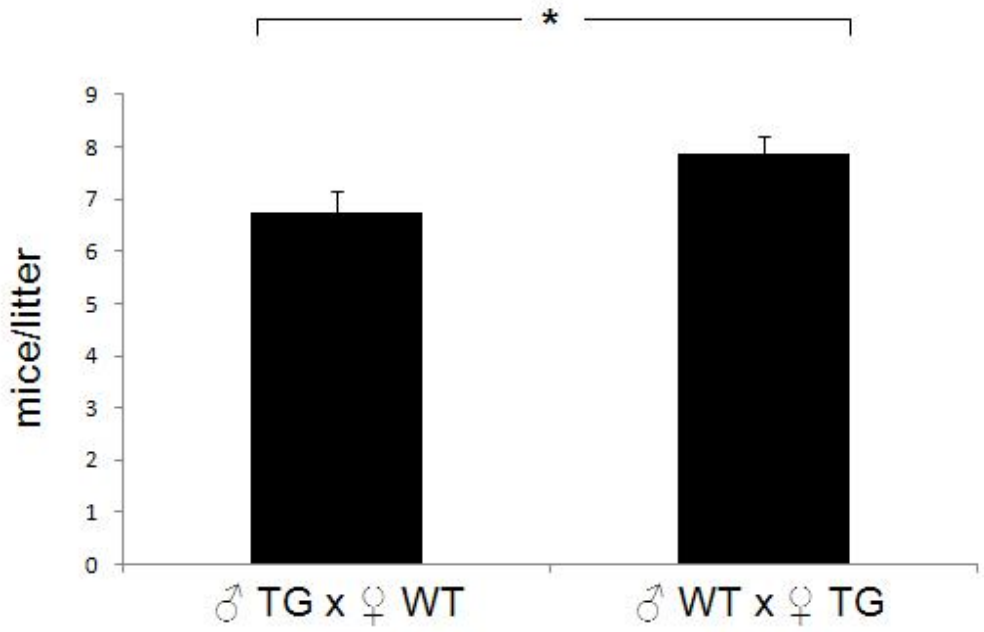
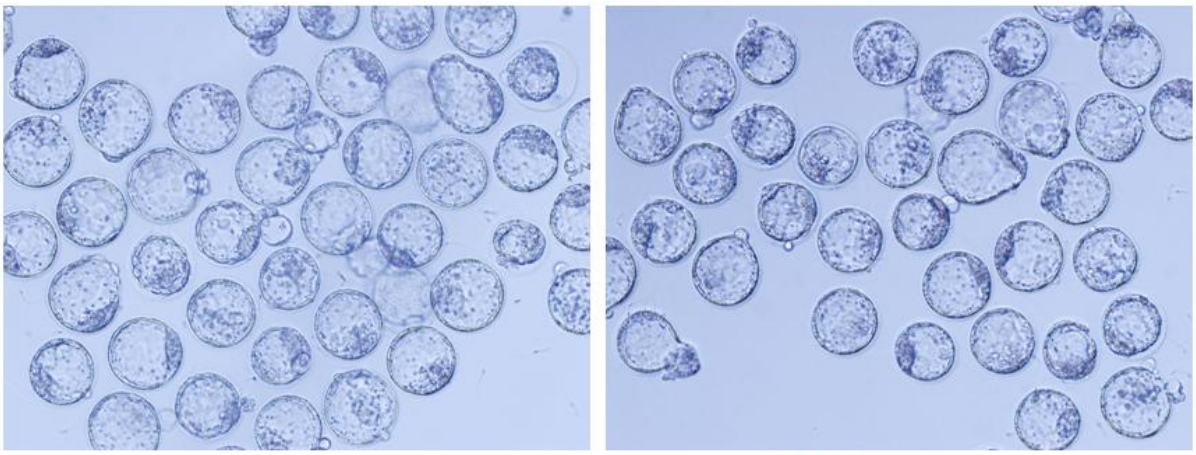
SUPPLEMENTARY FIGURES AND LEGENDS

Supplementary Figure S1. Fertility of *FOXO3* transgenic mice.



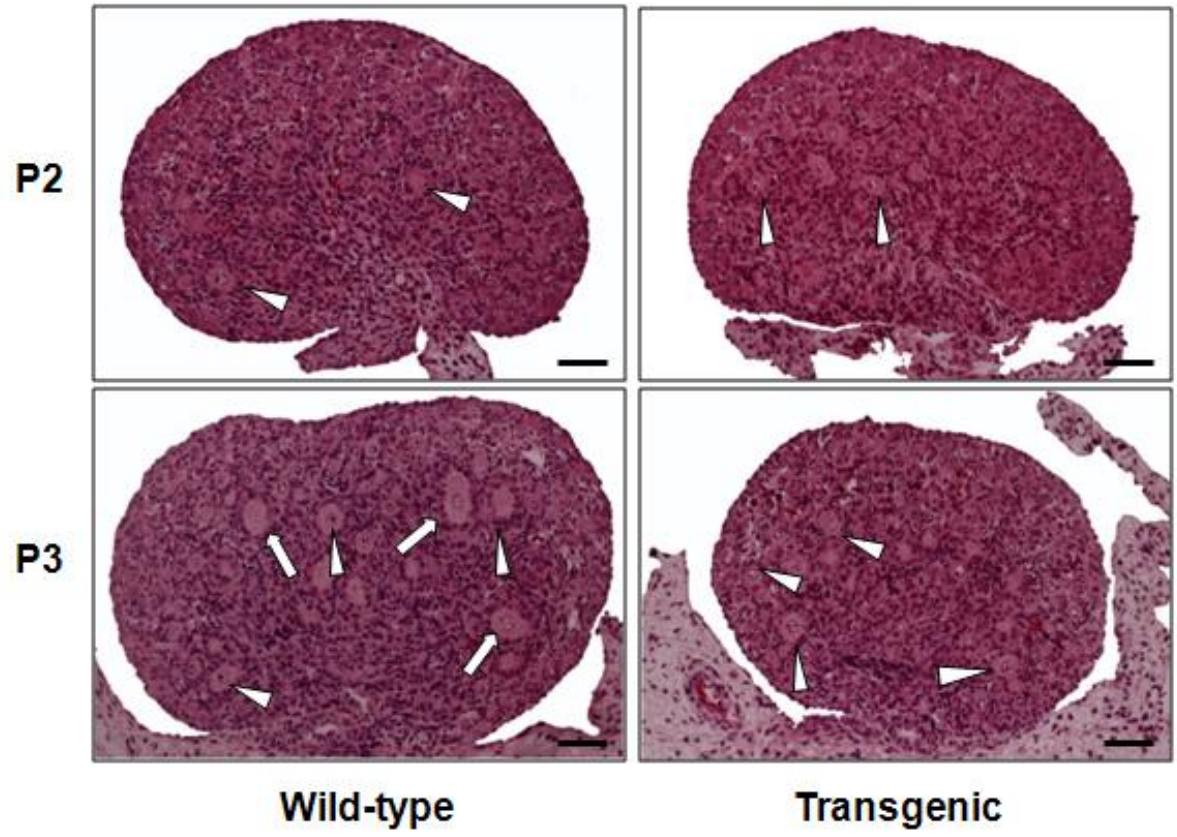
Average number of mice per litter resulting from breeding of 2-6 month old *FOXO3* transgenic animals with wild-type mates. Transgenic males and transgenic females were both fertile. TG = transgenic, WT = wild-type. Data are represented as mean values ± SEM. n=45, (*) $p<0.05$, unpaired *t*-test.

Supplementary Figure S2. Blastocyst morphology after in vitro fertilization.



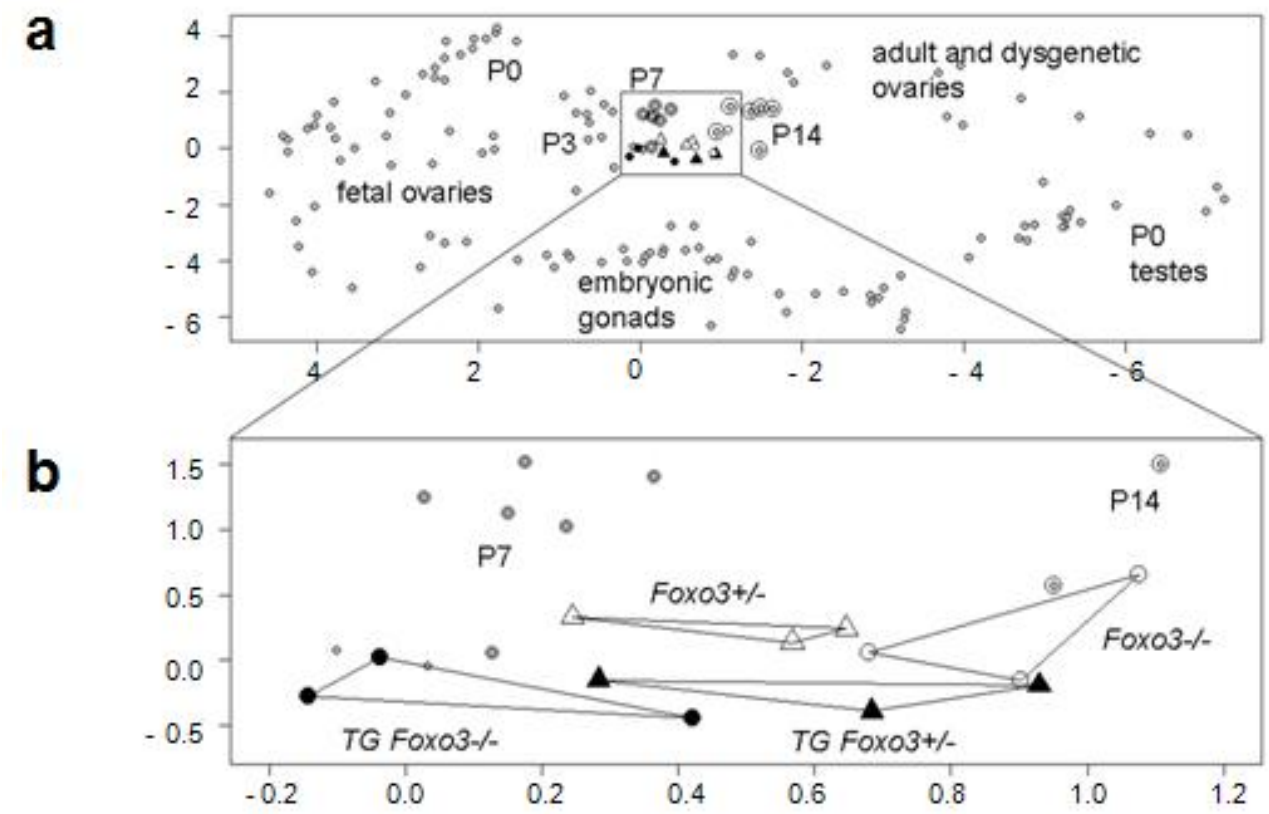
Picture of embryonic development at the blastocyst stage after in vitro fertilization of wild-type and transgenic oocytes. Eggs retrieves from *FOXO3* transgenic females showed similar competency with wild-type for blastocyst formation.

Supplementary Fig. S3. Delayed onset of follicle recruitment in *FOXO3* transgenic ovaries.



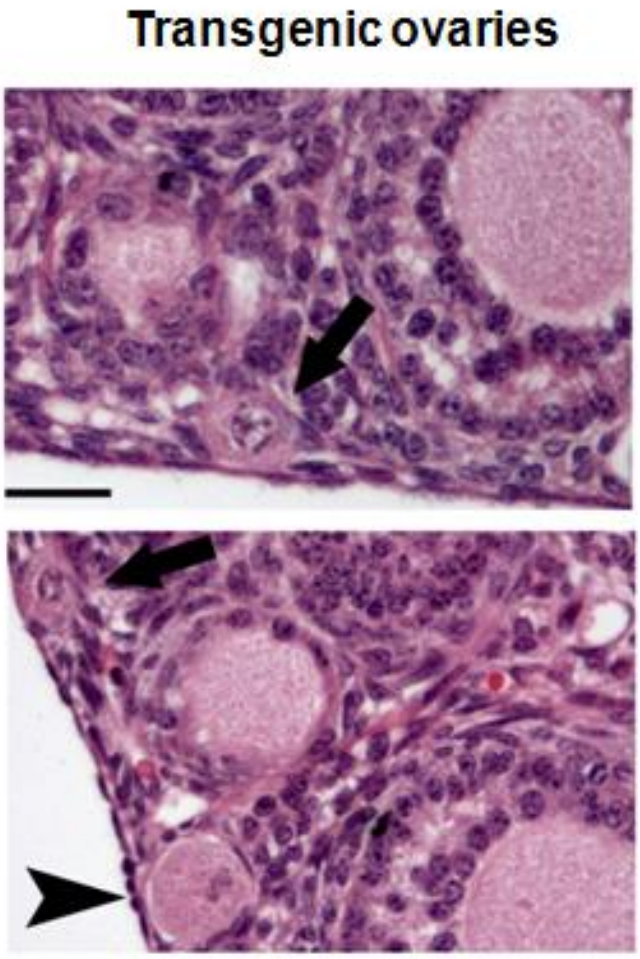
Hematoxylin and eosin staining of ovary sections showed similar appearance of the ovary at P2, whereas one day later wild-type ovaries appeared having more primary (arrowheads), and secondary follicles (arrows) compared to transgenic ovaries. P2 = 2 dpn; P3 = 3 dpn. Bar = 50 μm.

Supplementary Figure S4. Younger transcription profile of *FOXO3* transgenic ovaries.



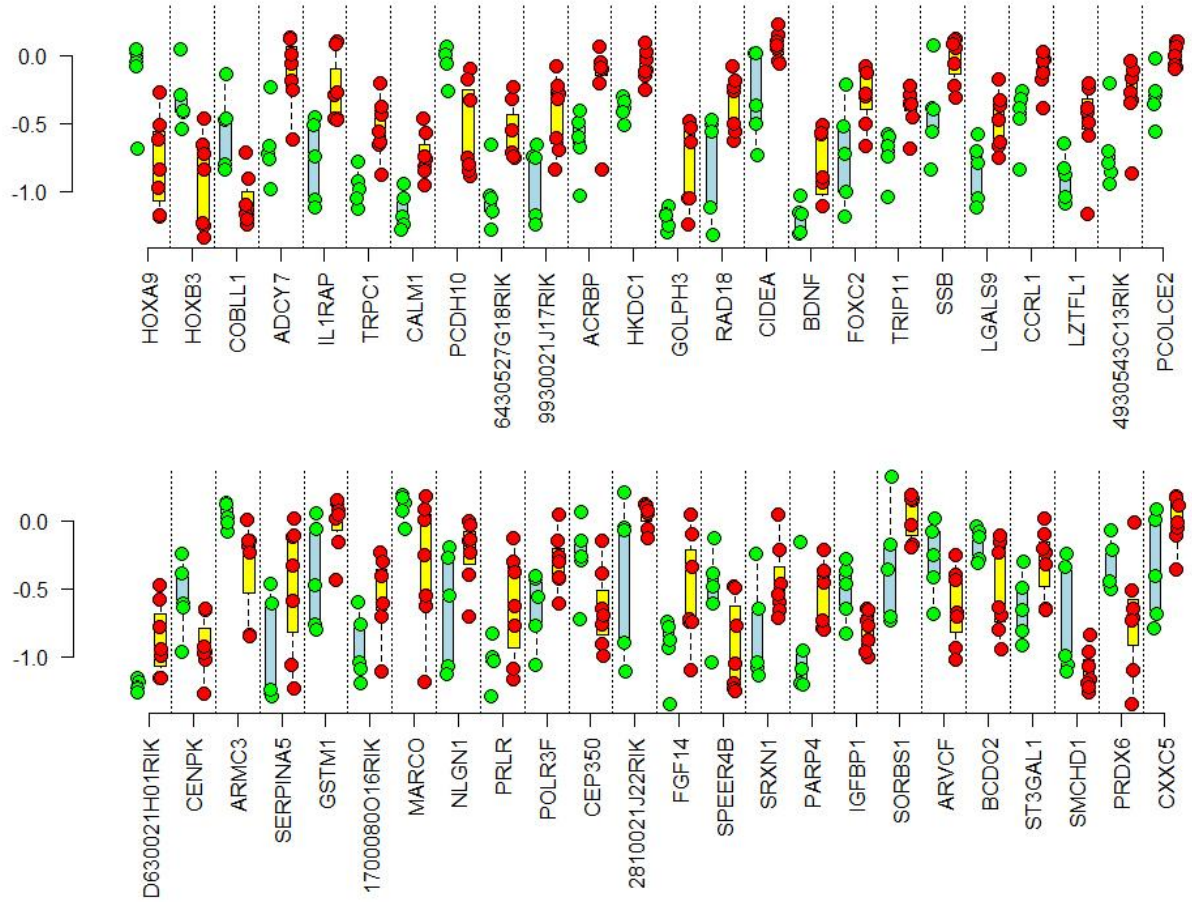
(A) Principal component analysis on 521 developmental genes showing differential aging rates in *Foxo3-/-*, *Foxo3+/-*, and corresponding transgenic ovaries (i.e., TG-*Foxo3-/-* and TG-*Foxo3+/-*). Complete graph for 141 previously reported datasets plus ovaries from the new *Foxo3*-related datasets. (B) Zoomed view for the P7-P14 ovary region. Legend as in Figure 4B; "doubled circles" indicate P7 or P14 ovaries from a different dataset. P0 = 0 dpn; P3 = 3 dpn; P7 = 7 dpn; P14 = 14 dpn.

Supplementary Figure S5. Presence of normal primordial follicles in *TG-FOXO3-/-* ovaries.



Hematoxylin and eosin staining of P14 TG-*Foxo3-/-* ovary sections showed the presence of normal primordial follicles (arrows). At P14, Foxo3-/- ovaries without the transgene would show only early growing primordial follicles (arrowhead). Bar = 20 μm.

Supplementary Figure S6. Differential aging profiles in *FOXO3* transgenic vs KO ovaries.



Top 48 genes associated with "differential aging" in *Foxo3-/-* and TG-*FOXO3-/-* mouse ovaries by predictive analysis of microarray. The total 12 replicates from the four genotypes tested (Foxo3-/- and Foxo3+/- mice carrying or not carrying the transgene) were divided into two groups depending on whether they clustered with younger (P7) or age-matched (P14) ovaries from published reports, according to the first principal component representing major gene expression changes in the developing ovary (see Methods and Supplementary Fig. S4). This corresponds to 5 green and 7 red dots, resp. The genes are ordered from left to right and top to bottom according to their absolute statistical score of differential expression as calculated by

predictive analysis of microarrays (PAM). The y-axis shows arbitrary units of gene expression levels from the normalized microarray dataset. Blue and yellow boxes represent the interval between the 25th and 75th percentile expression values in either group.

Supplementary Table S1. In vitro fertilization in wild-type and transgenic mice.

	No. oocytes	No. PN embryo (%)	No. embryos developed to (%)			
			2-cell	8-cell	Morula	Blastocyst
WT (n=3)	93	82(89)	69(84)	65(78)	65(78)	59(71)
TG (n=3)	81	70(86)	63(89)	58(83)	57(81)	54(77)

Fertilization rates were not different between wild-type and transgenic mice after superovulation and in vitro fertilization.