Cancer Epigenetics
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Epigenetic modifications:

Chromosomal changes that are heritable, but do not involve alterations in the DNA sequence.
# Epigenetic Modifications

1. **DNA methylation**

2. **Post-translational histone modifications**
   - Acetylation
   - Propionylation
   - Butyrylation
   - Proline isomerization
   - ADP-ribosylation
   - Methylation
   - Phosphorylation
   - Ubiquitination
   - Sumoylation
   - Deamination
DNA Methylation

A. DNA methyltransferases

B. Methylation

C. Normal DNA vs. Cancer DNA
Examples of histone modifications
Examples of histone modifications

Proline isomerization (by peptidylprolyl isomerase or PPIlase)
Examples of histone modifications

ADP-ribosylation
Examples of histone modifications

- Lysine
- Monomethyl lysine

S-adenosyl-L-methionine (AdoMet)
S-adenosyl-L-homocysteine (AdoHcy)

Methylation
Examples of histone modifications

PhosphoSerine: \( \text{C}_3\text{H}_6\text{NPO}_5 \)

PhosphoThreonine: \( \text{C}_4\text{H}_8\text{NPO}_5 \)

PhosphoTyrosine: \( \text{C}_9\text{H}_10\text{NPO}_5 \)

DehydroAlanine: \( \text{C}_3\text{H}_3\text{NO} \)

Phosphorylation
Examples of histone modifications

Ubiquitination
76 amino acids
Attaches to lysines
Examples of histone modifications

Sumoylation
SUMO (small ubiquitin-like modifier)
100 amino acids, attaches to lysines
Examples of histone modifications

Deamination of arginine
Converts it to citrulline
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acetylation (blue star)
phosphorylation (red box)
ubiquitination (green halfmoon)
methylation (black circle)
Di- or tri-methylation of H3 lysine 9 (H3K9) silences genes. Methylation of H3 lysine 4 (H3K4) activates genes.
Heritable

Unmethylated cytosine

DNA replication

Methylation

Not recognized by DNA methyltransferase
DNMT
DNA Methyltransferases

1. Maintenance methylases
2. De novo methylases
Bisulfite sequencing

Treatment of DNA with bisulfite converts cytosine residues to uracil, but leaves 5-methylcytosine residues unaffected.
Bisulfite sequencing

---TGAGGTGCC---AGGTAGCGA---

**Bisulfite treatment**
- Alkylation
- Spontaneous denaturation

---AUTUUAUGG---TUUATCGUT---

---TGAGGTGCUU---AGGTAGCGA---

---TGAGGTGCC---AGGTAGCGA---

---AUTUUAUGG---TUUATUGUT---

---TGAGGTGCUU---AGGTAGUGA---

Non-methylation-specific PCR
Methylation-specific PCR