p53 overexpression

refers to an increase in the levels of the p53 protein, which is a crucial tumor suppressor involved in regulating the cell cycle, promoting DNA repair, and inducing apoptosis (programmed cell death) in the presence of genomic damage.

 Basic Biology of p53 Gene: TP53 (on chromosome 17p13.1)

Protein: p53, often dubbed the “guardian of the genome”

Function: Acts as a transcription factor that responds to cellular stress.

 Causes of p53 Overexpression TP53 mutation:

Most common cause.

Mutated p53 protein is often non-functional but accumulates in the cell due to its prolonged half-life.

Seen in many cancers (e.g., glioblastoma, breast, lung, colon).

Non-mutational stress:

DNA damage, oncogene activation, or hypoxia can lead to p53 stabilization and transient overexpression.

Loss of MDM2 function:

MDM2 is a negative regulator that targets p53 for degradation.

Loss or inhibition of MDM2 can result in p53 accumulation.

 Detection Immunohistochemistry (IHC):

Common method for identifying p53 overexpression in tumor tissues.

High staining intensity suggests accumulation, often correlating with mutation.

 Clinical Implications Prognostic marker:

Overexpression often correlates with poor prognosis, especially when due to mutation.

Diagnostic aid:

Helps in differentiating tumor types, especially in neuro-oncology (e.g., distinguishing between low- and high-grade gliomas).

Therapeutic target:

Trials are ongoing for drugs that can restore normal p53 function or exploit mutant p53 pathways.