EPIGENETICS OF AN IMPRINTING DISORDER: BECKWITH-WIEDEMANN SYNDROME

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INTRODUCTION AND OBJECTIVES

Beckwith-Wiedemann syndrome (BWS) is an imprinting disorder with a prevalence of 1:10.340[1]. BWS is the result of epigenetic and/or genetic alterations that lead to dysregulation of the imprinted region of the short arm of the chromosome 11 (11p15.5).

There are two imprinted domains involved and are regulated by Imprinting Control Regions (ICR) – ICR1 and ICR2. The objective of this work is to revise the epigenetic regulation of these domains and consequently study if the epigenetic alterations that lead to BWS could be erased.

Beckwith-Wiedemann syndrome is an overgrowth disorder. The main symptoms are:

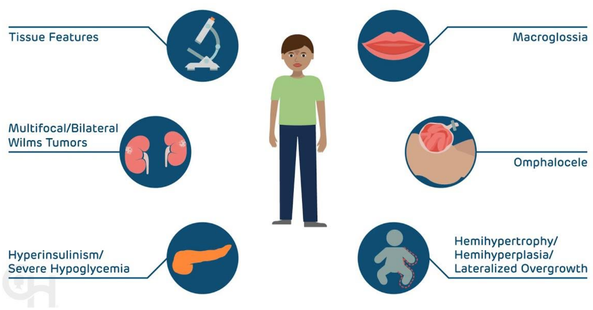
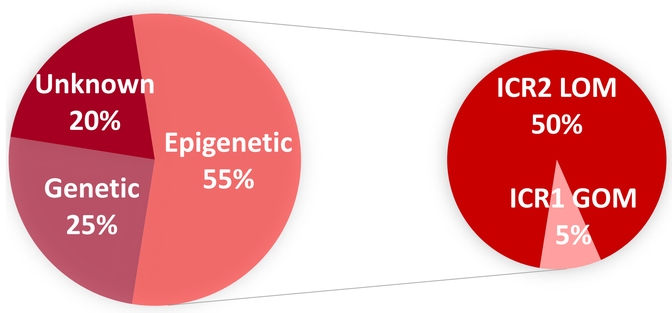
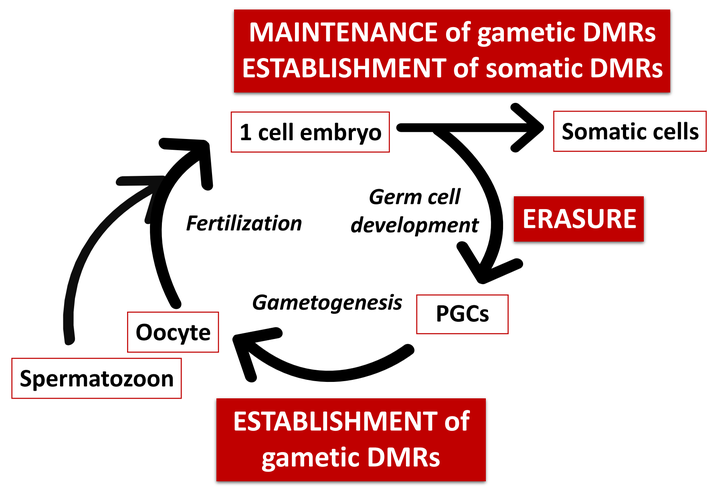


Figure 1: ref[2]

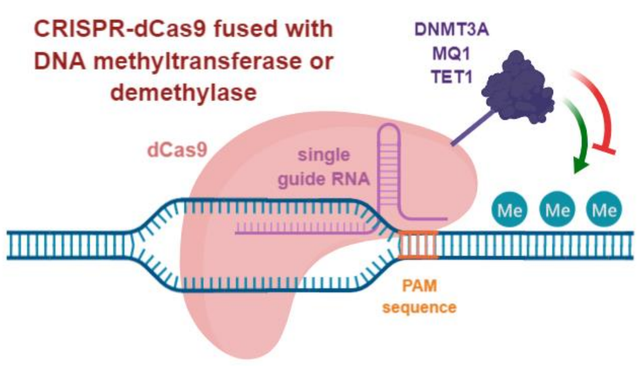
Which are the causes of Beckwith-Wiedemann syndrome?



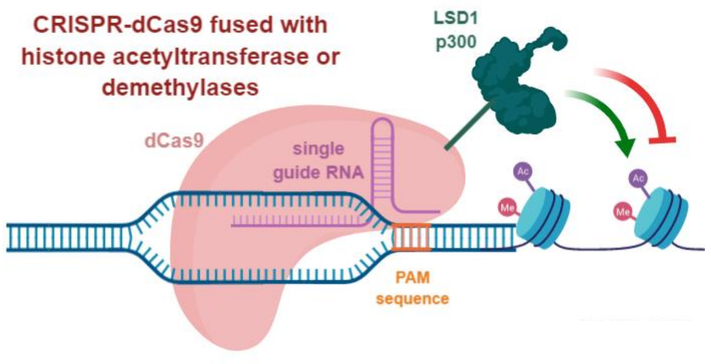
When is the methylation set?



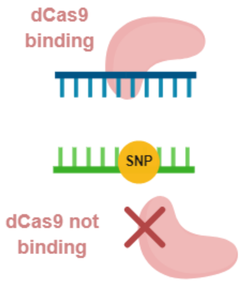
How can epigenetic marks be reverted?



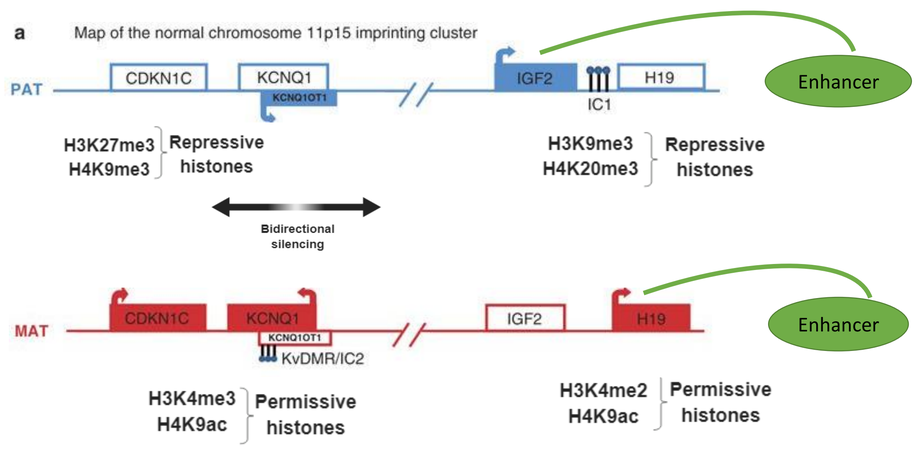
Changing epigenetic patterns have been fulfilled *in vitro* and *in vivo*.



However, the main challenge still is:
is it possible to develop an allele-specific epigenome editing tool?



Gain of methylation on ICR1 and loss of methylation on ICR2



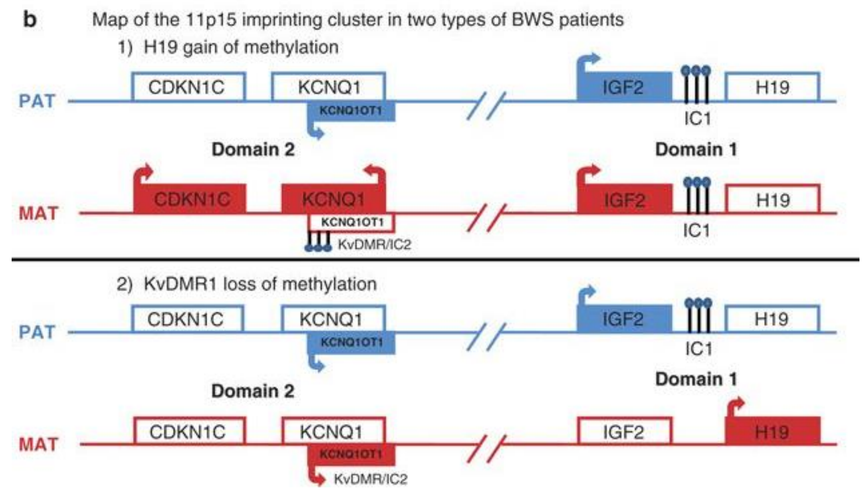


Figure 2: ref[3]

CONCLUSIONS

- ✓ The most promising tool to revert DNA methylation patterns is CRISPR-dCas9 fused with DNA methyltransferases, DNA demethylases and histone acetyltransferases and methylases. First results have been shown both *in vivo* and *in vitro* and allow the scientific community to be optimistic about this field.
- ✓ When it comes to allele-specific epigenome editing, there are still several challenges that need to be solved. It is not a very explored field, but the first approaches let us picture a future with allele-specific epigenome edition based on SNPs.
- ✓ If in the future therapies for BWS are developed, they will be highly personalized hence further research in the two imprinted domains of BWS is fundamental to determine accurate diagnoses and to establish a better genotype-phenotype correlation.

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