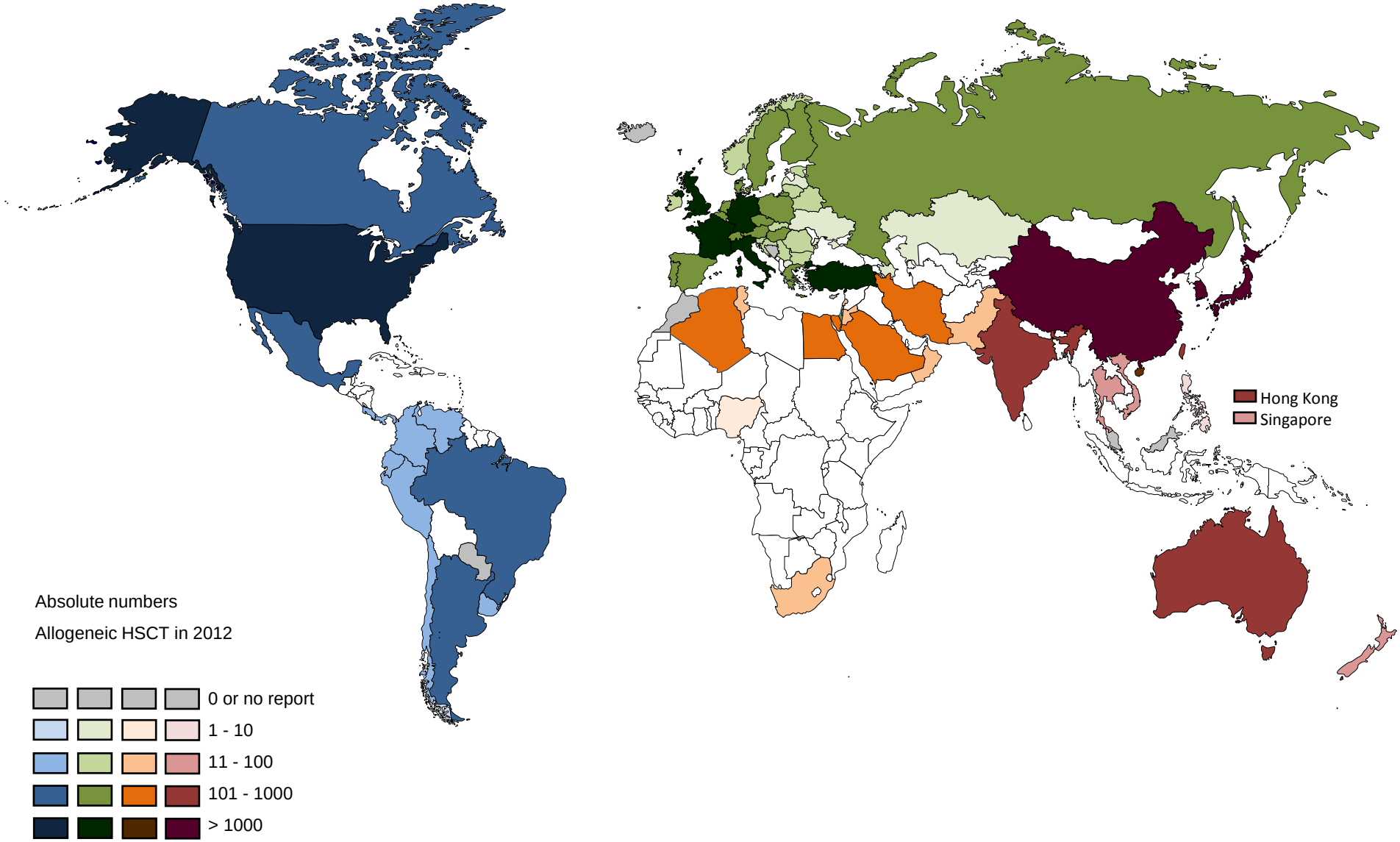Supplementary Figure 1a