**Important Definitions**

1) **Acetylation**: a reaction that introduces a functional acetyl group into an organic compound. It is also a post-translational chemical modification of histones, tubulins, and the tumor suppressor p53.

2) **Chromatin**: the complex of DNA and protein that composes chromosomes. Chromatin packages DNA into a volume that fits into the nucleus, allows mitosis and meiosis, and controls gene expression.

3) **CpG islands**: regions in DNA that contain many adjacent cytosine and guanine nucleotides. The “p” in CpG refers to the phophodiester bond between the cytosine and the guanine. These islands occur in approximately 40% of the promoters of human genes.

4) **DNA methylation**: the addition of a methyl group of DNA at the 5-carbon of the cytosine pyrimidine ring that precedes a guanine.

5) **Histone**: the main protein components of chromatin. The core histones—H2A, H2B, H3, and H4—assemble to form the nucleosome. The linker histone H1 locks the DNA into place and allows the formation of a higher-order structure.

6) **Transposons**: sequences of DNA that can move around within the genome of a single cell.

7) **Clastogenic**: an agent or process giving rise to or inducing disruption or breakages, as of chromosomes. Clastogens are mutagens, which cause chromosome effects including breaks, rearrangements and changes in number.

**Nickel Carcinogenesis**

I. **Introduction**

Ni compound has the ability to deliver a high concentration intracellularly as well as interact with the cell’s chromatin. One of the major causations of Ni exposure near the heterochromatin is its ability to silence the expression of genes by “inducing a loss of histone H4 and H3 acetylation and DNA hypermethylation.”

II. **Intracellular Response and Hypoxia**

Because soluble Ni ions generally do not enter the cell, soluble Ni ions have been found to exhibit less activity than the water-soluble nickel compounds. Ni ions derived from phagocytized particles exhibited “selectively in damaging genetically inactive heterochromatin.” Transcription factors induce HIF heterodimers to bind to the hypoxia response element, meaning that the cell is unable to cease its coding for proteins involved with energy metabolism or cell proliferation.

III. **Nickel Substitution**

Occasionally, nickel compounds are unable to enter the cell, especially the soluble Ni compounds. Nevertheless, Ni still can induce epigenetic change in the cell. It was found that soluble Ni ions turned on Ca signaling pathways and also activated HIF-1 transcription factor. Somehow Ni is able to increase Magnesium and iron concentrations inside the nucleus, although Ca never enters the cell.

**Arsenic Carcinogenesis**

I. **Introduction**

The metalloid arsenic may not be best known not for its carcinogenic effects, but for its toxic effects. Its toxicity stems from its ability to disrupt both oxidative phosphorylation and cause prolonged “neuropathy” the “sensory nerves.” However, long-term contact with the arsenic has also been linked with liver, lung and bladder cancer and, because arsenic has little mutagenic potential, research has focuses on arsenic’s ability to destabilize the genome through epigenetic changes.

II. **Intracellular Response**

Arsenic is known to be associated with hypermethylation, causing the silencing of genes. Some of these epigenetic changes include “methylation silencing” of the promoters of the genes RASSF1A, which regulates “microtubule dynamics…in cell division,” and PRSS3, which “may be important for cell motility and adhesion.” High level of arsenic is seen all around the world; however, scientists have found that Southeast Asia has been deeply affected, as seen in the presentation with regards to the skin lesions on people’s feet.