

DISCUSSION SESSION ON LECTURE #2: STUDY QUESTIONS

ASSIGNED PAPER: LaRonde-LeBlanc N, Santhanam AN, Baker AR, Wlodawer A, Colburn NH (2007) Structural basis for inhibition of translation by the tumor suppressor PDCD4. *Mol. Cell. Biol.* **27**: 147-156.

(1) Regulation of mRNA translation occurs mainly at the initiation step of protein synthesis. Initiation on the vast majority of cellular transcripts normally requires a 5'-"cap"? What is the chemical structure of the cap?

(2) To commence translation, the 5'-cap must associate with a cap-binding multi-protein complex, called eIF4F? What are the constituent proteins in eIF4F, and what function does each of them have in the process of translation initiation?

(3) Given that cell growth and proliferation demand new protein synthesis, does it make sense that a protein that prevents translation initiation could serve as both a tumor suppressor and as a promoter of apoptosis?

(4) What does this paper reveal about how eIF4A interacts with eIF4G? About how PDCD4 inhibits eIF4A? What is an MA3 domain?

(5) There are claims that two different protein kinases— c-Akt/PKB [see: Palamarchuk A et al. (2005) *Cancer Res.* 65: 11282-11286] and p70^{S6K} [see: Dorrello NV et al. (2006) *Science* 314: 467-471] phosphorylate and regulate the function and stability of PDCD4. Based on the information revealed in this paper, which of these two kinases is less likely to play a physiologically relevant role modulating PDCD4 activity?

QUANTITATIVE QUESTION: If you program an *in vitro* translation reaction (at high Mg²⁺, which obviates the need for a normal initiation codon) with a synthetic random hetero-copolymer composed of equal amounts of A and U, what amino acids would be incorporated into the resulting product, and in what ratio?