>12B4  | CDR3-H109         | 4 (1;0;3)         | CDR1-V30          | 1 (1;0;0)         | CDR1-H31          | 8 (2;1;5)         |                   |                   | CDR1-H31          | 16 (2;0;14)       | CDR1-H31          | 1 (0;0;1)         |                   |                   |
|                  | CDR3-V114         | 8 (2;0;6)         | CDR1-H31          | 36 (6;0;30)       | CDR3-G107         | 4 (0;0;4)         |                   |                   | CDR1-N34          | 3 (0;0;3)         | CDR1-N34          | 7 (2;0;5)         |                   |                   |
|                  |                   |                   | CDR1-S32          | 15 (4;1;10)       | CDR3-S108         | 10 (2;1;7)        |                   |                   | CDR1-Y38          | 41 (2;0;39)       |                   |                   |                   |                   |
|                  |                   |                   | CDR3-S108         | 10 (1;0;9)        | CDR3-H109         | 6 (1;0;5)         | Not observed      | Not observed      | CDR3-G107         | 10 (2;1;7)        |                   |                   | Not observed      | Not observed      |
|                  |                   |                   | CDR3-H109         | 7 (0;0;7)         | CDR3-V114         | 8 (1;0;7)         |                   |                   | CDR3-S108         | 3 (1;0;2)         |                   |                   |                   |                   |
|                  |                   |                   | CDR3-V114         | 6 (0;0;6)         | CDR3-L116         | 15 (0;0;15)       |                   |                   |                   |                   |                   |                   |                   |                   |
| V-Kappa<br>10D5  | CDR3-S108         | 1 (1;0;0)         | CDR1-V30          | 2 (1;0;1)         | CDR1-H31          | 10 (2;1;7)        |                   |                   | CDR1-H31          | 12 (2;0;10)       | CDR1-N34          | 5 (1;0;4)         |                   |                   |
|                  | CDR3-H109         | 5 (1;0;4)         | CDR1-H31          | 35 (6;0;29)       | CDR3-G107         | 8 (0;0;8)         |                   |                   | CDR1-N34          | 5 (1;0;4)         |                   |                   |                   |                   |
|                  | CDR3-V114         | 14 (3;1;10)       | CDR1-S32          | 17 (4;2;11)       | CDR3-S108         | 12 (2;1;9)        |                   |                   | CDR1-Y38          | 43 (3;0;40)       |                   |                   |                   |                   |
|                  |                   |                   | CDR1-S34          | 1 (1;0;0)         | CDR3-H109         | 3 (1;0;2)         | Not observed      | Not observed      | CDR3-G107         | 10 (2;1;7)        |                   |                   | Not observed      | Not observed      |
|                  |                   |                   | CDR3-S108         | 11 (3;0;8)        | CDR3-V114         | 8 (1;0;7)         |                   |                   | CDR3-S108         | 3 (1;0;2)         |                   |                   |                   |                   |
|                  |                   |                   | CDR3-H109         | 9 (1;0;8)         | CDR3-L116         | 15 (0;0;15)       |                   |                   |                   |                   |                   |                   |                   |                   |
|                  |                   |                   | CDR3-V114         | 5 (1;0;4)         |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |
| V-Kappa<br>WO-2  | CDR3-S108         | 1 (1;0;0)         | CDR1-V30          | 1 (1;0;0)         | CDR1-H31          | 11 (3;0;8)        | CDR1-H31          | 1 (0;0;1)         | CDR1-H31          | 14 (3;0;11)       |                   |                   |                   |                   |
|                  | CDR3-L109         | 14 (2;0;12)       | CDR1-H31          | 33 (6;0;27)       | CDR3-A107         | 11 (0;0;11)       |                   |                   | CDR1-N34          | 5 (2;0;3)         |                   |                   |                   |                   |
|                  | CDR3-V114         | 16 (4;1;11)       | CDR1-S32          | 16 (4;2;10)       | CDR3-S108         | 12 (2;1;9)        |                   |                   | CDR1-Y38          | 39 (2;0;37)       |                   |                   |                   |                   |
|                  |                   |                   | CDR3-S108         | 11 (2;0;9)        | CDR3-L109         | 7 (1;0;6)         |                   |                   | CDR3-A107         | 8 (2;0;6)         | Not observed      | Not observed      | Not observed      | Not observed      |
|                  |                   |                   | CDR3-L109         | 14 (0;0;14)       | CDR3-V114         | 10 (1;0;9)        |                   |                   | CDR3-S108         | 2 (0;0;2)         |                   |                   |                   |                   |
|                  |                   |                   | CDR3-V114         | 5 (1;0;4)         | CDR3-L116         | 18 (0;0;18)       |                   |                   |                   |                   |                   |                   |                   |                   |

<sup>a</sup>Amino acid positions and CDR-IMGT delimitations are according to the IMGT unique numbering for V-DOMAIN

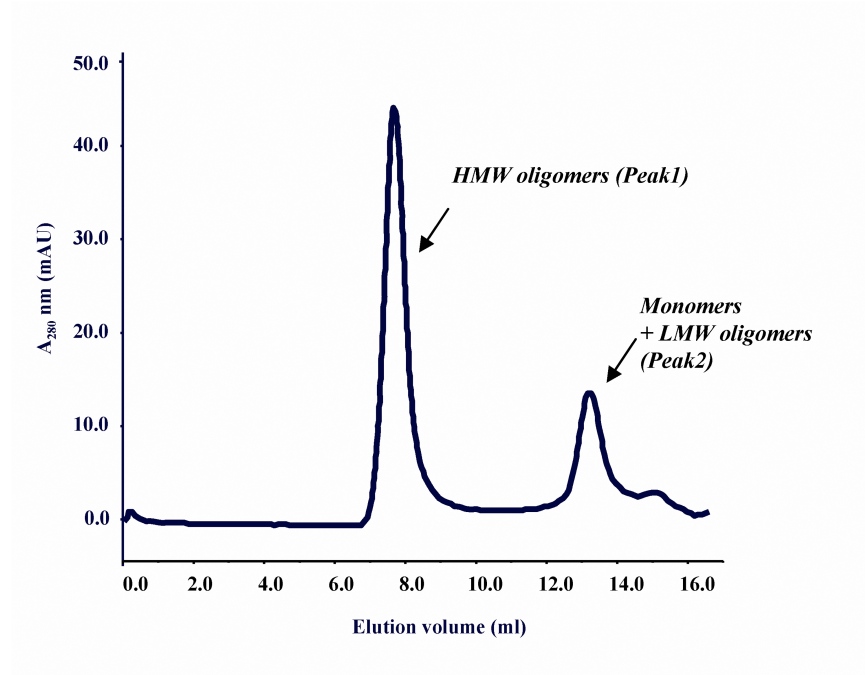
<sup>b</sup>Atom contact type: total number of atom contact (polar; hydrogen; non-polar)

## **Supplemental figure captions**

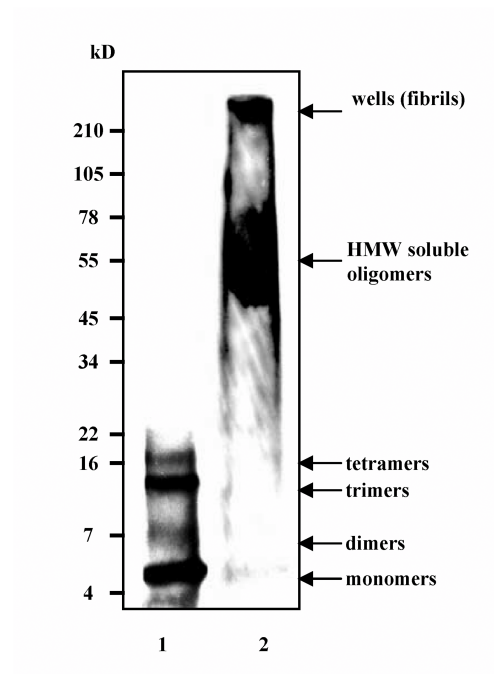
Supplemental figure 1: (A) High Molecular Weight (HMW) and Low molecular Weight (LMW) biotinylated  $A\beta_{1-42}$  oligomers separated by size exclusion chromatography (Superdex 75 HR 10/30 column). (B) LMW biotinylated  $A\beta_{1-42}$  oligomers fraction (Peak2-lane1) and HMW biotinylated  $A\beta_{1-42}$  oligomers fraction (Peak-lane2) were run on a Tris-tricine gel (4-16%) and immunoblotted with the 6E10 antibody. Each fraction was used directly for the SPR analysis.

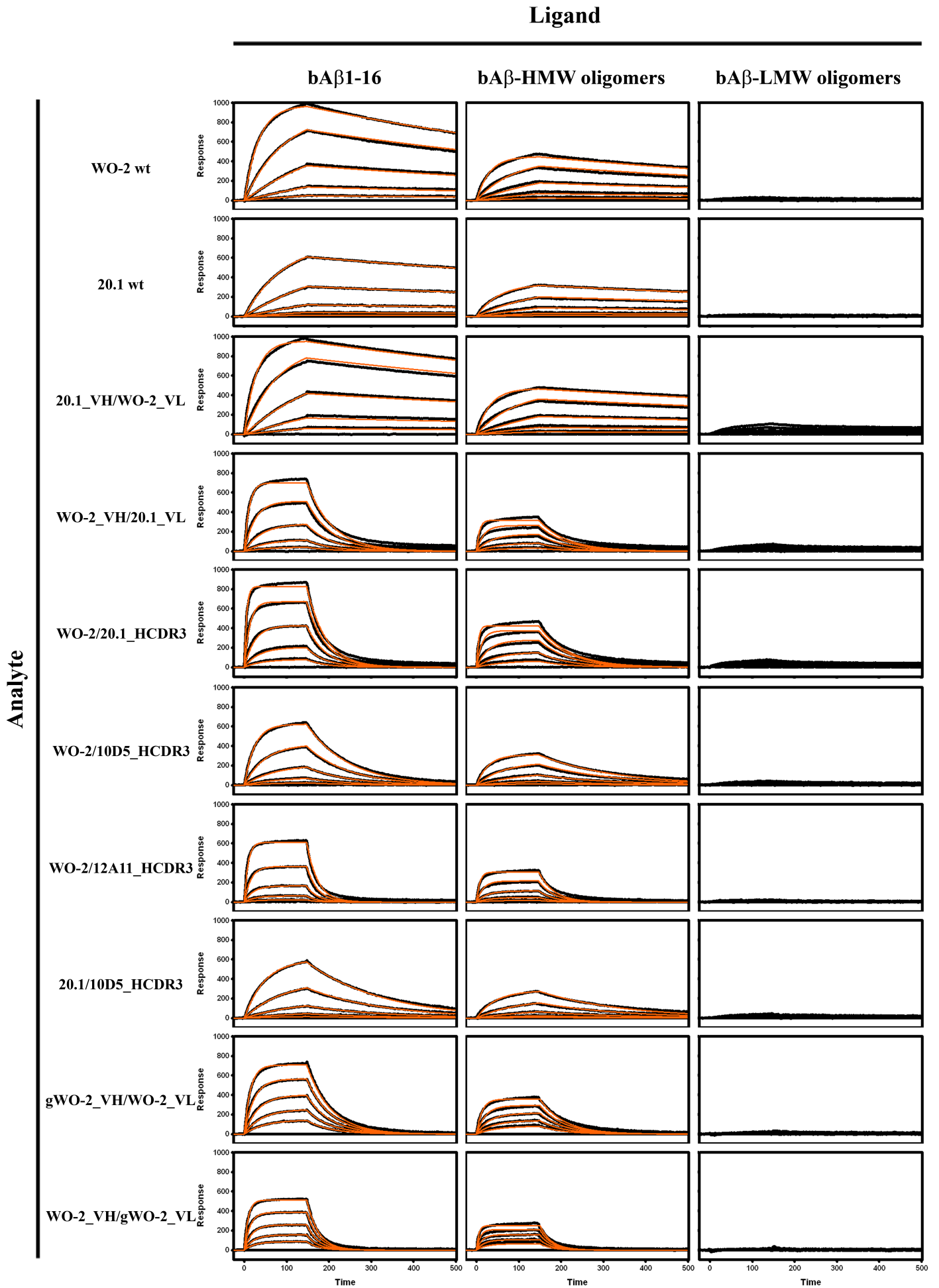
Supplemental figure 2: Kinetic analysis of rFabs binding to immobilized biotinylated  $A\beta_{1-16}$  peptide (b $A\beta_{1-16}$ -right panel), HMW biotinylated  $A\beta_{1-42}$  oligomers (b $A\beta$ -HMW oligomers-middle panel) and LMW biotinylated  $A\beta_{1-42}$  oligomers (b $A\beta$ -LMW oligomers-left panel).  $A\beta_{1-16}$ -biotin peptide, b $A\beta$ -HMW oligomers and b $A\beta$ -LMW oligomers were captured on a NeutrAvidin coated chip (NLC, BioRad) at a ligand density of  $\sim 90$  RU;  $\sim 600$  RU and  $\sim 1000$  RU respectively. Binding responses (black lines) were fit globally to a simple 1:1 interaction model (red lines) using Scrubber software v2.0c ([www.biologic.com.au](http://www.biologic.com.au)).

**A**



**B**





Supplemental Figure.2