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Environmental Effects of Dredging Technical Notes

Methods for the Assessment of the Genotoxic Effects of Environmental Contaminants; Glossary and References

Purpose

This technical note is the third in a series of three that outline and describe the principal methods that have been developed to test the potential of environmental contaminants to cause mutagenic, carcinogenic, and teratogenic effects. The first in this series (EEDP-04-24) describes methods used to discern genotoxic effects at the subcellular level, while the second (EEDP-04-25) describes methods used to discern genotoxic effects at the cellular and organ/organism level.

Recent literature citations for each topic referenced in this series of technical notes are provided in this technical note, in addition to a glossary of terms. The information in these technical notes is intended to provide Corps of Engineers personnel with a working knowledge of the terminology and conceptual basis of genotoxicity testing. To develop an improved understanding of the concepts of genotoxicity, readers are encouraged to review "A Primer in Genotoxicity" (Jarvis, Reilly, and Lutz 1993), presented in Volume D-93-3 of the *Environmental Effects of Dredging* information exchange bulletin.

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Additional Information

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Glossary

Adduct - a chemically modified macromolecule. An adduct is formed when a compound covalently binds to DNA, hemoglobin, bile, etc.

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Amino acid - an organic acid having the general structure of HO_2C-CHR-NH_2 linked together polymerically to form proteins. The R group determines the specific amino acid. Amino acids are obtained from the diet (essential amino acids) or are synthesized by the body from essential amino acids (nonessential amino acids).

Analog - a compound structurally similar to another.

Antigen-antibody reaction - an antigen is a foreign compound that enters the body. In response to an antigen, particular cells in the body synthesize antibodies, or proteins that bind to the antigen and are highly specific for the antigen. The antigen-antibody complex is recognized by other types of cells in the body, which engulf the antigen-antibody complex for removal from the body. This immune-response principle the body uses to fight infection has been applied to the detection of particular compounds (antigens) of interest. Antibodies to the compound or enzyme of interest are synthesized using biotechnology techniques. The antibodies are labeled with a fluorescent tag that allows visualization using fluorescence techniques.

Autoradiography - a method of visualizing distinct areas of radioactivity in a sample using photographic techniques. Radioactive compounds emit energy in the form of gamma rays or alpha or beta particles, depending on the type of isotope. This energy will expose photographic film in the same manner as visible light, giving a "picture" of the location of radioactivity in a sample.

Bioluminescence - a biochemical reaction occurring in an organism that results in the formation of light energy. An example is the light produced by a firefly.

Biomarker - generally, some biological event that can be used to signal the exposure of an organism to a particular contaminant.

Carcinogen - a compound shown to cause the formation of cancer in an organism.

Cardiac output - blood flow from the heart.

Chromosome - the condensed form of DNA and its associated proteins visible during cell division.

Complementary RNA or DNA (cRNA, cDNA) - a strand of RNA or DNA that is composed of bases complementary to a particular segment of RNA or DNA. RNA is composed of four bases: guanine (G), which is complementary to cytosine (C), and adenine (A), which is complementary to uracil (U). DNA is composed of these same bases, except thymine (T) is substituted for uracil. Complementary bases noncovalently bind (hybridize) with each other. A segment of cDNA for a piece of DNA whose sequence is CCGATAAGT would be GGCTATTCA. cDNA and cRNA are often used as probes.

Conjugation - the covalent bonding of an endogenous molecule to a xenobiotic molecule to facilitate excretion of the xenobiotic.

Covalent bonding - an interaction of two or more separate molecules whereby they become one distinct molecule. For example, two hydrogen and one oxygen atoms may covalently bond to form water.

Cryostatic - techniques that are performed at freezing temperatures.

Cytochrome P450 - a family of enzymes located primarily in the liver that normally function in steroid metabolism, but which also metabolize xenobiotic compounds.

Cytosol - the aqueous portion of a cell and the components dissolved therein. The cytosol is isolated from tissues using ultracentrifugation.

DNA - deoxyribonucleic acid, an extremely long molecule composed of four nucleotides (adenine, thymine, cytosine, guanosine) which contains the genetic makeup of an organism.

Electrophoresis - a method used to separate large electrically charged molecules such as DNA, RNA, or proteins. Electrophoresis uses direct electrical current to cause the charged molecules to migrate through a gel toward the oppositely charged pole of the apparatus.

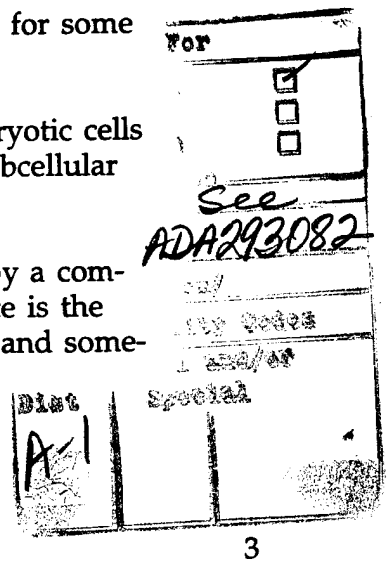
Endoplasmic reticulum - a flat, membranous, netlike system within the cytoplasm of a cell that, among other functions, contains cytochrome P450.

EROD induction assay - ethoxyresorufin-*O*-deethylase, or EROD, is a particular cytochrome P450 enzyme that is normally present in the liver in very small quantities, but is induced upon exposure to planar aromatic compounds such as dioxins, furans, and PCBs. For the EROD induction assay, liver hepatoma (cancer) cells grown in culture are dosed with sample extracts and analyzed for EROD activity using a fluorometer. This assay detects picogram (parts per trillion) quantities of 2,3,7,8-TCDD, the most potent EROD inducer, rivaling gas chromatography/mass spectrometry in sensitivity.

Etiologic agent - a compound that can be shown to be the cause for some effect.

Eukaryote - a cell that comprises a multicellular organism. Eukaryotic cells are much more complex than prokaryotic cells, containing more subcellular components.

Fluorescence - the emission of light of a particular wavelength by a compound after absorption of light of another wavelength. Fluorescence is the basis for detection of many compounds and is extremely sensitive and somewhat specific.



Fluorometer - an instrument used to measure fluorescence.

Genome - the DNA of a cell.

Glucose - a simple sugar (monosaccharide) that is utilized by cells for energy.

Glutathione - a tripeptide, γ-glutamylcysteinylglycine, that is found in virtually all species. Glutathione is extremely important in that it helps regulate the reduction-oxidation potential of the cell, acts as an amino acid transport system for the body, and functions in phase II metabolism.

Glycogen - the storage form of glucose. After periods of glucose intake (eating) when blood glucose levels are high, the body stores excess glucose by linking, or polymerizing, the glucose molecules together into a branched chain configuration making glycogen. Glycogen is stored in the liver and muscle.

Hybridize - noncovalent bonding of complementary segments of nucleic acids.

Hyperplasia - an excessive proliferation of normal cells.

Hypertrophy - an enlargement of cellular diameter without accompanying nuclear changes.

Induction - production of a particular protein in response to some stimulus.

Initiation - conversion of a normal cell to a cancerous cell. Initiation is an irreversible change involving the interaction of a carcinogen with DNA, priming the cell for cancer development via promotion.

Lagging - a term used to describe the leaving behind of part of a chromosome during the migration of chromosomes in anaphase during mitosis.

Luminometer - an instrument used to measure bioluminescence.

Macromolecules - large molecules that comprise a cell. Macromolecules include DNA, RNA, and proteins.

Messenger RNA - a strand of RNA that is complementary to a particular segment of DNA (gene) and acts as a template for the translation (production) of a particular protein.

Mutagen - a compound that can cause a mutation, or a change in a specific DNA nucleotide, for example, adduct formation.

Nucleoside - a building block of DNA and RNA. A nucleoside is one of the five nitrogen bases (adenine, guanine, uracil, cytosine, and thymine) linked to a sugar compound called ribose (for RNA) or deoxyribose (for DNA).

Nucleotide - a nucleotide is a nucleoside with a phosphate group attached. Nucleosides must be converted to nucleotides before they can be incorporated into DNA or RNA.

Phase I metabolism - the metabolism of xenobiotic compounds by enzymes which include cytochrome P450. Phase I metabolism usually results in the addition or exposure of a polar functional group, for example, an -OH group, on the xenobiotic. Phase I metabolism readies the xenobiotic for urinary excretion or phase II metabolism.

Phase II metabolism - the metabolism of xenobiotic compounds whereby an endogenous molecule is conjugated with a xenobiotic. Phase II metabolism readies the xenobiotic for biliary excretion.

Probe - a relatively short strand of RNA or DNA that is complementary to a particular gene of interest and is labeled with a fluorescent or radioactive tag. The probe is incubated with isolated DNA or RNA from an organ and hybridizes with the gene of interest. The gene may then be visualized using fluorescent microscopy or autoradiography.

Prokaryote - a bacterial cell. Prokaryotic cells are much simpler than eukaryotic cells, lacking many of the subcellular structures of the eukaryotic cell. One-celled organisms are prokaryotic.

Promotion - the process by which a chemical facilitates the growth and development of initiated cells into a tumor. Promoters do not interact directly with DNA, but generally stimulate an increase in DNA synthesis and/or cell replication in the target cells.

Promutagen - a compound which, when metabolized, is converted into a mutagen.

Teratogen - a compound causing defects in reproduction, resulting either in reduced productivity due to fetal mortality or in the birth of offspring with physical, mental, behavioral, or developmental defects.

Translation - the biosynthesis of amino acids.

Ultracentrifugation - a technique involving centrifugation at extremely high speeds, up to 250,000 times the force of gravity, used to isolate cellular components.

Xenobiotic - a compound foreign to the body. Examples of xenobiotics are pesticides, PAHs, and dioxins.

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