## The Dummerstorf high-fertility mouse line 1 – a worldwide unique model for increased female reproductive performance

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The development and maturation of ovarian follicles is a complex and highly regulated process. During recent decades, several mouse models provided insights into the regulation of folliculogenesis. In contrast to the commonly used transgenic or knockout mouse models, the Dummerstorf high-fertility mouse line 1 (FL1) is a worldwide unique selection experiment for increased female reproductive performance and high fertility. FL1 mice almost doubled the number of ovulated oocytes compared to the unselected control mouse line.

To gain insights into the cellular mechanisms leading to the high fertility phenotype, granulosa cells were isolated from antral follicles and used for mRNA sequencing. To obtain a global picture of how the phenotype is achieved gonadotropins, growth factors and other hormones associated with follicular development were analyzed.

While FSH and IGF1 levels are significantly decreased in FL1 females, LH levels are elevated. No differences were found in insulin, prolactin and oxytocin levels in FL1 mice compared to the control mouse line.

FL1 females are characterized by various alterations on endocrine and molecular levels, which have the potential to improve the follicular development. Our results indicate that the crosstalk between different intracellular signaling pathways in granulosa cells is improved, follicular atresia in FL1 is decreased due to enhanced granulosa cell survival and by improving the efficiency of intracellular signaling, glucose metabolism and signal transduction, FL1 mice have advantages in reproductive performance. The understanding of these mechanisms and their interplay might be of fundamental interest for the understanding of proper fertility in human.