Age-related DNA methylation changes in mouse spermatozoa

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Abstract
DNA methylation plays important roles in the production and functioning of spermatozoa. Recent studies have suggested that DNA methylation patterns in spermatozoa can change with age, but the regions susceptible to age-related methylation changes remain to be fully elucidated. In this study, we conducted genome-scale DNA methylation profiling of spermatozoa obtained from C57BL/6N mice at 8 weeks (8w), 18 weeks (18w) and 17 months of age (17m). There was no substantial difference in the global DNA methylation patterns between 18w and 17m samples except for a slight increase of methylation levels in long interspersed nuclear elements in the 17m samples. We found that maternally methylated imprinting control regions (mICRs) and spermatogenesis-related gene promoters had 5-10% higher methylation levels in 8w samples than in 18w or 17m samples. Analysis of individual sequence reads suggested that these regions were fully methylated (80-100%) in a subset of 8w spermatozoa. Similar atypical methylation patterns are known to be observed in a subset of postnatal spermatogonia, which might be the source of the atypical DNA methylation in 8w spermatozoa. Our findings provide new insights into the stability and plasticity of DNA methylation in spermatozoa.