Fighting the Enemy Within

Basic Life Science and Issues : Presentation

Group 4

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Chapter Abstraction

Fighting the Enemy Within

11th chapter of *The Epigenetics Revolution*

"Epigenetic perspective of Cancer and its treatment"

Introduction: Cancer

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Characteristics of Oncogenesis

- Multi-step process
- Defections must be accumulated

  Inherited oncogenes are slowly expressed
  e.g.) BRCA1 mutation

- Tumour suppressor gene - Switched off
- Alteration with epigenetic access

Epigenetic Approach for Oncogenesis

- DNA Methylation

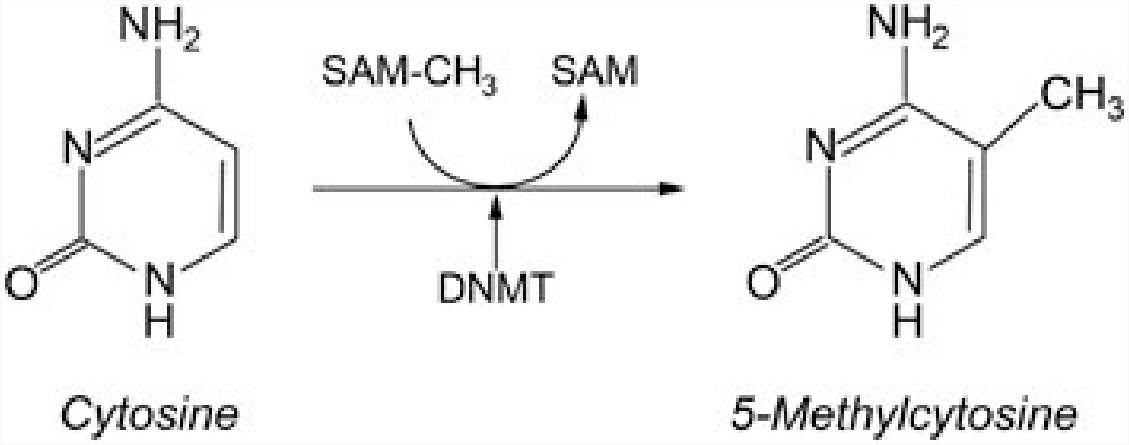
  Hypermethylation of CpG island

- Repressive Histone Modification

  Histone deacetylation

DNA Methylation

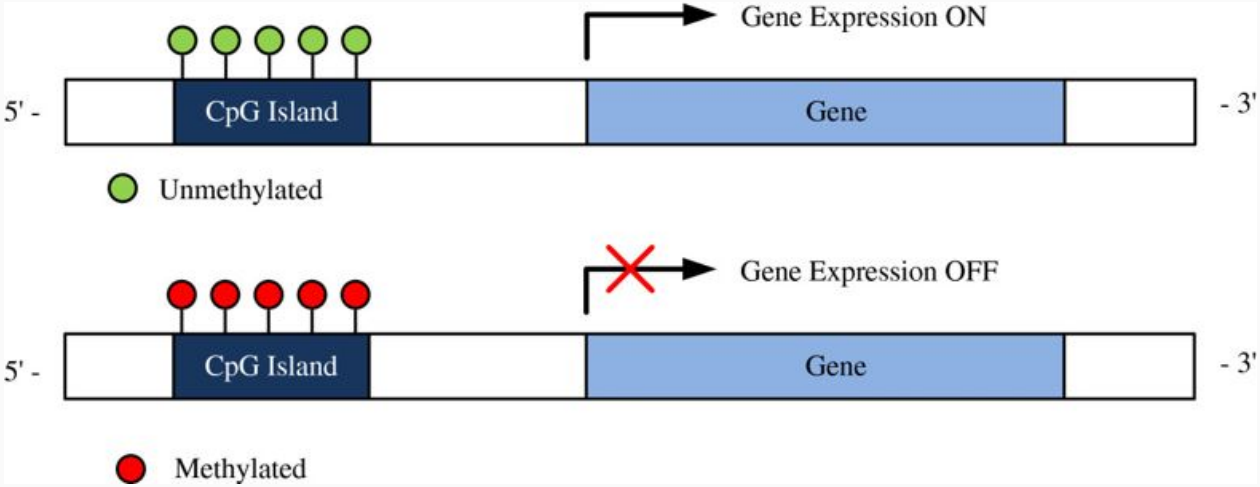
Cytosine before Guanine can be methylated



Methyl group is bond on 5’ carbon atom

DNA Methylation

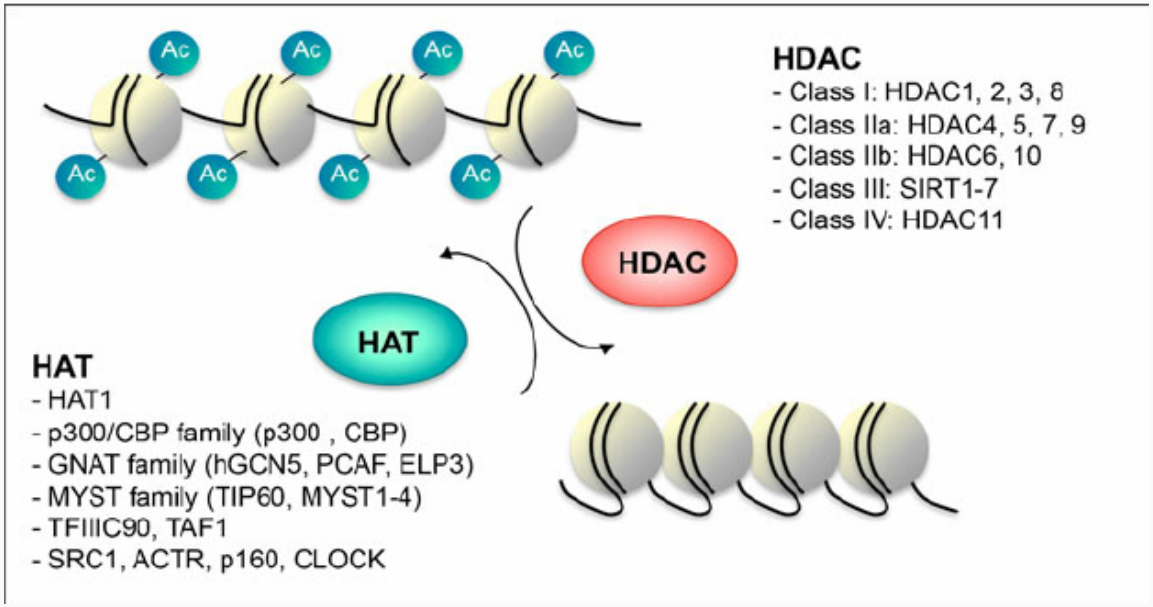
CpG dinuclotide cluster (CpG island, CGI) are usually located in the promoter regions of genes in a DNA sequence.



Hypermethylated CGI disables specific gene expression.

Histone deacetylation

Histones are related with gene regulation.

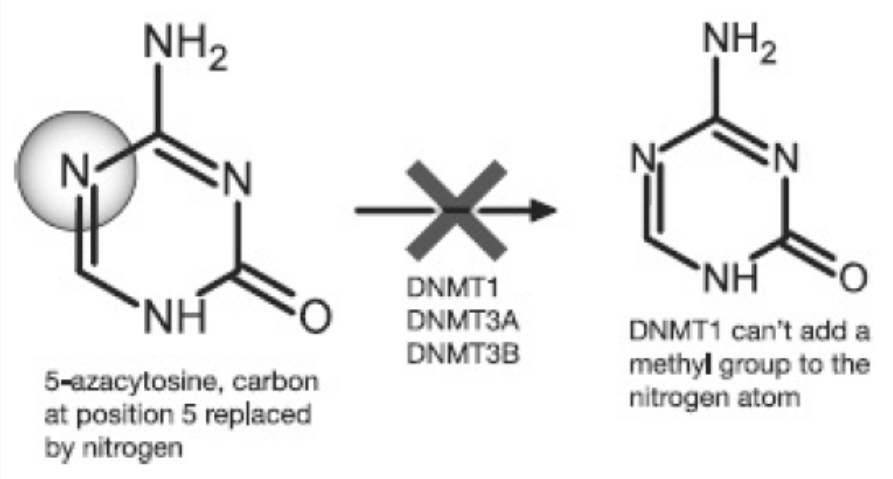


Less acetylated histones lead less expression.

Approach for Treatment

- DNMT enzyme inhibitors

  5-azacytidine, 2-aza-5'-deoxycytidine

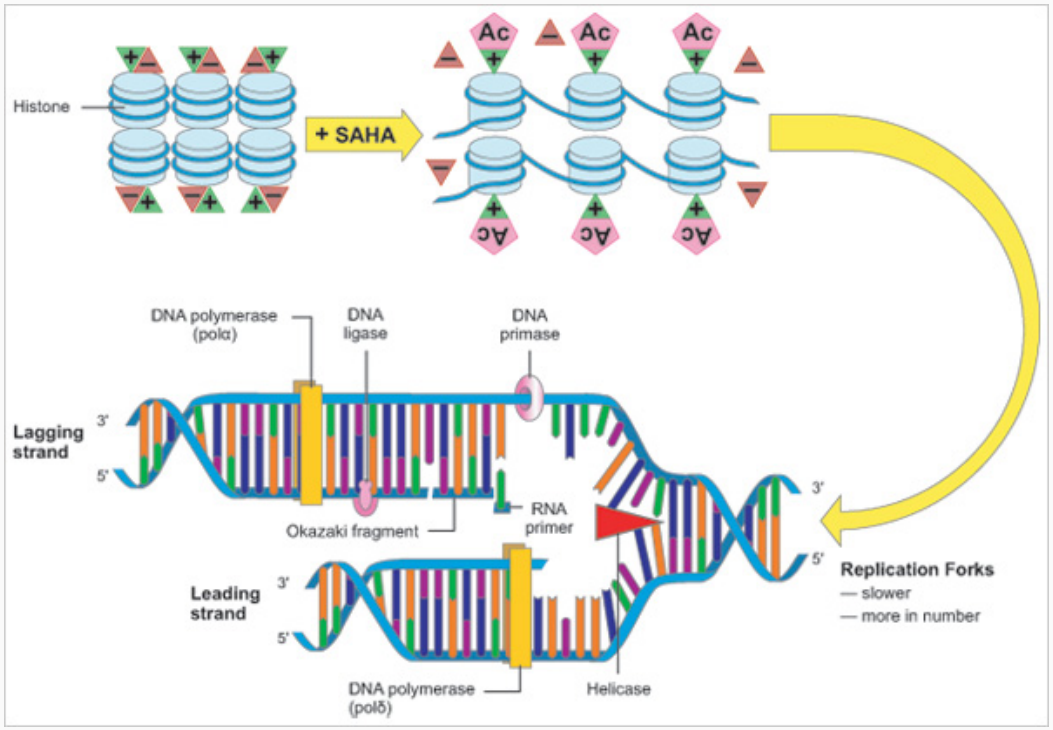


methylation inhibited by 5-azacytidine

Approach for Treatment

- HDAC inhibitor

  SAHA, Romidepsin



No easy wins

- Oncogenesis has numorous mechanisms

  Case by case, person by person

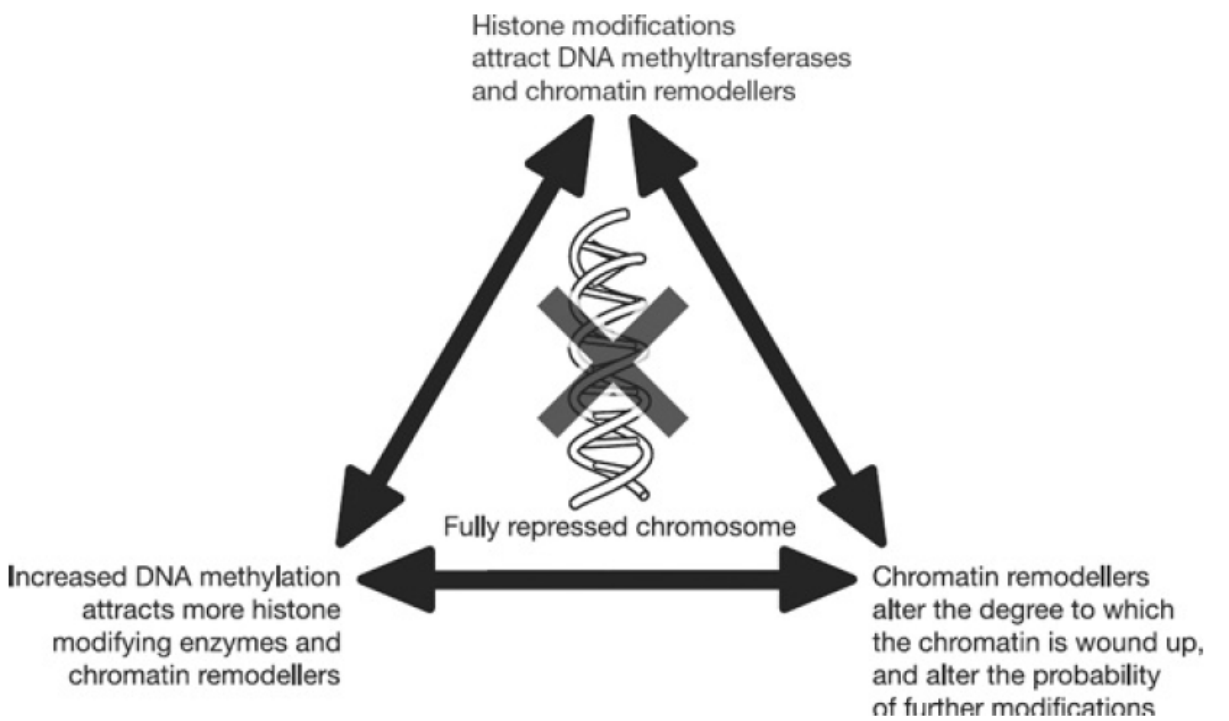
- The solutions are preferrable for haematological cancer
- Also these solutions should be used in different fields

  DMNT inhibitors for bone marrow, HDAC inhibitors for T-cell lymphoma

Chromosome Repression Model

There are many enzymes that involved in histone alteration

(Writer, Reader, Eraser...)



And these interact each other, forms vicious cycle.

Chromosome Repression Model

Writer Enzymes Do...

- EZH2 methylates #27 Lysine of Histon H3
- DNA methylation enzymes are attracted

Eraser Enzymes Do...

- LSD1 demethylates H3K4 of Histon tail
- Demethylated H3K4 receives DNMT3L
- DNMT3L attracts DNMT3A, DNMT3B

Alternative Approach

- 5-azacytine, SAHA cannot be complete destroyer
- But the cycle can be disturbed when the agents are used simultaneously

Conclusion

Epigenetical approach in Oncology...

- Needs further research
- However, several agents are currently effective
- It can open new way to curing cancer

References

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[3] Kazantsev, Aleksey G; et al. (2008). *Therapeutic application of histone deacetylase inhibitors for central nervous system disorders*, Nature Reviews. Drug Discovery London Vol. 7 Iss. 10 854-68.

Q & A

Thank you!