

EPIGENETICS AT EPIZYME

EPIZYME & EPIGENETICS

Epizyme is a pioneer in the field of epigenetic research, having been singularly focused on understanding the role epigenetics plays in cancer development and proliferation for more than a decade.

With a long-term vision to rewrite treatment for cancer and other serious diseases through the development of epigenetic medicines, Epizyme focuses on the genetic drivers of disease to 'reprogram' malignancies, converting them into more normal, healthy cells or to accelerate cell death.

Our proprietary drug discovery platform allows us to identify epigenetic targets that are critical for specific cancers.

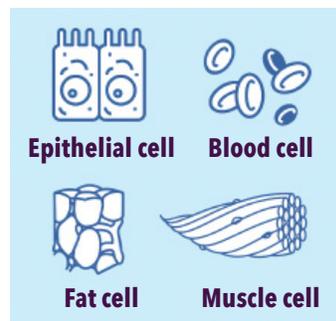
EPIGENETICS DIRECTS CELL FUNCTION

There is tremendous diversity in the types of cells, tissues and organs in the body. Since every cell contains the same exact DNA, there are several mechanisms that allow for this diverse functioning to take place.

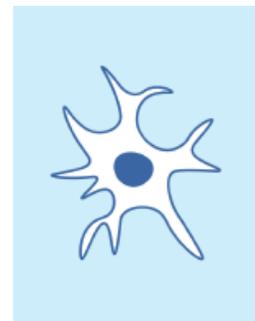
Epigenetics is one vital mechanism that exists. It is a broad and dynamic regulatory system in the body that modulates gene expression.¹

EPIGENETICS PLAYS A ROLE IN MANY BIOLOGICAL PROCESSES, INCLUDING:^{1,2}

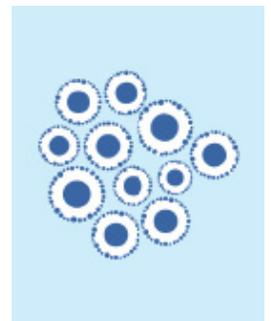
Cell differentiation



Aging



Cancer



EPIGENETICS MODULATES GENE EXPRESSION

Each cell in the human body carries identical genetic information located in the nucleus in the form of long strands of DNA.

Stretched out, human DNA is over 2 meters long and must be tightly packaged to fit within the nucleus. It does so by wrapping around nuclear proteins called histones to form a structure known as chromatin, which is dynamic and its structure can be changed by chromatin modifying proteins.³

Epigenetic modulations occur when chromatin modifying proteins alter DNA packaging and accessibility to transcriptional proteins without changing the DNA sequence. This can turn gene expression on or off.⁴



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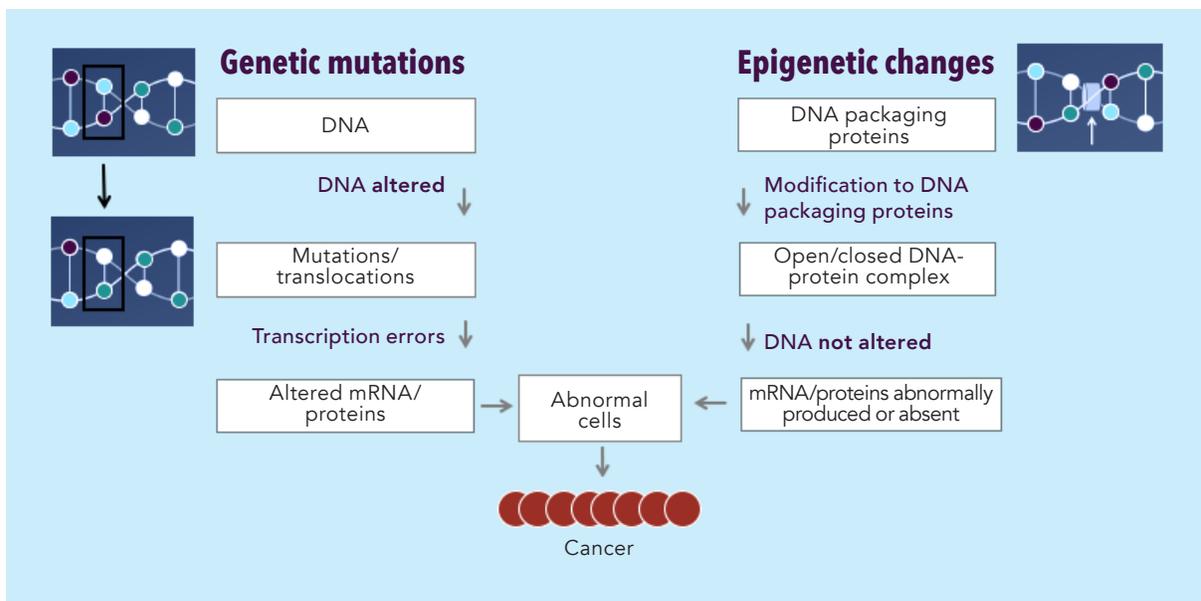
EPIGENETICS AT EPIZYME

EPIGENETICS IN CANCER

Both genetic variations and epigenetic changes can contribute to cancer.⁵

- **Genetic mutations** alter DNA, which may result in altered protein products that are no longer able to function normally.⁶
- **Epigenetic changes** make chromatin more or less accessible to the machinery that ultimately turns genes on or off without altering the DNA sequence. This can result in the abnormal production or absence of the protein products coded by such genes.^{2,4}

In either instance, these alterations in the cell can lead to abnormal cell proliferation. This proliferation may introduce premalignancies that may ultimately lead to cancer development.⁵



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References

1. Soufi, A.; Dalton S. Cycling through developmental decisions: how cell cycle dynamics control pluripotency, differentiation and reprogramming. *Development*. 2016. 143: 4301-4311. Accessed December 17, 2019.
2. Kadoch C, et al. PRC2 and SWI/SNF Chromatin Remodeling Complexes in Health and Disease. *Biochemistry*. 2006;55:1600-1614. Accessed December 17, 2019.
3. Annunziato AT. DNA Packaging: Nucleosomes and Chromatin. *Nature Education*. 2008; 1(1):26. Accessed December 17, 2019.
4. Li B, et al. The Role of Chromatin during Transcription. *Cell*. 2007;128(4):707-719. doi:https://doi.org/10.1016/j.cell.2007.01.015. Accessed December 17, 2019.
5. Aly AE. Cancer Epigenetic. Accessed December 11, 2019.
6. Rote NS. Cancer biology. In: McCance KL, Huether SE, eds. *Pathophysiology: The Biologic Basis for Disease in Adults and Children*. 8th ed. St Louis, MO: Elsevier; 2019:346-378.