



#### Additional data 1. Random collision frequencies in gene-rich regions for large separations distances.

Random collision frequencies were determined by 3C-qPCR after a primer extension step (see Methods) at two *Usp22* genomic sites (sites F1 & F-28) (Fig.1A) in liver samples issued from 16.5 dpc embryos (grey data points) or 30 days old mice (white data points). Data analysis was as described in the legend of Fig1B. Red squares represent the floating mean (45kb windows, shift of 22.5kb). We determined the higher and the lower points of the floating mean for site separations above 40kb and calculated the average random collision frequencies (values are indicated in the figure) of sites located 40kb around these points (horizontal black bars).  $p$ -values (Mann-Whitney  $U$ -test) account for the significance of the differences observed between these averages. Error bars are s.e.m.