



Figure 3. Dynamics of 5mC/5hmC/5fC/5caC in paternal and maternal genomes during preimplantation development. DNA demethylation of the zygote, gauged by 5mC levels, occurs by a passive mechanism in the female pronucleus, diluting the marks with the passage of every cell cycle. The male pronuclear genome becomes demethylated actively by the action of the Tet enzymes. Tet3 is expressed in the oocyte and zygote. After fertilization, Tet3 is relocated from the cytoplasm to the paternal nucleus to convert 5mC to 5hmC/5fC/5caC. Subsequently, paternal and maternal genomes undergo replication-dependent dilution of 5hmC/5fC/5caC in males and 5mC in females. It is possible that replication-independent active DNA demethylation may occur in a loci-specific manner in zygotes, but the exact mechanism is currently unclear. DNA methylation patterns in ICM are reestablished by de novo DNA methyltransferases Dnmt3a and Dnmt3b at the blastocyst stage.