Question 1:

What activities of p53, related and important to its functioning as a DNA sequence-specific TF, does the CTD modulate?

❍ It assists in linear diffusion along DNA and rapid search for sequence-specific binding sites.

❍ It participates in the control of p53 half-life by providing the secondary interaction site for E3 Ligase Mdm2 that targets multiple lysines within it for ubiquitination leading to degradation of p53 protein.

❍ The CTD represents a docking site for many transcriptional co-factors and chromatin modifiers.

❍ The CTD is important for stabilization of sequence-specific interaction between p53 and DNA.

● All of the above

Explanation:

The CTD controls p53 transcriptional activity on many different levels including acceleration of the search for cognate DNA binding sequences within genomic DNA, control of stability of p53-DNA complexes, control of p53 stability, and stimuli- and promoter-specific interaction with numerous transcriptional coactivators.

Question 2:

What features of the CTD are responsible for its multifunctionality?

❍ Low number of lysine residues that are not involved in any intra-molecular interactions.

❍ High number of evolutionary conserved polar residues.

● Conformational flexibility along with a unique amino acid composition characterized by

the presence of a number of lysines and arginines

Explanation:

Conformational flexibility of the CTD due to lack of well-defined structure under native conditions and a rather unique amino acid composition with a high number of positively charged residues seem to be the most critical features of the CTD that are responsible for its multifunctionality.

Question 3:

What is the structure of the CTD of p53?

❍ The CTD has a well-defined globular structure.

● The CTD is intrinsically disordered and may undergo local disorder-to-order transition upon interaction with a number of ligands.

Explanation:

The CTD is unfolded/disordered under normal physiological conditions. Interactions with numerous ligands of protein and non-protein nature have been shown to result in local folding within the CTD. The exact shape of the induced structures varies depending on the modification status of the CTD and the interacting partner.

❍ The structure of the CTD is unknown.

Question 4:

What type of post-translational modification within the CTD of p53 is known to be dependent on p300 HAT?

❍ Serine and threonine phosphorylation.

❍ Lysine and arginine methylation.

● Lysine acetylation.

Explanation:

p300 is a histone acetyl transferase that specifically acetylates a number of lysine residues within the CTD in response to activation of the p53 pathway.

❍ Only arginine dimethylation