RJA 1st Report

Pg 7

- Logical to introduce epigenetics before then describing genome wideepigenomics
- Give more precise ref for Waddington
 - Waddington C. H. (1942). The epigenetype. Endeavour 1, 18-20.
- "Some consider..." too vague give reference
- Generally put reference inserts at the end of a phase or sentence to make reading easier—particularly when not a superscript number style
- "... an organism can generally be thought..." too vague what are the 'general' exceptions
- 200 cell types historic new see 2i in
 - e https://www.humancellatlas.org/files/NIH_reponse_regev.pdf and for further discussion
 - http://www.cell.com/cell systems/abstract/S2405-4712(17)30091-
- ".. to list exhaustively here" too vague list major categories i) DNA modifications, ii) Histone Variants iii) PTM of Histone tails and then describe each category
- Histone Code include combinatorial methods > Segmentation

Pg 8

- "likely DNA methylation." too informal be more definitive and include refs to support statements
- the addition of methyl group at the 5 Carbon of cytosine DNA methylation
- Be more explicate re non-CpG how frequent where prientate reader with refs, etc.
- Repeated sentence "probably most well studied" line 4
- Explain why DNA methylation easier to study that chromatin marks
- Refs re mutability
 - Duncan BK, Miller JH. Mutagenic deamination of cytosine residues in DNA. Nature 1980
- Partial sentence starting "CpG islands..."
- "Dubbed" too informal "defined as"
- Logical order discussing DMRs in CGI shores before within CGI themselves

Pg 9

- Figure meaning not clear enough

Pg 10

- Orphan CGI need to include refs on alternate promoters
 - Illingworth et al. (2010) Orphan CpG Islands Identify Numerous Conserved Promoters in the Mammalian Genome
 - Maunakea et al. (2010) Conserved role of intragenie DNA methylation in regulating alternative promoters
- Details re CGI here need to come before CGI shores
 - Need to include Lister et al. (2009) and Schultz et al. (2015) Nature
- Sentence structure "DNA methylation is highly dependent..."
- SNP/CpG SNP influence on allelic methylation need to cite
 - Kerkel et al (2008) Nat Genet
 - o Shoemaker et al (2010) Genome Res.
 - Schalkwyk et al. (2010) AJHG
- transcription factors. "2.5"



Pg 13

- "[@]"
- "For other reviews see..." not appropriate in this context.
- Consistent capitalization "Regions"
- Definite re RRBS bias



Pg 14

- Example of epimutation
 - o Hypermethylation of *BRCA1* promoter has been identified in 10-15% of sporadic non-familial BC [Dobrovic *et al.* (1997) Cancer Res; Rice *et al.* (2000) Carcinogenesis]
- Sentence structure "The divergence..."
- "global" H4 H3 acetylation
- "nice" too informal
- "This has allowed..."
- Incongruous lumping 2 studies from 1982 and 2006 together what was first found what was later supported
- Christensen et al. tissue type include elsewhere as discussing ageing here
- Rakyan et al. include bivalent domains
- "...490 significant DMRs" in fact incorrect nomenclature used in this paper—they are DMPs only
- *A lot of history here could reduce to strongest points to reduce word count

- Rakyan "et al." and Bocklandt "et al."
- Affinito et al. in sentence
- Garagani et al. not adding much
- Describe Horvath study in more depth
- "...Zaghlool"
- "quite a large number" too vague
- "findings indicated that"
- Array bias in results
- ... linear."



Pg 17

- Early studies not cell type corrected
- Need to have consistent direction otherwise not replication
- Comparing non array to array studies needs to be pointed out

Pg 20/22

- Age variability need to cite
 - o Slieker et al. (2016) Genome Biology
- Much of this page is more appropriate for a Discussion section not Literature Review



- "I hypothesise ..." not in Literature Review section
- Best practice is to avoid singular personal pronoun in scientific writing as is seen as a collective endeavor (Horvath Genome Biol. being a notable exception!)
- "capaciSty"
- "This finding is in agreement with the finding..."