Supplementary informatuon S1 (table) | **Evidence for and against DNA demethylation in mammailian cells**

Enzyme	Evidence supporting demethylation	Evidence against demethylation
Direct removal		
MBD2	- *In vitro* assays (1)	- Stably binds to methylated DNA (2,3) - Normal methylation patterns in null mice (4)
5meC glycosylases		
DME ROS1/DML1 DML2 DML3	- *In vitro* assays (5–9) - Loss of function mutants exhibit expression of imprinted genes and hypermethylation (5, 10)	
TDG		- Excision activity is much lower against 5meC compared to thymine (11)
MBD4		- Excision activity is much lower against 5meC compared to thymine (12) - Null zygotes exhibit paternal genome demethylation (13)
Deaminases		
AID APOBEC1	- *In vitro* oligonucleotide and *E. coli* assay (14) - Deamination and BER of methylated when expressed in zebrafish embryos (15) - Subtle hpermethylation in AID-deficient PGCs (16)	- Knockout of AID or APOBEC1 are viable and fertile (18–21) - Majority of demethylation is maintained in AID-deficient PGCs (16)
Dnmt3a Dnmt3b	- *In vitro* assays (17)	- Deamination reaction can only occur in the absence of SAM (17)
Nucleotide excision repair		
Gadd45a	- Loci-specific and global demethylation after overexpression, hypermethylation after knockdown (22) - Knockdown of NER machinery results in hypermethylation (23)	- Lack of direct biochemical evidence - Irreproducibility (25) - No expected hypermethylation in knockout mouse (26)
Gadd45b	-Deficiency results in promoter hypermethylation (24)	- Lack of direct biochemical evidence - Null zygotes undergo paternal genome demethylation (27)
Oxidative demethylation		
Tet1 Tet2 Tet3	- *In vitro* assays (28, 29) - 5hmC is present in ES cells and Purkinje neurons (28, 30)	
Radical SAM		
Elongator	- Paternal genome is not demethylated after knockdown in zygotes (27)	- Lack of direct biochemical evidence

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