Extended Data Figure 1 | Ethanol-induced genomic instability. **a**, Left, representative images of bone marrow metaphase spreads from wild-type mice treated with mitomycin C (MMC); *n* shows the number of SCE events per metaphase. Right, comparison between number of SCEs in the bone marrow of wild-type and *Aldh2*$^{-/-}$ mice treated with ethanol (5.8 g kg^{-1}) or MMC (1 mg kg^{-1}). Triplicate experiments, 25 metaphases per mouse, $n = 75$; *P* calculated by two-sided Mann–Whitney test; data shown as mean and s.e.m. Ethanol causes a strong homologous recombination response in *Aldh2*$^{-/-}$ mice, comparable to that observed in wild-type mice exposed to MMC. **b**, Left, representative images of bone marrow metaphase spreads from wild-type and *Fanca*$^{-/-}$ mice; *n* shows the number of SCE events per metaphase. Right, quantification of SCEs (duplicate experiments, 25 metaphases per mouse, $n = 50$; *P* calculated by two-sided Mann–Whitney test; data shown as mean and s.e.m.). Mice deficient in cross-link repair (*Fanca*$^{-/-}$, or *Fancd2*$^{-/-}$ in Fig. 1a) show a small but significant increase in the number of spontaneous SCE events, indicating that a homologous recombination repair response occurs in the absence of the Fanconi anaemia pathway. **c**, Scheme depicting the formation of micronucleated erythrocytes. Micronuclei (Mn) generated by fragmentation or mis-segregation of chromosomes during erythrocyte maturation remain in the erythrocyte after extrusion of the main nucleus. These fragments can be detected by a DNA stain (PI^{+}). During maturation, red-cell progenitors lose CD71 expression. Therefore, peripheral CD71^{+} red cells represent immature, short-lived reticulocytes (Ret) and CD71^{-} cells represent mature, long-lived normochromic erythrocytes (NCEs). **d**, Proof-of-principle experiment showing the induction of micronucleated reticulocytes 48 h after MMC treatment (1 mg kg^{-1}). *P* calculated by two-sided Mann–Whitney test; data shown as mean and s.e.m.; $n = 29$, 8, 20 and 9 mice, left to right. **e**, Treatment of *Aldh2*$^{-/-}$ mice with ethanol (5.8 g kg^{-1}) leads to potent micronucleus formation. This induction is comparable to that observed in wild-type mice that were treated with the aneugen vincristine (Vcn, 0.2 mg kg^{-1}, 48 h) or clastogenic γ-irradiation (IR, 400 rad, 48 h)[46]. *P* calculated by two-sided Mann–Whitney test; data shown as mean and s.e.m.; $n = 29$, 15, 10, 11, 25 and 15 mice. **f**, List of chromosomal aberrations observed in the bone marrow of 8-to-12-week-old untreated *Aldh2*$^{-/-}$*Fancd2*$^{-/-}$ and control mice. **g**, List of chromosomal aberrations observed in the bone marrow of 8-to-12-week-old *Aldh2*$^{-/-}$*Fancd2*$^{-/-}$ and control mice 48 h after ethanol treatment (5.8 g kg^{-1}, injected intraperitoneally, IP). In **f** and **g**, three mice and 30 metaphases per mouse were analysed per condition, and the numbers represent the fraction of abnormal metaphases per mouse. **h**, Bar chart classifying the type of aberrations for each genotype (90 metaphases per condition). **i**, Examples of different types of chromosomal aberrations.