





Fig. S4









NIH/3T3-iCRISPRa-sgNgn2 Ethanol

NIH/3T3-iCRISPRa-sgNgn2 40HT





NIH/3T3-iCRISPRi-sgScr Ethanol
NIH/3T3-iCRISPRi-sgScr 4OHT

NIH/3T3-iCRISPRi-sgMymx Ethanol

NIH/3T3-iCRISPRi-sgMymx 40HT

С

a



DEG of sgKlf4 4OHT vs sgScr 4OHT GO enrichment\_DOWN\_BP





neutrophil homeostasis

positive regulation of natural killer cell activation



DEG of sgKlf4 4OHT vs sgKlf4 Ethanol

-log10(pvalue)

Ν

DEG of sgKlf4 4OHT vs sgScr 4OHT

GO enrichment\_UP\_BP

DEG of sgKlf4 4OHT vs sgScr Ethanol

GO enrichment\_UP\_BP

-log10(pvalue)

N

С

cellular response to retinoic acid positive regulation of DNA biosynthetic process vesicle docking exocytic process response to retinoic acid regulation of DNA biosynthetic process placenta development regulation of neuron projection development protein polyglutamylation regulation of interleukin-8 biosynthetic process

negative regulation of leukocyte cell-cell adhesion negative regulation of cell-cell adhesion negative regulation of DNA binding transcription factor activity detection of calcium ion interleukin-8 biosynthetic process potassium ion export negative regulation of T cell mediated immunity positive regulation of T-helper 1 type immune response negative regulation of muscle adaptation neuronal ion channel clustering

> DEG of sgKlf4 4OHT vs sgKlf4 Ethanol GO enrichment\_DOWN\_BP





negative regulation of endopeptidase activity epidermal cell differentiation negative regulation of peptidase activity negative regulation of proteolysis epidermis development keratinization regulation of endopeptidase activity negative regulation of cysteine-type endopeptidase activity involved in apoptotic process regulation of peptidase activity negative regulation of hydrolase activity

b

С

a

b

С



mitochondrial respiratory chain complex I assembly

DEG of sgPrdm4 4OHT vs sgScr Ethanol GO enrichment\_UP\_BP -log10(pvalue) 0 N

regulation of cell cycle G1/S phase transition cell cycle G1/S phase transition negative regulation of response to DNA damage stimulus negative regulation of cell cycle G1/S phase transition transition metal ion homeostasis regulation of cell cycle phase transition regulation of G1/S transition of mitotic cell cycle sequestering of zinc ion cellular ketone body metabolic process regulation of sequestering of zinc ion







meiotic nuclear division meiotic chromosome segregation meiotic cell cycle process meiotic cell cycle nuclear division homologous chromosome segregation organelle fission maintenance of organelle location chromosome organization involved in meiotic cell cycle

synaptonemal complex assembly

#### DEG of sgPrdm4 4OHT vs sgPrdm4 Ethanol GO enrichment\_DOWN\_BP



#### DEG of sgPrdm4 4OHT vs sgPrdm4 Ethanol GO enrichment\_UP\_BP -log10(pvalue) 0 ω ი ŝ 5

-

mitochondrial respiratory chain complex assembly protein targeting to ER establishment of protein localization to endoplasmic reticulum NADH dehydrogenase complex assembly mitochondrial respiratory chain complex I assembly SRP-dependent cotranslational protein targeting to membrane cotranslational protein targeting to membrane protein localization to endoplasmic reticulum

oxidative phosphorylation

respiratory electron transport chain

response to estroger bicarbonate transport aging

regulation of epithelial to mesenchymal transition

positive regulation of transmembrane receptor protein serine/threonine kinase signaling pathway

# pigmentation

in utero embryonic development

neuron death

positive regulation of epithelial to mesenchymal transition SMAD protein signal transduction

-log10(pvalue)



negative regulation of smooth muscle cell proliferation

heart development

















