Extended Data Figure 7: Viable structually variant sex chromosomes in humans.

The presence of the 12 broadly expressed, dosage-sensitive X–Y pair genes and other chromosomal features on structurally variant sex chromosomes are indicated by filled circles. **a,** Viable non-mosaic deletions of X–Y pair genes from the human Y chromosome. The human Y chromosome is susceptible to structural rearrangements due to homology mediated crossing-over between repeated sequences. Crossing-over between tandem repeats creates interstitial deletions, whereas crossing-over in palindrome arms causes the formation of isodicentric chromosomes and isochromosomes. Each Y-linked member of the 12, broadly expressed, dosage-sensitive X–Y gene pairs is deleted in one or more variants, thus no single X–Y pair gene is haplolethal. **b,** Viable deletions of X–Y pair genes from the human X chromosome in females are shown. Reported cases of X chromosome deletions in females are consistent with a collective haplolethality for all 12 broadly expressed, dosage-sensitive X–Y gene pairs in humans. Familial cases, where a variant X chromosome has been transmitted from mother to daughter, are unlikely to be mosaic. The most extensive deletion among familial cases eliminates 7 of 12 genes. The most extensive de novo deletion variants eliminate 11 of 12 genes, but mosaicism for 46,XX cells cannot be excluded. No variants remove *RPS4X* because of viability effects mediated by its position between the centromere (CEN) and X-inactivation centre (XIC) on the long arm, rather than haplolethality of *RPS4X* alone.