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## **Crosstalk between *Pax6* haploinsufficiency and paternal aging in modulating offspring behavior: a possible role for epigenetic modification**

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Human epidemiological studies have indicated that advanced paternal age is related in their offspring to elevated rates of various psychiatric disorders such as schizophrenia, autism, early onset of bipolar disorder, reduced IQ, and impaired social functioning in adolescence. Both genetic and epigenetic mechanisms are assumed to be involved in these transgenerational effects. Currently, we are focusing on elucidation of the epigenetic mechanism how paternal aging and paternal *Pax6* haploinsufficiency cause vocal communication deficits in F1 offspring, which was abolished when F2 offspring was born to young F1 male mice. We have identified a common change of H3K79 tri-methylation (H3K79me3) in both wild type (WT) and *Pax6* mutant spermatocytes and sperm. Furthermore, a notable association was observed between H3K79 tri-methylation of sperm versus age of male mice, and versus vocal communication deficits in offspring. Based on these lines of evidences we favor to propose a scenario that altered regulation of gene expression by H3K79me3 might be a pathophysiological basis of vocal communication deficits by advanced paternal aging. Identification of target genes whose expressions are regulated by H3K79me3 will be warranted.

### **References:**

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