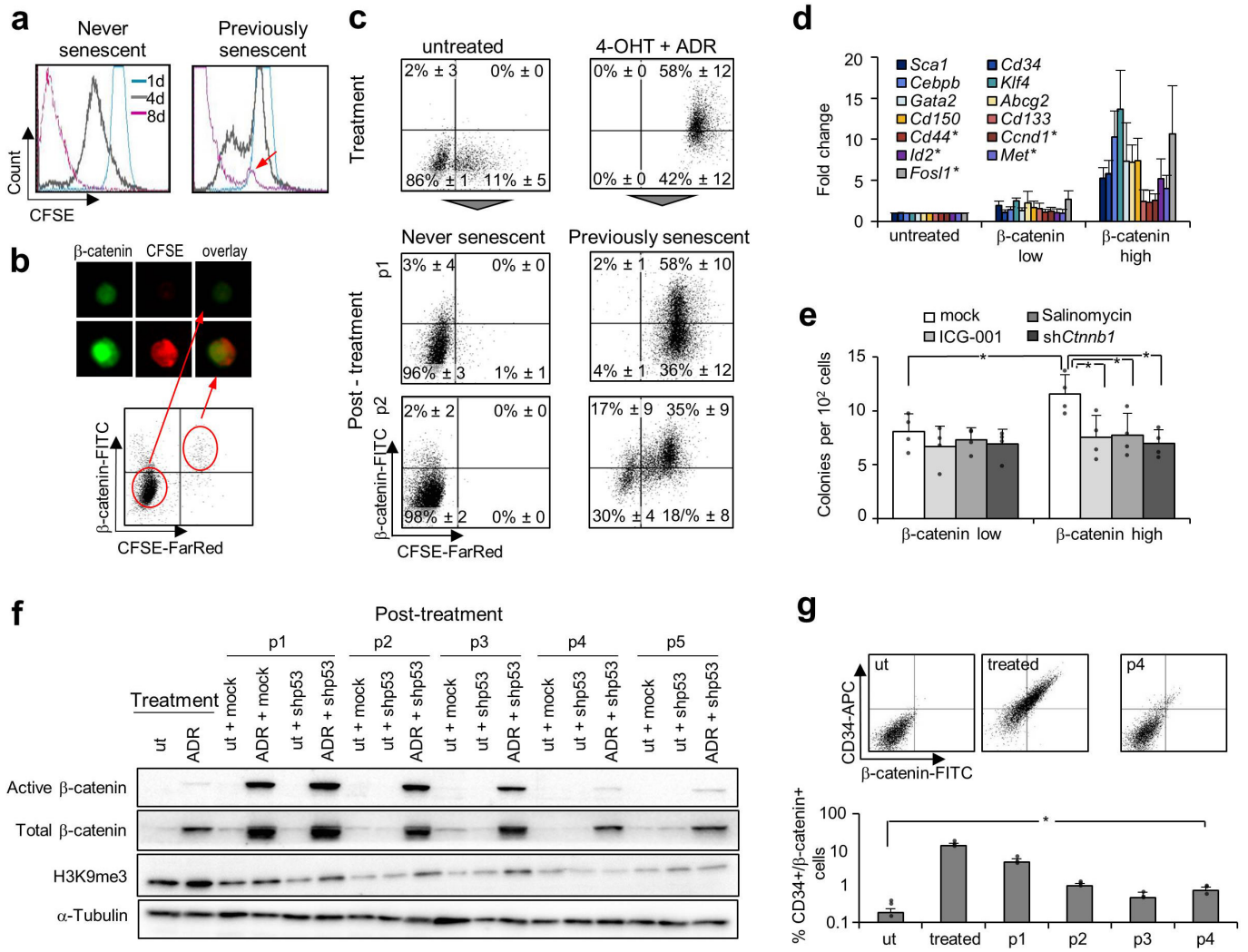

Extended Data Figure 8 | The previously senescent cell population maintains a stable fraction of Wnt-active stem cells over time. **a**, Detection of a slowly dividing subpopulation in previously senescent but not in never senescent lymphoma cells (arrow) by the CFSE membrane dye 1, 4 or 8 days after stopping the ADR ± 4-OHT treatment. Experiment performed in triplicates. **b**, CFSE^{high} previously senescent cells exhibited more profound nuclear β-catenin expression, indicating acquired stemness (passage 3 after 4-OHT/ADR removal; compare with **c**). One out of three independent experiments, each performed in triplicate. **c**, Co-staining with β-catenin and CFSE as in **b** in *Suv39h1*$^{-}$;*Bcl2*;*Suv39h1*-ER^{T2} cells, untreated or exposed to ADR ± 4-OHT for five days ('treatment') and subsequently passaged in 4-OHT/ADR-free medium (p1–2; each passage reflects seven days in culture). The slowly cycling (CFSE^{high}) population was positive for β-catenin and persisted over time, although their relative percentage drops owing to outgrowth of their (CFSE^{low}) progeny. Numbers reflect mean percentages from three independent lymphomas ± s.d. **d**, **e**, Higher expression of ATSC- or Wnt-related (asterisks) transcripts by qPCR (**d**) and higher clonogenic capacity, which can be neutralized by indicated pharmacological or genetic Wnt inhibitors (**e**) in flow-sorted, β-catenin high versus β-catenin low previously senescent cells (passage 3 after 4-OHT/ADR removal). Mean expression levels normalized to untreated cells and mean colony numbers respectively ± s.d., $n = 4$ biologically independent samples. Two-tailed, unpaired *t*-test with Welch's correction, $^{*}P < 0.05$. **f**, Immunoblot analysis of β-catenin and H3K9me3 levels in human RCK8 lymphoma cells exposed to ADR for 5 days to induce senescence ('treatment'), then stably transduced with an shp53- or mock lentivirus, and further propagated in ADR-free medium ('post-treatment', p1–5, each reflecting seven days in culture). The senescence-associated high levels of active and total β-catenin achieve a low but stable level at later passages. It is noteworthy that stably senescent ADR-pretreated, mock-infected cells were only blotted in p1. One representative out of three independent experiments shown, with α-tubulin as a loading control. For gel source data, see Supplementary Fig. 1. **g**, Co-expression of β-catenin and the stem-cell marker CD34 detected by flow cytometry in ADR-pretreated, shp53-infected RCK8 cells as in **f**, demonstrating a small but stable steady-state fraction of double-positive cells at later passages, explaining the lastingly enhanced colony-forming potential of previously senescent versus never senescent cells. Representative flow cytometry plots from three independent experiments (top) and mean percentages of double-positive cells ± s.d. (bottom) at the indicated passages ($n = 3$ independent experiments). Two-tailed, unpaired *t*-test with Welch's correction. $^{*}P < 0.05$.