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HST.161 Molecular Biology and Genetics in Modern Medicine
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Reading assignment #5—Imprinting, X inactivation and Epigenetics

Answer question 1 and two of the remaining three questions (i.e. 2,3 or 2,4 or 3,4)

1. In Buiting et. al., the authors reach the conclusion that approximately 1 in 1,500,000 million spermatozoa should carry a maternal imprint which was not erased in the paternal germline. Explain the logic which leads to this conclusion. Explain how the data in Figure 2 is supportive of this conclusion. (Please note that the review by Horsthemke and Buiting on imprinting defects on chromosome 15 is also provided to you to help understand the mechanisms underlying imprinting on chromosome 15.)

2. In the review of Rett syndrome by Williamson and Christodoulou, it is noted that pathogenic mutations in exon 1 of MeCP2 are only rarely associated with Rett syndrome. Propose a reason why this is likely to be the case.

3. In the opinion piece by Reik and Lewis, the authors suggest that chromosomal imprinting was developed during mammalian evolution in parallel with non-random X chromosome inactivation but *random* X chromosome inactivation was developed at a later point in eutherian mammal evolution. Explain their reasons for holding this point of view.

4. Based on your reading of the review by Robertson explain how the loss of imprinting of the IGF2 can contribute to either tumorigenesis in Wilms tumor or anatomical malformation in Beckwith-Weideman syndrome.