Figure S1. Neutralization of J6 with and without HVR1 by antibody against the J6 HVR1 epitope. J6 (yellow triangles) and J6$_{\Delta HVR1}$ (purple triangles) recombinants were incubated with dilution series of the J6.36 antibody, along with 8 replicates of virus only. 48h after inoculation of Huh7.5 cells with the virus/antibody mixes or virus only the number of FFU were visualized by HCV-specific immunostaining and the counts were normalized to the mean count of virus only. Isotype-matched control antibody was included at the highest concentration of the specific antibody and was found to have no effect on infection. Data-points are means of four replicates with standard deviation (SD). Four-parameter non-linear curve regression was used to fit the data points, top value set to 100 and bottom value set to 0 (Graphpad PRISM, v4.03). The calculated IC$_{50}$-titers of neutralization are shown in Table 1.

Figure S2. Neutralization of H77, J6, and S52 with and without HVR1 by domain A, B, C, D, and E specific HMAbs. (A-E) H77 (red triangles) and H77$_{\Delta HVR1}$ (green triangles), (F-J) J6 (yellow triangles) and J6$_{\Delta HVR1}$ (purple triangles), (K-O) S52 (brown triangles) and S52$_{\Delta HVR1}$ (blue triangles) recombinants were incubated with dilution series of CBH4G, CBH5, CBH7, HC84.26, or HC33.4 (subscript indicates antibody specificity), along with 8 replicates of virus only. 48h after inoculation of Huh7.5 cells with the virus/antibody mixes or virus only the number of FFU were visualized by HCV-specific immunostaining and the counts were normalized to the mean count of virus only. Isotype-matched control antibody was included at the highest concentration of the specific antibody and was found to have no effect on infection. Data-points are means of four replicates with standard deviation (SD). Four-parameter non-linear curve regression was used to fit the data points, top value set to 100 and bottom value set to 0 (Graphpad PRISM, v4.03). The calculated IC$_{50}$-titers of neutralization are shown in Table 1.

Figure S3. Neutralization of H77, J6, and S52 with and without HVR1 by antigenic region 1-5 specific HMAbs. (A-E) H77 (red triangles) and H77$_{\Delta HVR1}$ (green triangles), (F-J) J6 (yellow triangles) and J6$_{\Delta HVR1}$ (purple triangles), (K-O) S52 (brown triangles) and S52$_{\Delta HVR1}$ (blue triangles) recombinants were incubated with dilution series of AR1B, AR2A, AR3A, AR4A, or AR5A (subscript indicates antibody specificity), along with 8 replicates of virus only. 48h after inoculation of Huh7.5 cells with the virus/antibody mixes or virus only the number of FFU were visualized by HCV-specific immunostaining and the counts were normalized to the mean count of virus only. Isotype-matched control antibody was included at the highest concentration of the specific antibody and was found to have no effect on infection. Data-points are means of four replicates with standard deviation (SD). Four-parameter non-linear curve regression was used to fit the data points, top value set to 100 and bottom value set to 0 (Graphpad PRISM, v4.03). The calculated IC$_{50}$-titers of neutralization are shown in Table 1.

Figure S4. Neutralization of H77, J6, and S52 with and without HVR1 by E1-specific HMAbs. (A-B) H77 (red triangles) and H77$_{\Delta HVR1}$ (green triangles), (C-D) J6 (yellow triangles) and J6$_{\Delta HVR1}$ (purple triangles), (E-F) S52 (brown triangles) and S52$_{\Delta HVR1}$ (blue triangles) recombinants were incubated with dilution series of IGH520 or IGH526 (subscript indicates antibody specificity), along with 8 replicates of virus only. 48h after inoculation of Huh7.5 cells with the virus/antibody mixes or virus only the number of FFU were visualized by HCV-specific immunostaining and the counts were normalized to the mean count of virus only. Isotype-matched control antibody was included at the highest concentration of the specific antibody and was found to have no effect on infection. Data-points are means of four replicates with standard deviation (SD). Four-parameter non-linear curve

regression was used to fit the data points, top value set to 100 and bottom value set to 0 (Graphpad PRISM, v4.03). The calculated IC_{50}-titers of neutralization are shown in Table 1.
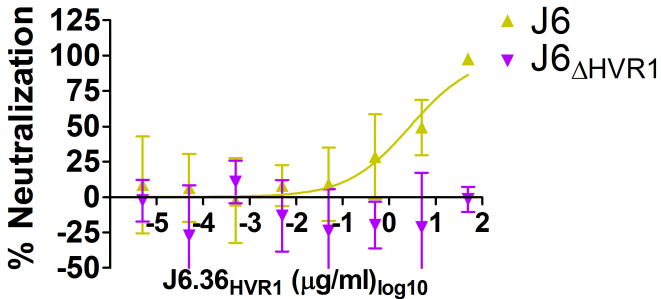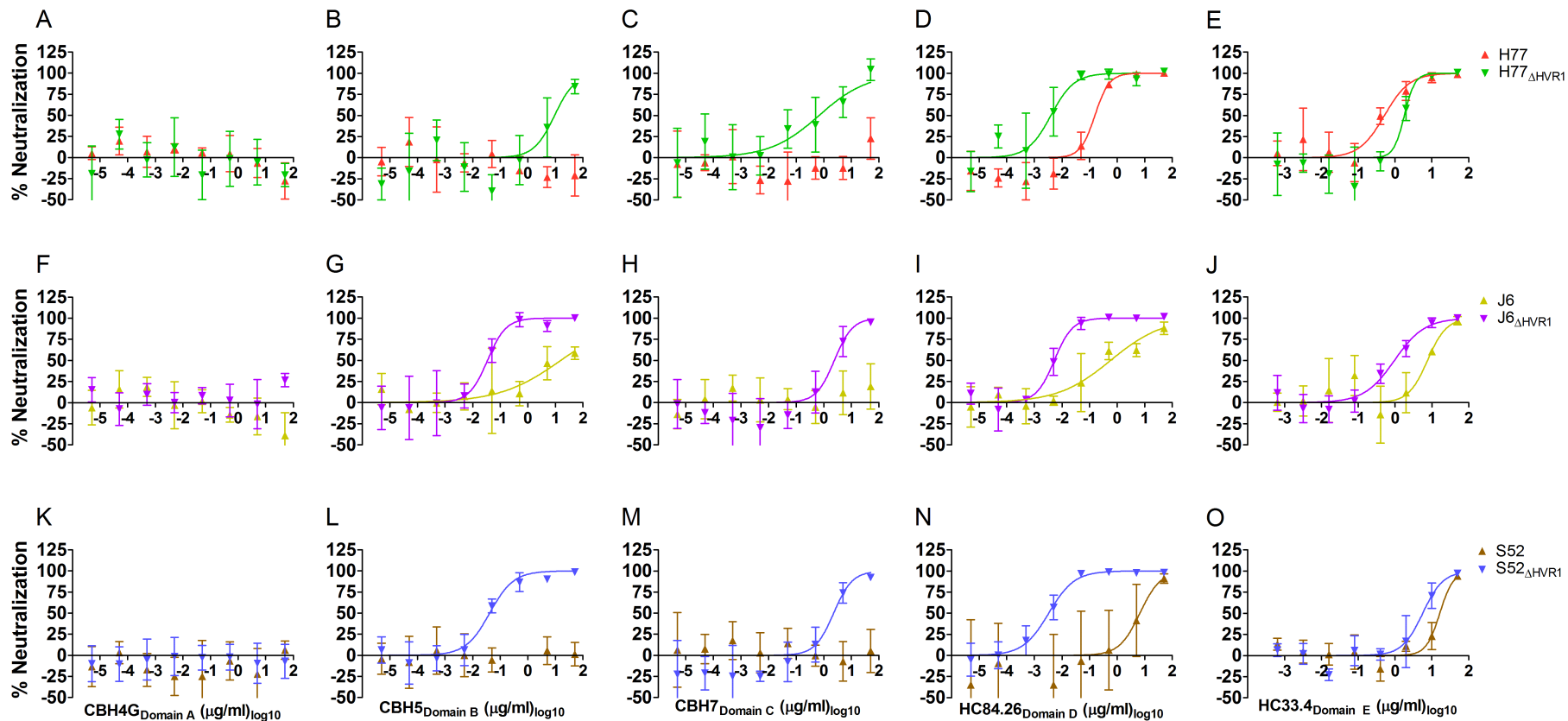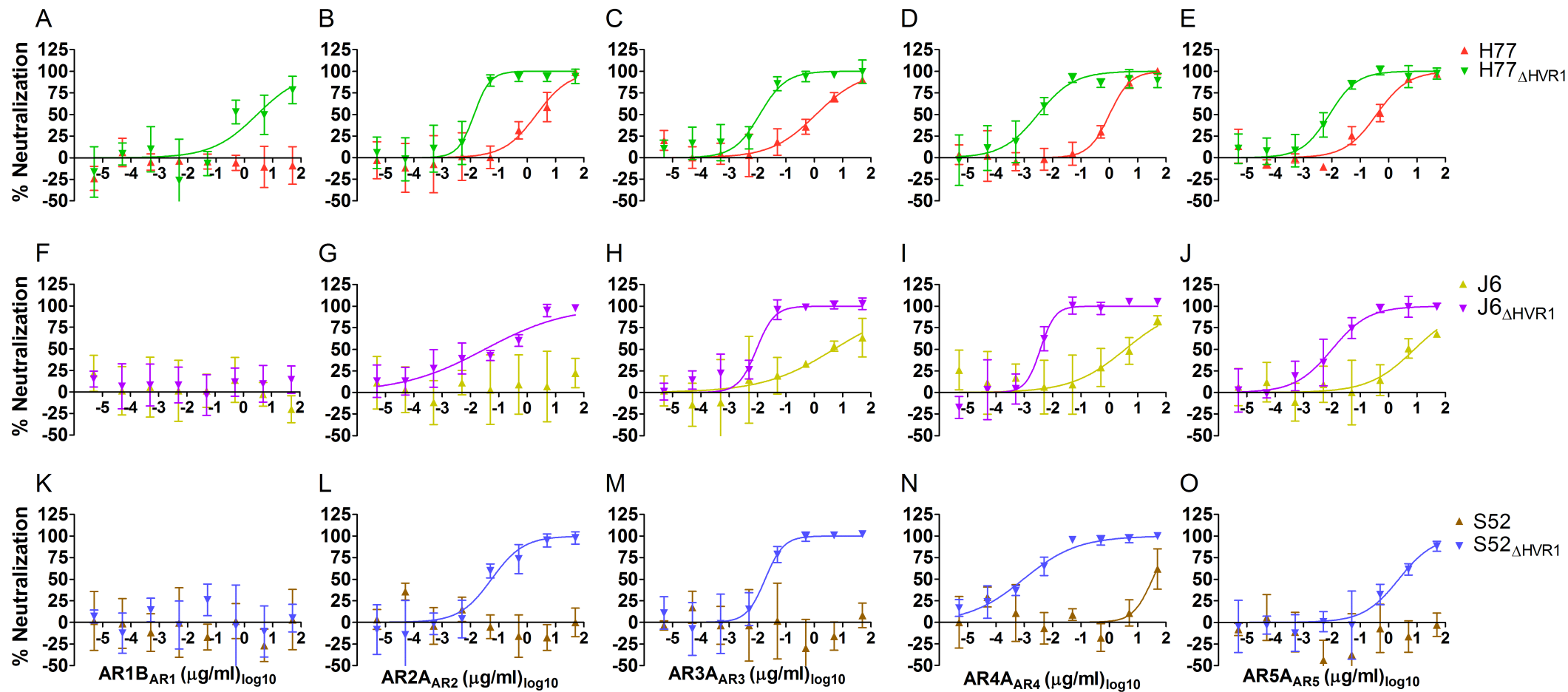
Figure S1

Figure S2

Figure S3

Figure S4