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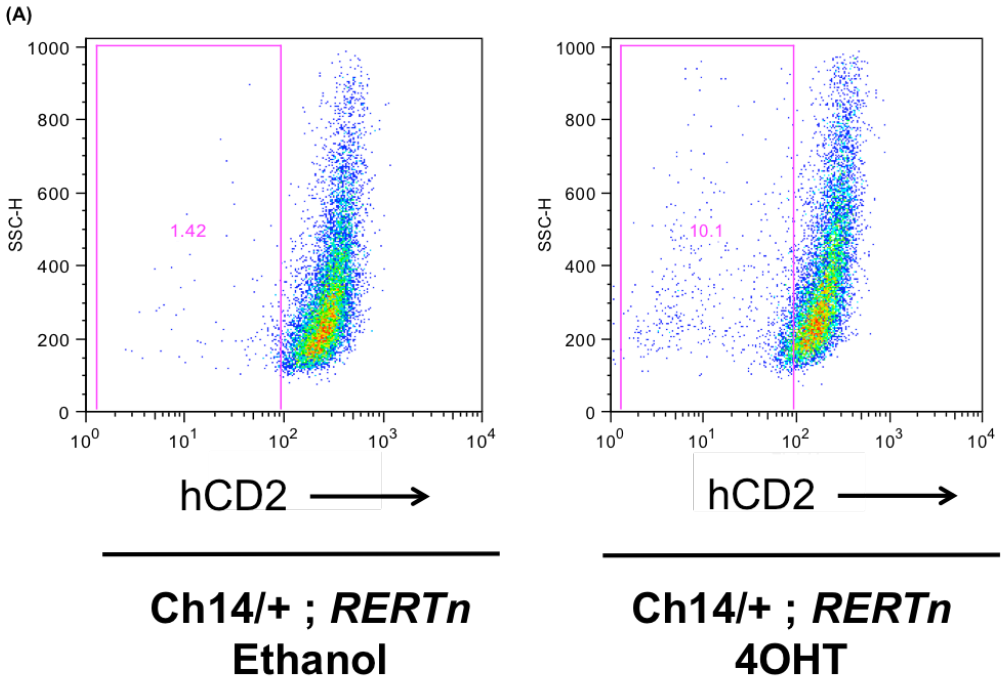
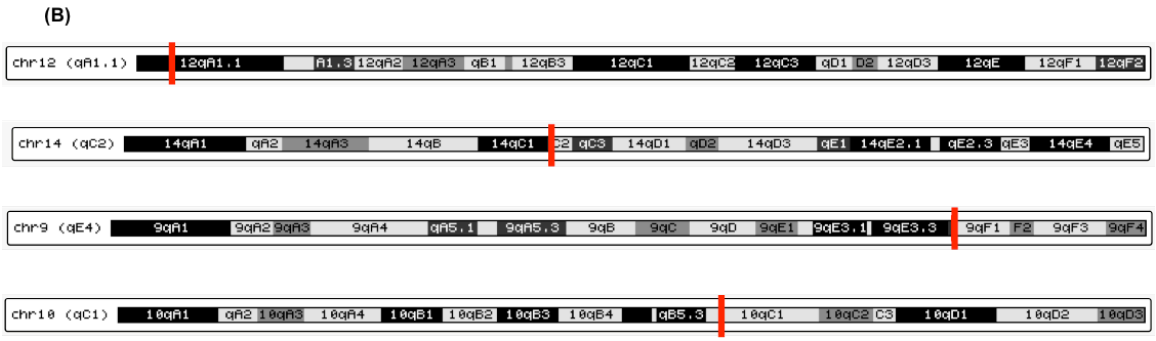
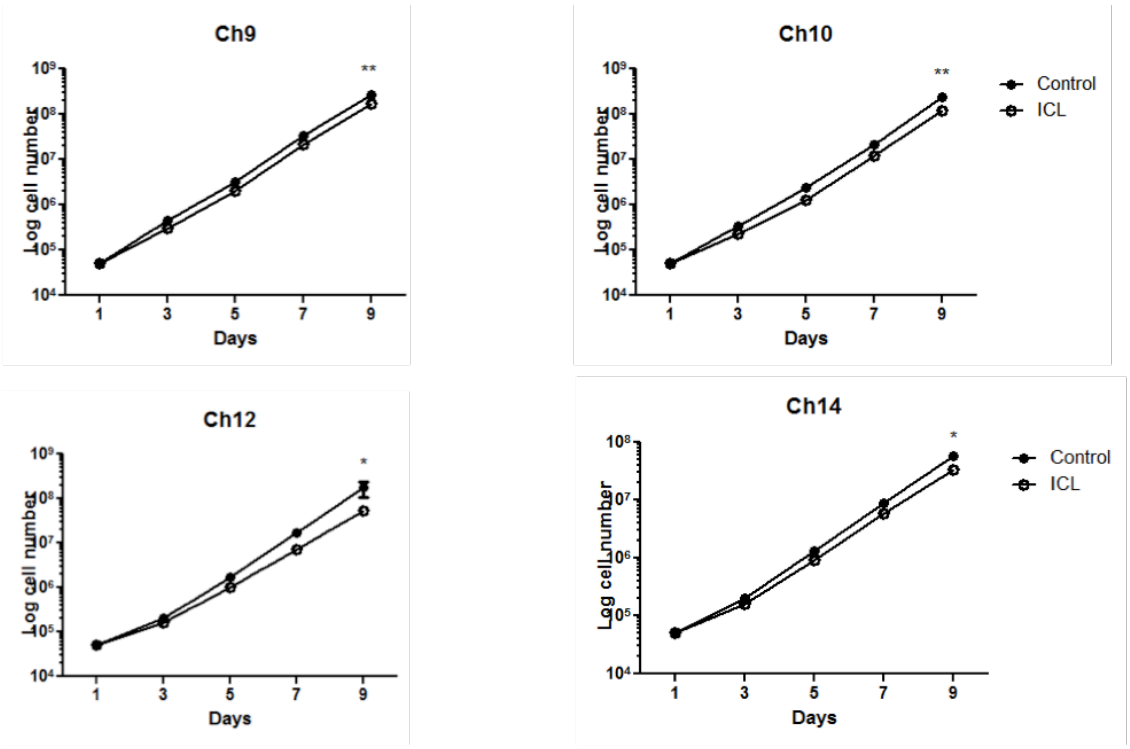
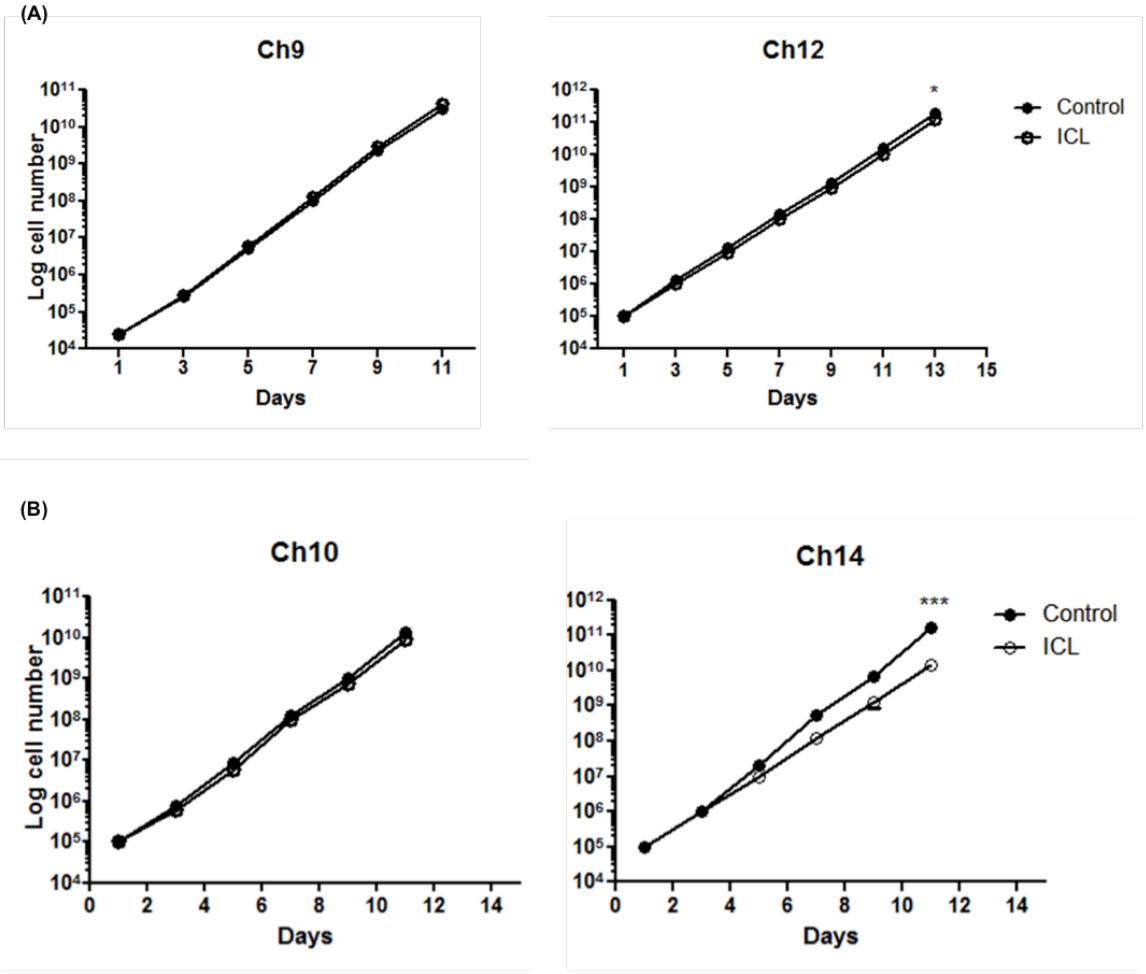




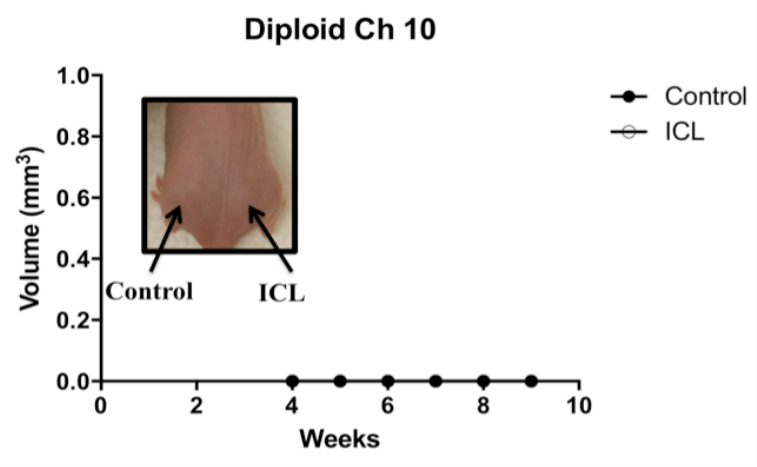
Appendix Figure S1

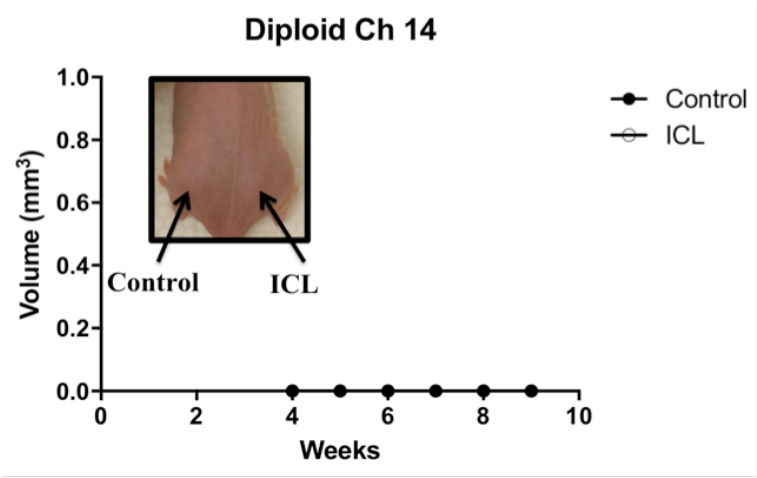


Appendix Figure S2



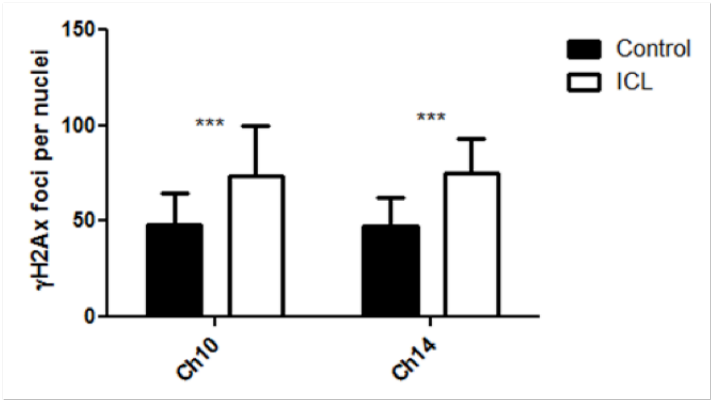
Appendix Figure S3





Appendix Figure S4

(A)



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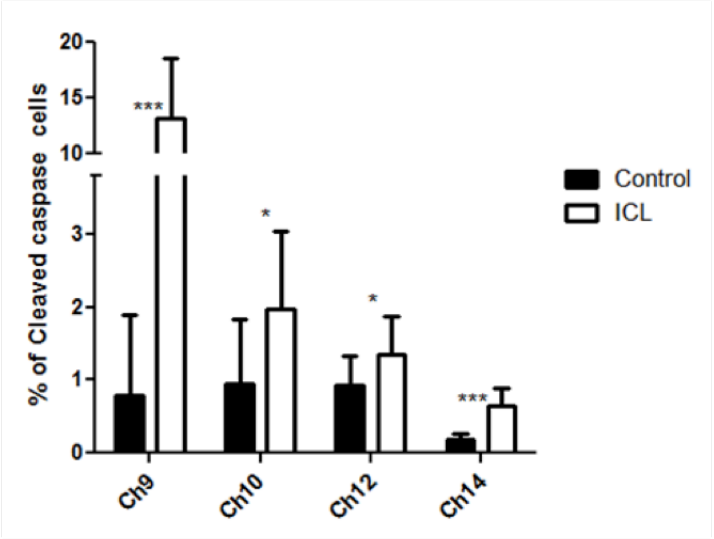

Appendix Figure S5

Appendix Figure S1: Generation of ICL in MEFs by Cre recombination

(A) Representative FACS plot showing loss of hCD2 marker expression of Ch14 ICL MEFs after treatment with 4-hydroxy tamoxifen (4OHT) for 14 days to induce Cre, compared to Ethanol treated control cells. Compared to Figure 1C, there is no difference in the side scatter between the Ethanol and 4OHT treated MEFs. (B) Location of the iLoxP sites denoted by red lines on all four chromosome lines.

Appendix Figure S2: *In vitro* growth characteristics of early passage ICL MEFs

Growth curve of the early passage ICL lines Ch9, 10, 12 and 14 under adherent *in vitro* culture conditions (n=3 for each dataset and error bars denote SD, $p<0.005$ for Ch9 and 10; $p<0.05$ for Ch12 and 14).

Appendix Figure S3: *In vitro* characteristics of late passage ICL MEFs and tumor explants

(A) Growth curve of the late passage ICL lines Ch9 and Ch12 under adherent *in vitro* culture conditions (n=3 for each dataset and error bars denote SD, $p<0.05$ for Ch12 and ns for Ch9). (B) Growth curve of the control and ICL tumor explants for Ch10 and Ch14 lines in culture conditions, measured every two days (n=3 for each dataset and error bars denote SD, $p<0.0005$ for Ch14 and ns for Ch10).

Appendix Figure S4: Tumorigenic potential of diploid ICL MEFs

Tumor growth curve after sh-p19 immortalized diploid ICL cell and control cells were injected into flanks of athymic nude mice (n = 5 per group).

Appendix Figure S5: DNA damage and Cleaved caspase immunofluorescence on ICL MEFs

(A) Quantification of γH2AX foci in Ch10 and Ch14 ICL lines grown under ultra-low adherence sphere forming conditions after cytospin onto glass slides (n=25 for each dataset and error bars denote SD, $p<0.0001$ for both Ch10 and Ch14). (B) Quantification of the percentage of cleaved caspase positive cells (n=10 and error bars denote SD, $p<0.0001$ for Ch9, $p<0.05$ for Ch10, $p<0.05$ for Ch12 and $p<0.0005$ for Ch14).