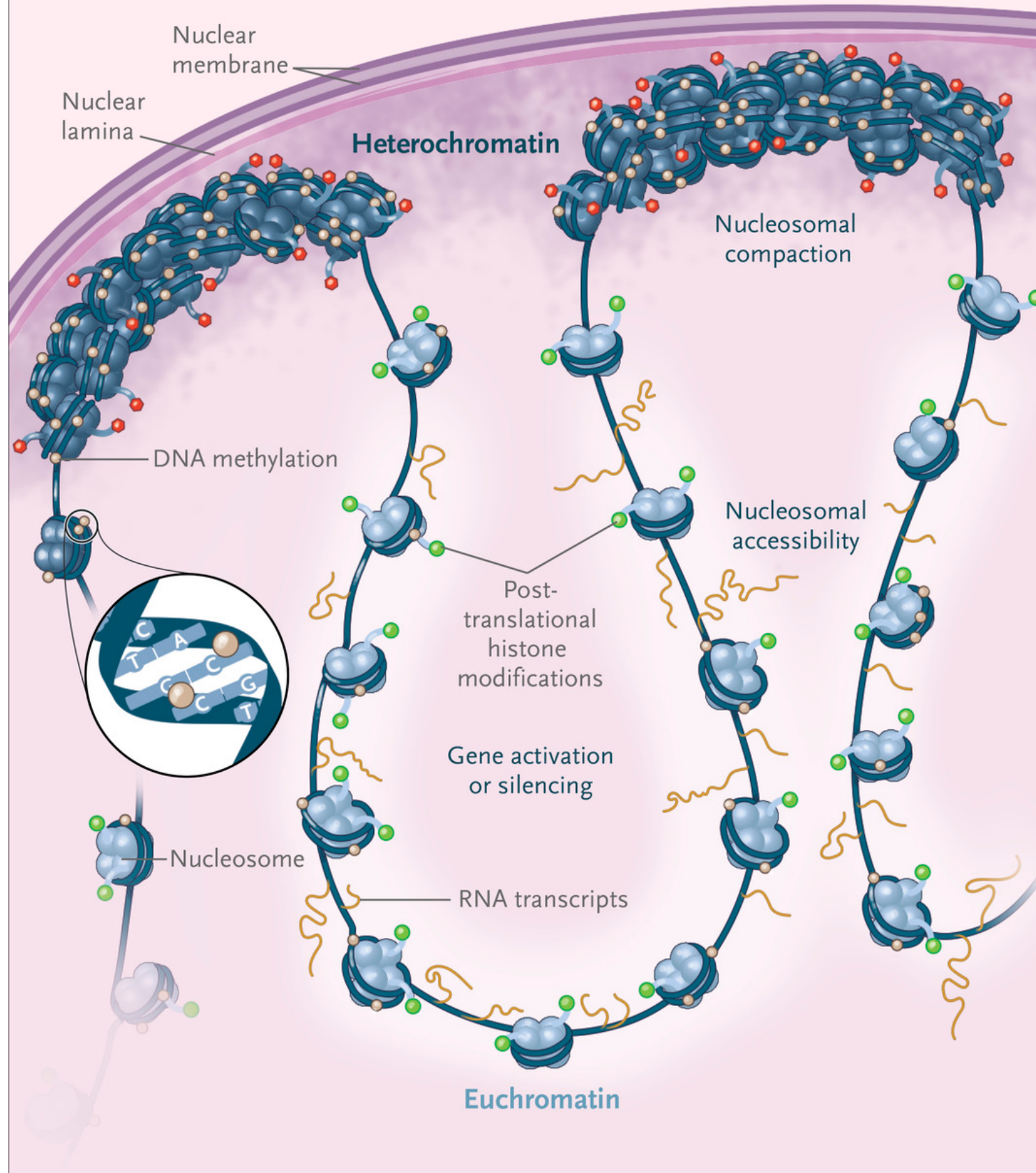
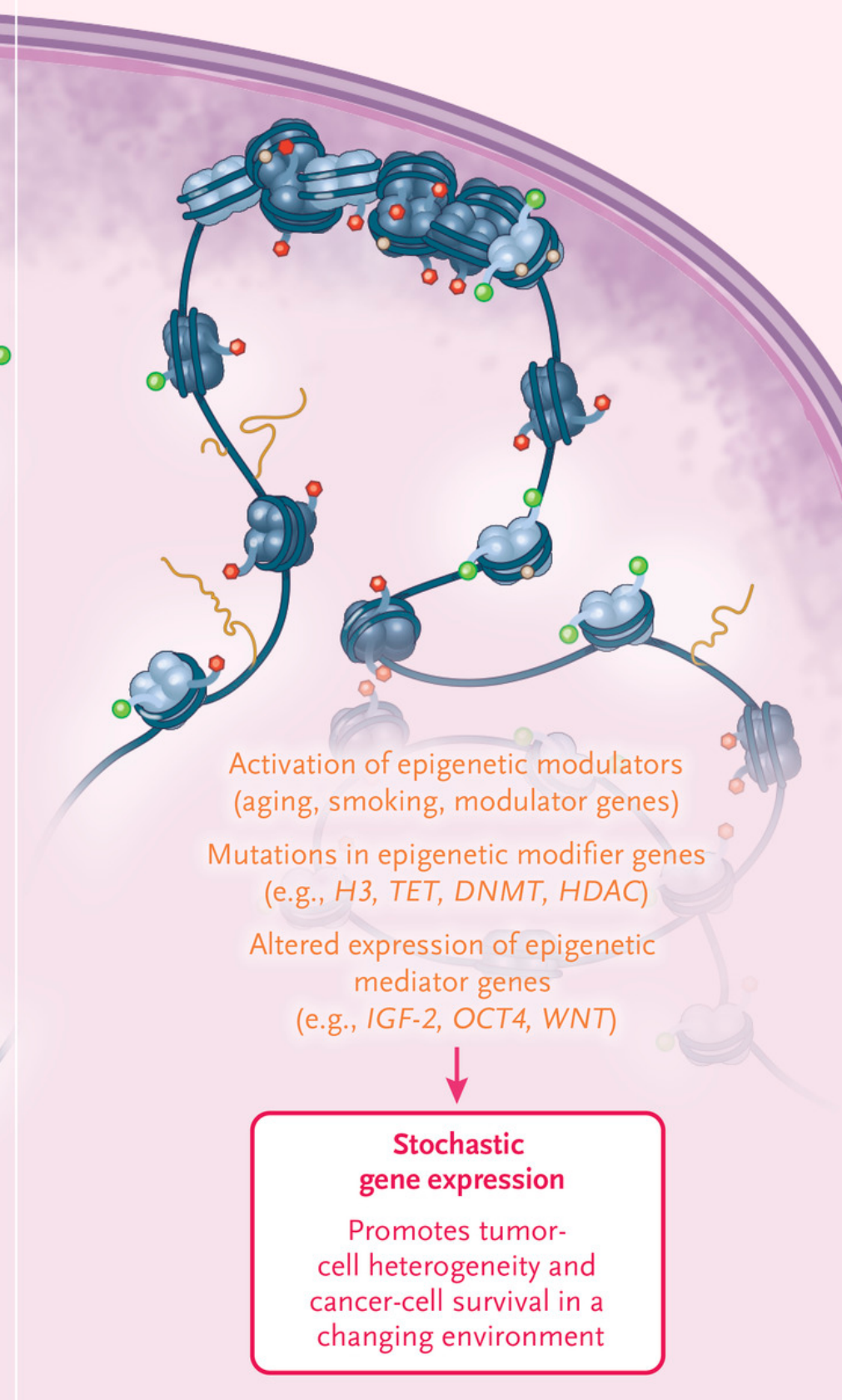


A Normal Cells



B Cancer Cells



The Cellular Nature of Epigenetic Information.

The DNA double helix is modified at the nucleotide cytosine by DNA methylation (brown dots). The nucleosomes around which the DNA is coiled undergo post-translational modifications of their component histones (green dots, depicting activation marks; red dots depict silencing marks), leading to gene activation (light-blue nucleosomes, with RNA transcripts originating nearby) or silencing (dark-blue nucleosomes). Higher-order chromatin structure involves nucleosomal compaction often near the nuclear membrane (heterochromatin) or nucleosomal accessibility (euchromatin). The nuclear periphery is primarily repressive but probably also contains transcriptionally permissive subcompartments. Higher-order large blocks of heterochromatin often involve large epigenomic domains termed lamina-associated domains (LADs) and large, organized chromatin lysine (K) modifications (LOCKS). In cancer, both large and smaller heterochromatic domains become euchromatic. In addition, epigenetic modulators such as environmental exposure and aging, as well as cancer mutations in epigenetic modifier genes, affect the expression of epigenetic mediators controlling pluripotency and cellular self-renewal. All these factors lead to increased stochastic gene expression in cancer, promoting tumor-cell heterogeneity and cancer-cell survival in a changing environment (e.g., as a result of metastasis or chemotherapy).