Supplementary Figure 1. $CXCL12_2$ treatment does not affect CXCR4-negative B16-F1 lung metastasis.

CXCR4-luc-B16-F1 cells (4×10^5) or pLNCX2-luc-B16-F1 cells (4×10^5) were injected i.v. into the tail vein of C57BL/6 mouse with the indicated concentrations of $CXCL12_2$. Mice were treated with an identical dose by intravenous tail vein injection the following day. Lungs were harvested 14 days after inoculation, and luciferase activity was measured to evaluate metastatic tumor (n=4).

Supplementary Figure 2. CXCR4-B16-F1 and pLNCX2-B16-F1 calcium flux induced by CXCL12 and $CXCL12_2$.

Calcium response of CXCR4-B16-F1 (A-C) and pLNCX2-B16-F1 (D-F) cells to 500 nM wtCXCL12 (A, D), 500 nM $CXCL12_2$ (B, E), or vehicle (C, F) in the presence (black dots) or absence (white dots) of 5 μM AMD3100 (n=8).

Supplementary Figure 3. $CXCL12_2$ maintains dimeric structure in the presence of mouse serum.

$CXCL12_2$ (10 μM) and wtCXCL12 (10 μM) were incubated in 90% mouse serum for the indicated times, and then analyzed by Western blot analysis using a specific antibody to hCXCL12 (R&D Systems ELISA DuoSet). Full length blot of Fig. 3A is shown.

Supplementary Figure 4. Smt-wtCXCL12 is degraded quickly in mouse serum.

Smt-wtCXCL12 was incubated with 90% mouse serum or heat-inactivated mouse serum. Western blot was performed using anti-hCXCL12 antibody (R&D Systems ELISA DuoSet). Full length blot of Fig. 3B and Fig. 5A is shown.

Supplementary Figure 5. $CXCL12_2$ inhibits wtCXCL12-induced chemotaxis in Transwell migration assay containing mouse serum.

The migration of THP-1 monocytes to 10 nM wtCXCL12 was inhibited by increasing concentrations of $CXCL12_2$. Experiments were performed in the presence of 1% mouse serum with both chemokines added to the lower chamber (n=3).