

Supplemental Information

**Cytokine and chemokine signatures associated
with hepatitis B surface antigen loss
in hepatitis B patients**

Sachiyo Yoshio¹, Yohei Mano¹, Hiroyoshi Doi¹, Hirotaka Shoji¹, Tomonari Shimagaki¹,

Yuzuru Sakamoto¹, Hironari Kawai¹, Michitaka Matsuda¹, Taizo Mori¹, Yosuke

Osawa¹, Masaaki Korenaga¹, Masaya Sugiyama², Masashi Mizokami², Eiji Mita³,

Keiko Katayama⁴, Junko Tanaka⁴ and Tatsuya Kanto^{1*}

Figure S1

Serum CXCL9, CXCL10, CXCL11, CXCL13 and IL-21 levels for each viral genotype in the patients with acute HBV infection. Serum CXCL9, CXCL10, CXCL11, CXCL13, and IL-21 levels for AH patients (including the sAH and pAH groups) were compared among genotype A(n=21), B(n=7), and C (n=21). Samples obtained at the peak of alanine aminotransferase (ALT) elevation were subjected to analyses. Box and whisker plots show median, lower and upper quartiles, and minimum and maximum values. There was no statistical significance by Kruskal-Wallis test.

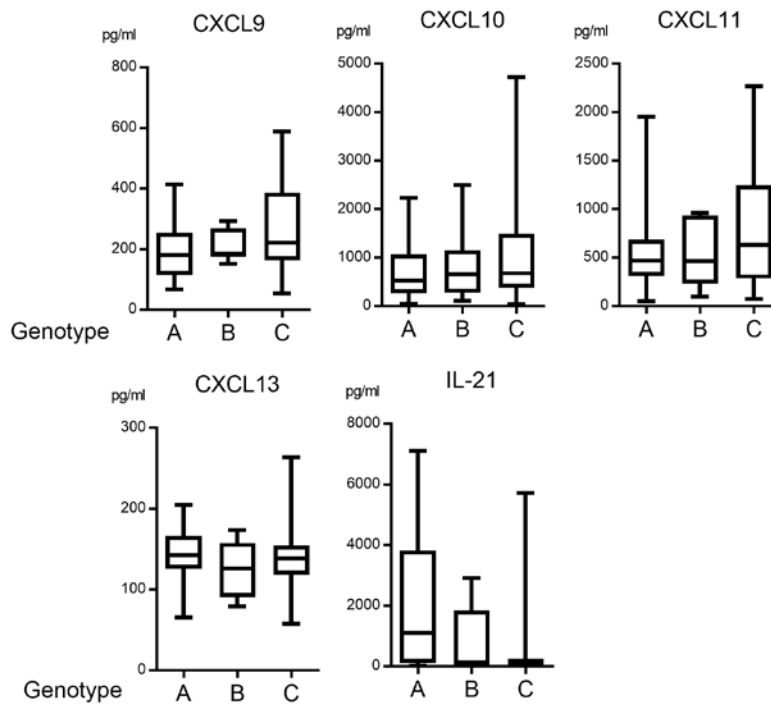
Supplemental Figure 1

Figure S2

Serum CXCL9, CXCL10, CXCL11, CXCL13 and IL-21 levels for patients with acute and chronic HBV infection. A. Serum CXCL9, CXCL10, CXCL11, CXCL13, IL-21, ALT, HBV DNA and HBsAg levels were compared between the HBeAg-positive/anti-HBe-negative sAH patients (n=18) and the HBeAg-positive/anti-HBe-negative pAH patients (n=8) groups. * $p < 0.05$, ** $p < 0.001$, *** $p < 0.0001$ by Mann-Whitney non-parametric U test. B. Serum CXCL9, CXCL10, CXCL11, CXCL13, IL-21, ALT, HBV DNA and HBsAg levels were compared among the HBeAg-positive/anti-HBe-negative (n=18), HBeAg-positive/anti-HBe-positive (n=16), and HBeAg-negative/anti-HBe-positive (n=7) sAH groups. * $p < 0.05$, ** $p < 0.001$ by Kruskal-Wallis test. C. Serum CXCL9, CXCL10, CXCL11, and CXCL13 levels were compared between HBeAg-negative (n=3) and HBeAg-positive (n=5) CH patients at hepatic flare.

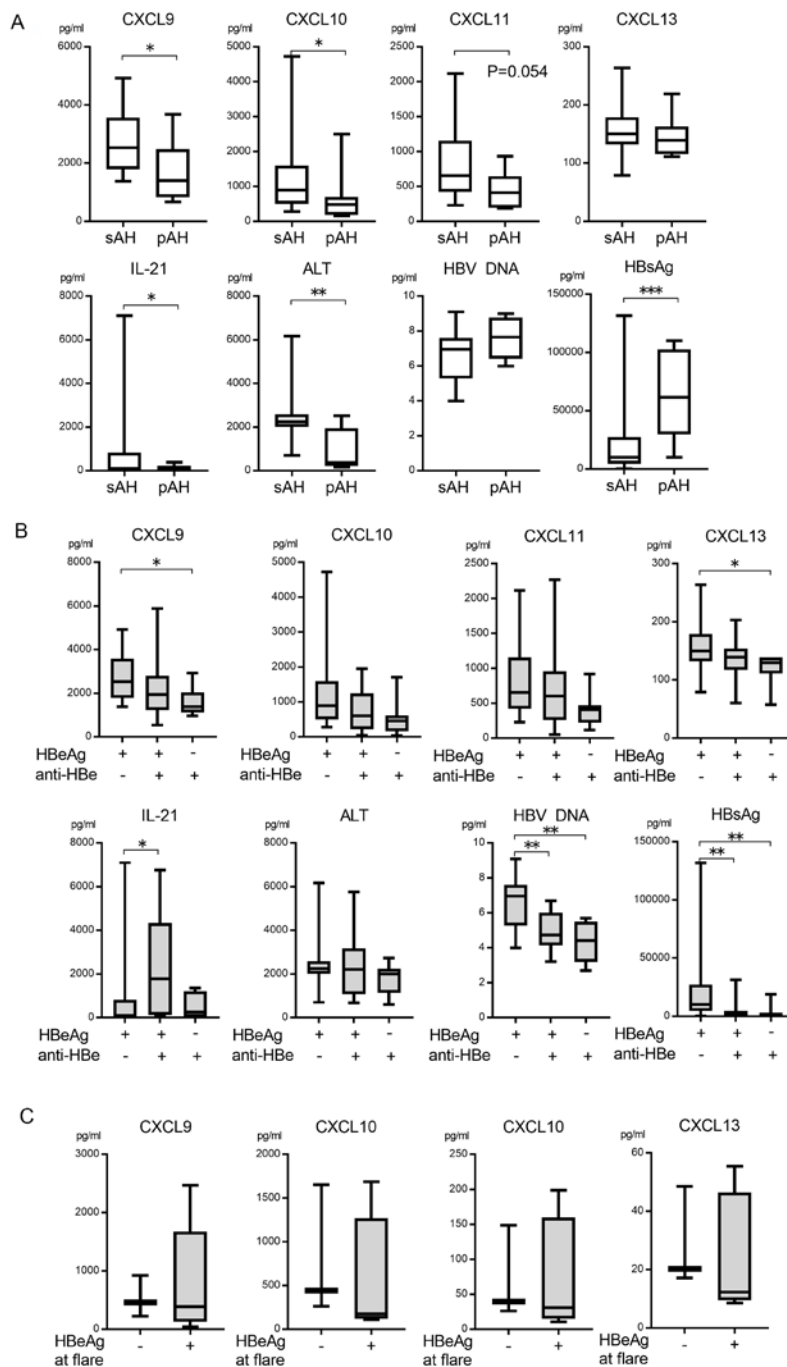
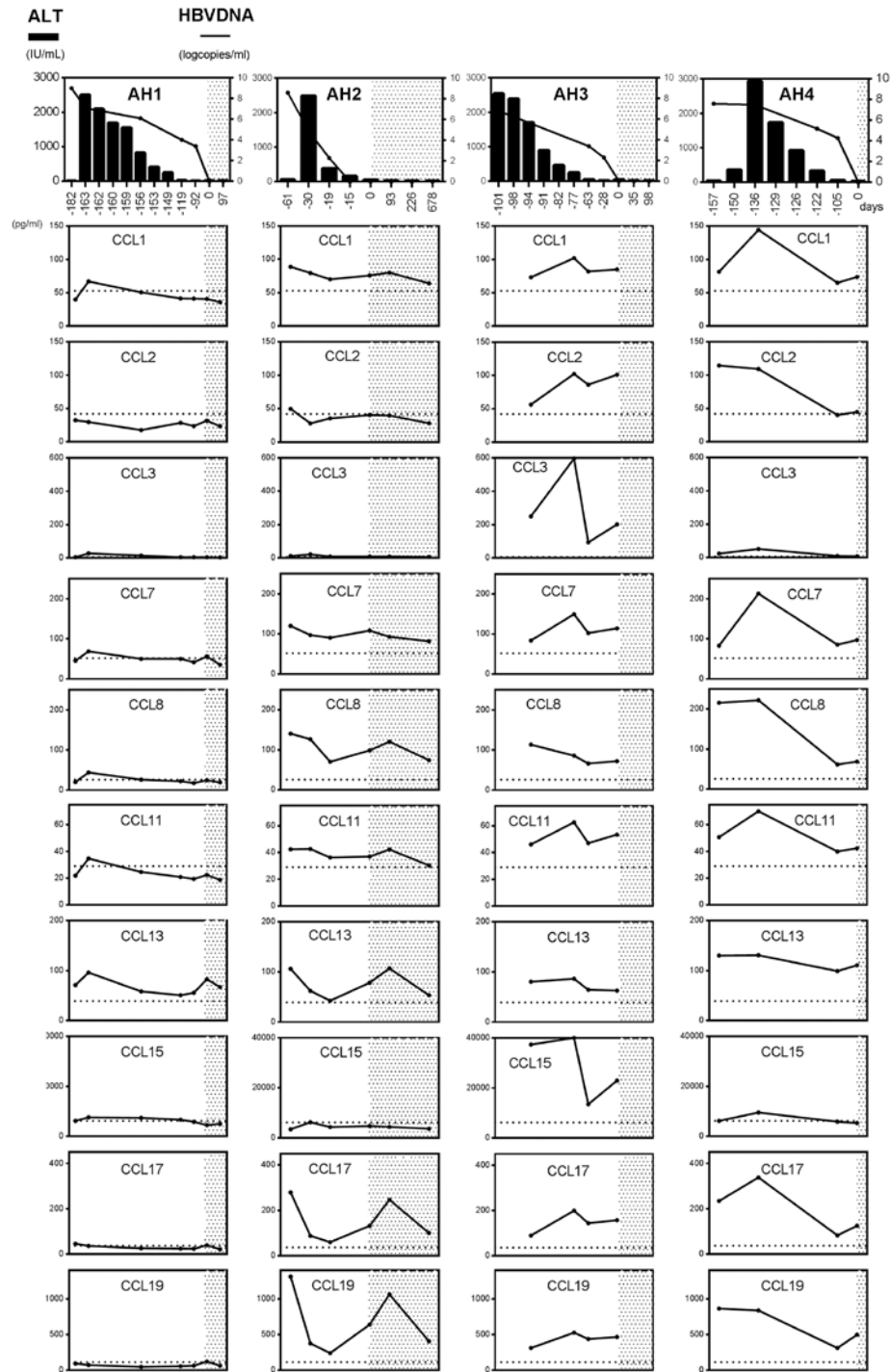
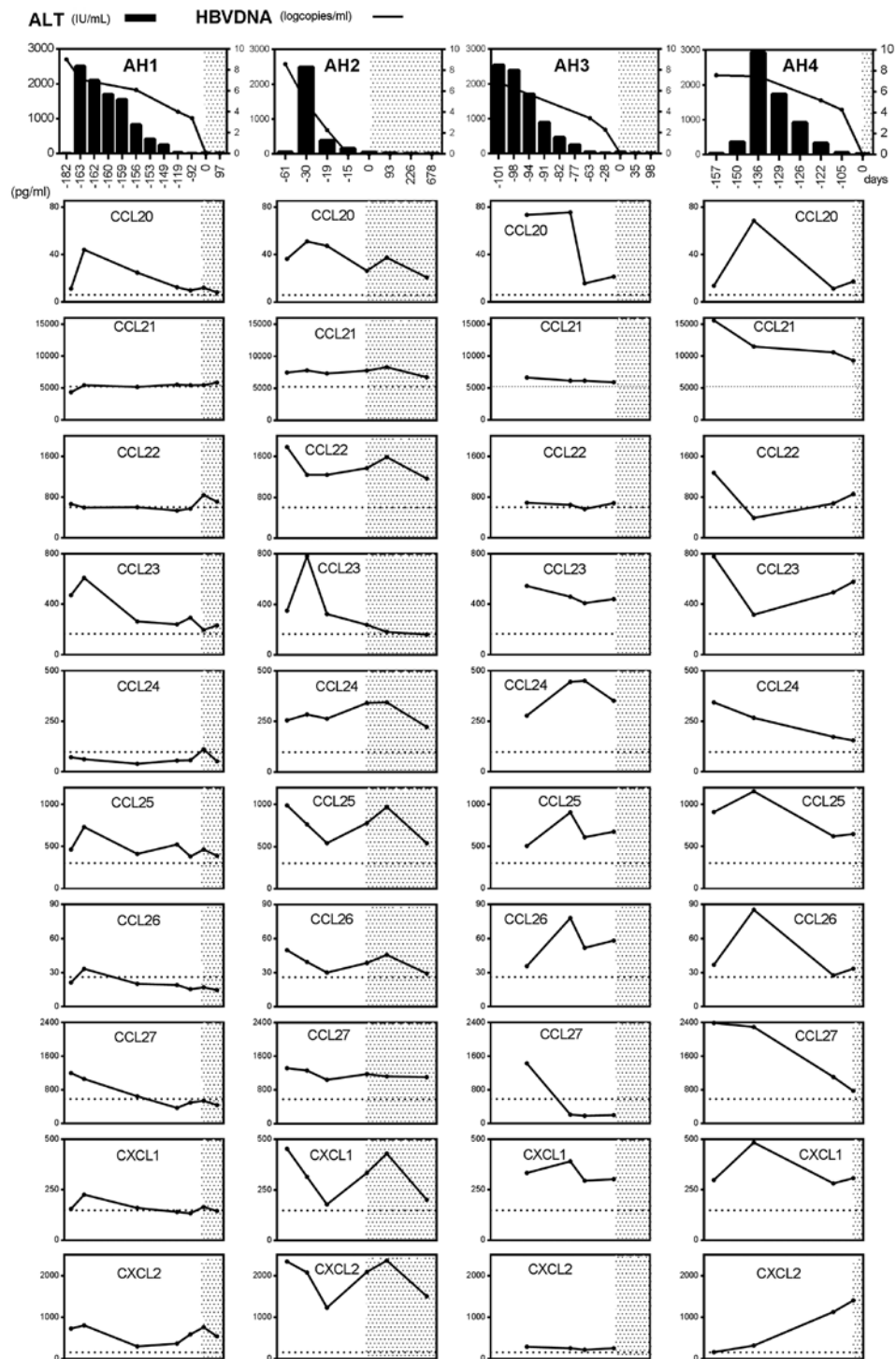
Supplemental Figure 2

Figure S3

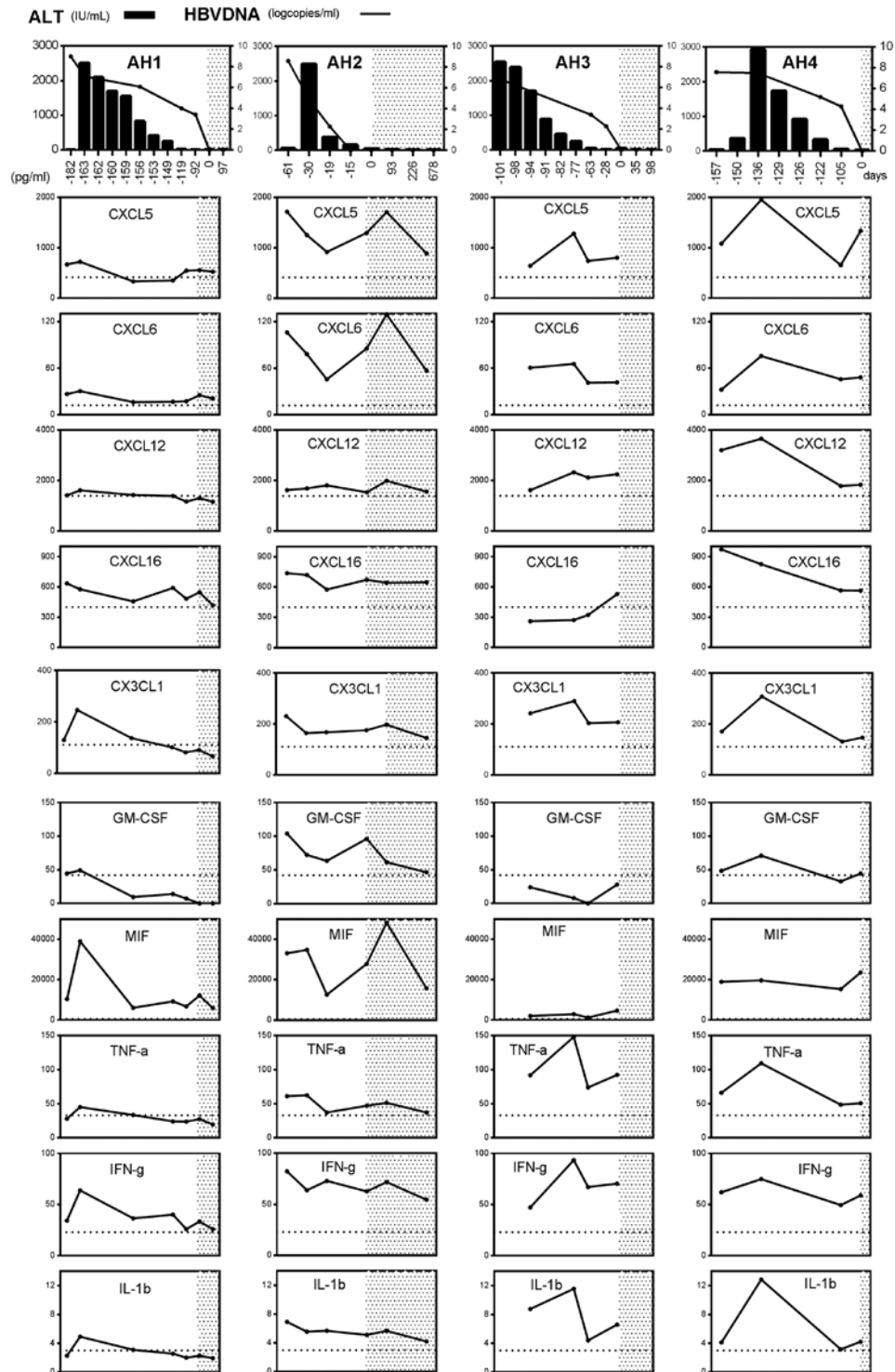
Longitudinal and comparative analysis of serum chemokines/cytokines in patients with self-limited HBV infection. The changes of 36 chemokines/cytokines, except for CXCL9, CXCL10, CXCL11, CXCL13 and IL-21, in Cases AH1, AH2, AH3 and AH4 are shown (A-D). Dotted lines in the panels indicate the average chemokine concentration in healthy volunteers. The shaded area depicts the time period of HBsAg-negative. The left vertical axes are for alanine aminotransferase (ALT), and the right vertical axes are for HBV DNA.

Supplemental Figure 3A

Supplemental Figure 3B



Supplemental Figure 3C



Supplemental Figure 3D

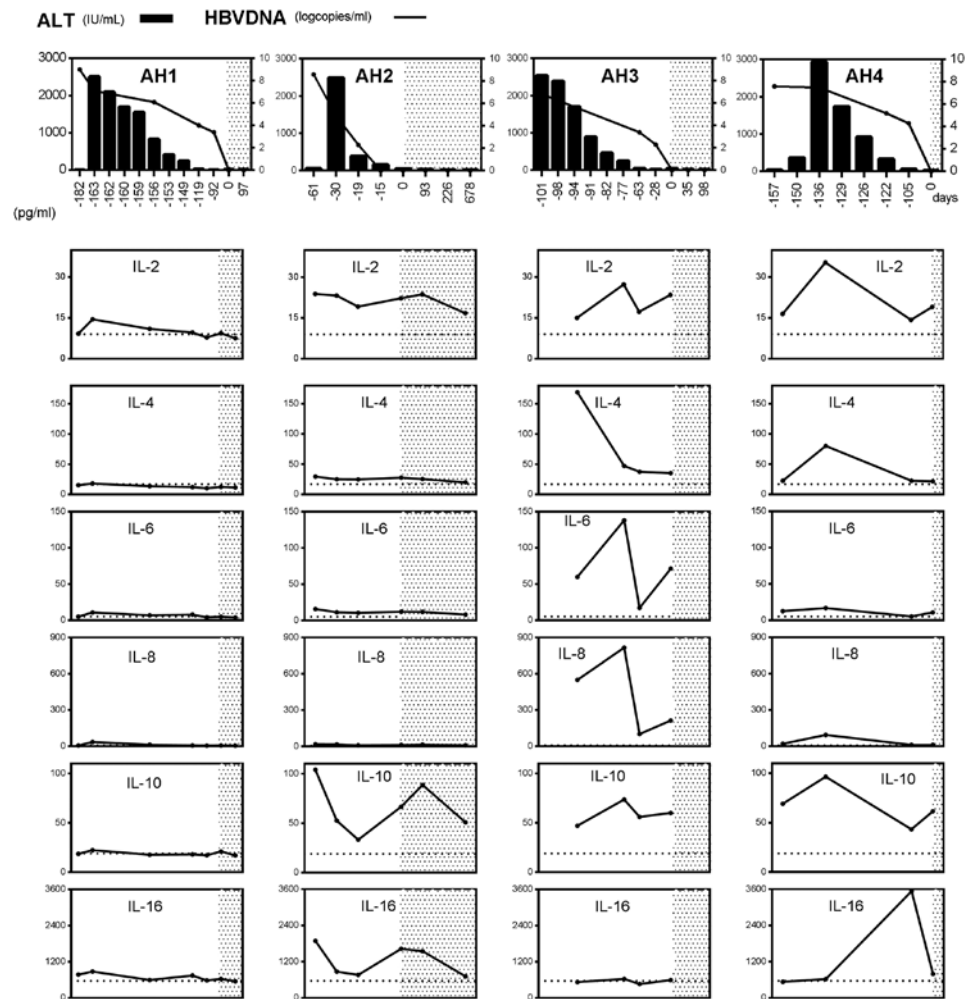
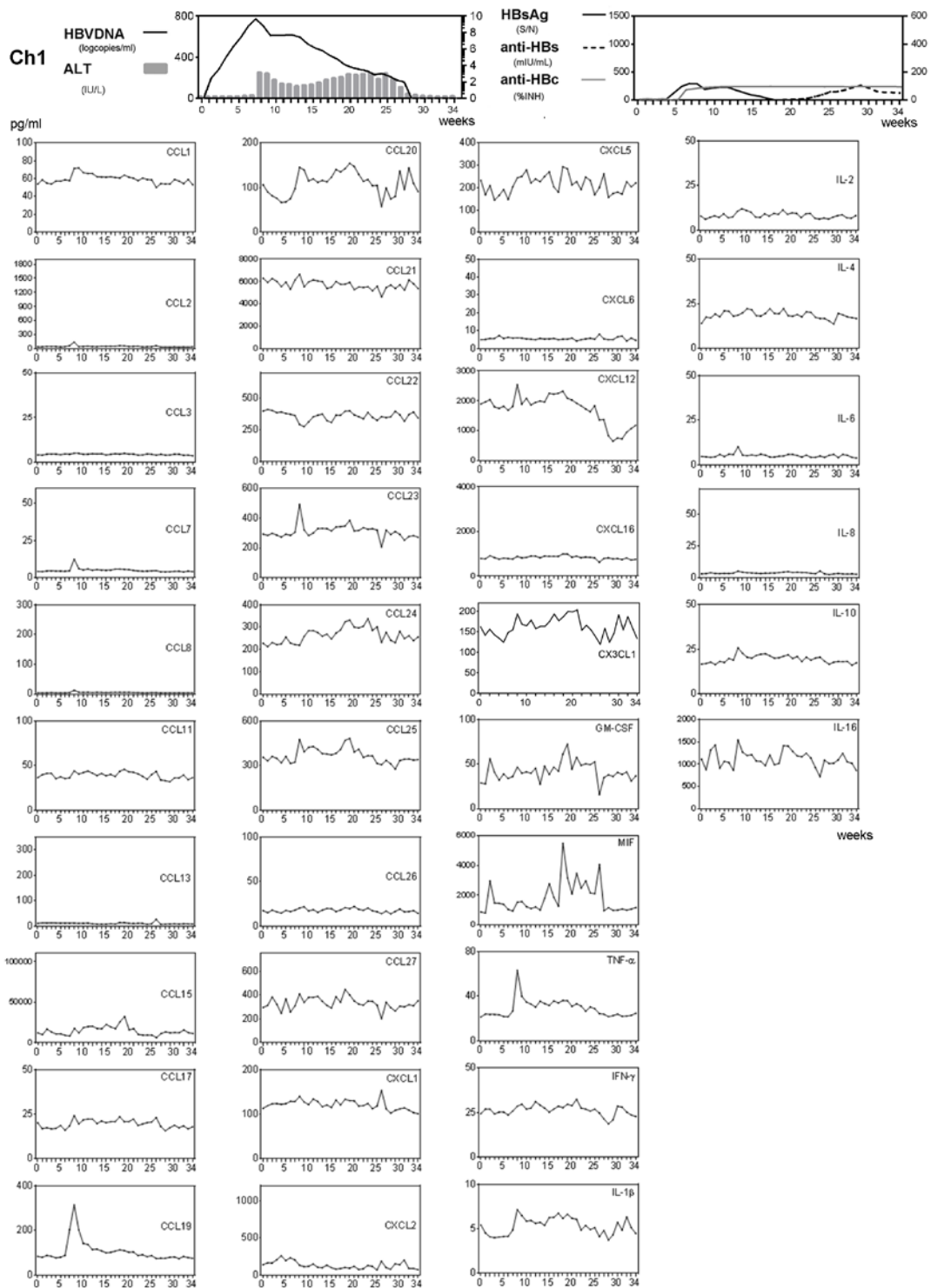


Figure S4**Sequential analyses of serum chemokines/cytokines of HBV-inoculated chimpanzees.**

The changes of 36 chemokines/cytokines, except for CXCL9, CXCL10, CXCL11, CXCL13 and IL-21, in Cases Ch1 (A), Ch2 (B), and Ch3 (C) are shown.

Supplemental Figure 4A

Supplemental Figure 4B

