



Figure S4. CircPOK plays as a proto-oncogene through the ILF2/3 complex. **a** Expression of circPOK (chart on the left) and Pokemon-protein (western blot in the middle) in $p53^{-/-}$ $Zbtb7a_Ex2^{F/F-CTR}$ MSCs over-expressing circPOK, or the empty vector as control. The chart on the right shows the expression of Pokemon-protein target genes in circPOK-GTG expressing cells, compared to cells of control (Empty cells = bar at 1). **b** Schematic representation of the possible ORF spanning the back-splice junction of circPOK. **c** Expression of Pokemon-protein in CTR cells or in cells transduced with shRNA targeting

the Exon2 of *Zbtb7a*. Two independent Antibodies (Ab) have been used to identify possible proteins translated from the circPOK transcript. **d** Polysome fractions and RT-qPCR analysis of LinPOK, circPOK, and circPVT1 as control. The panel on the right represent the polysome profiling, with indicated the relevant fractions analyzed by RT-qPCR. **e** RIP assays to measure the interactions between circPOK and ILF2 or ILF3. **f** Visualization of circPOK through circFISH assays, and co-localization with ILF3 measured by performing I.F. staining. Cells have treated with RNaseR before staining, to remove the signals coming from the linear transcripts, and in the way that only the circRNA is detected. **g** Flow-cytometry analysis of CD31+ endothelial cells in tumors originated from *p53^{-/-}Zbtb7a_Ex2^{F/F-CRE}* MSCs expressing circGFP or circPOK-GTG. **h** Expression levels of ILF2 (on the left) and ILF3 (on the right) mRNA upon knock down with specific shRNAs. **i** Measure of anchorage-independent proliferation of *p53^{-/-}Zbtb7a_Ex2^{F/F-CRE}* MSCs expressing circPOK-GTG and knocked down for the expression of ILF2 or ILF3. **j** Expression levels of ILF2 and ILF3 in *p53^{-/-}Zbtb7a_Ex2^{F/F-CRE}* MSCs expressing circGFP, circPOK and cDNA-POK. **k** Co-IP assays to measure the interactions between ILF2 and ILF3 in *p53^{-/-}Zbtb7a_Ex2^{F/F-CRE}* MSCs expressing circGFP or circPOK-GTG. **l** Localization of ILF2 and ILF3 in the nucleus and cytosol of *p53^{-/-}Zbtb7a_Ex2^{F/F-CRE}* MSCs expressing circGFP or circPOK-GTG.