Codjo Hountondji, J Chromatogr Sep Tech 2017, 8:3(Suppl)
DOI: 10.4172/2157-7064-C1-025

Affinity labeling studies and mass spectrometric analyses on human 80S or E. coli 70S ribosomes reveal how the ribosomes translate cancer

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Increasing evidence points to a connection between protein synthesis and cancer cell growth. For example, increasing the rate of protein synthesis is favorable to the increase in size of the cancer cells and hence to their subsequent division. Since the ribosome, with its functional sites A, P and E, is responsible for protein synthesis in all kingdoms of life, it may be considered as a target of new cancer therapeutics. Here, by combining affinity labeling studies and mass spectrometric analyses on human 80S or *E. coli* 70S ribosomes, we have demonstrated the following: (i) ribosomal proteins rP-eL42 of human 80S ribosomes and rP-bL12 of E. coli 70S ribosomes can be affinity labeled in situ with the CCA-end of tRNAox, a tRNA analogue bound to the P-site; (ii) the residue of eL42 or bL12 cross-linked with tRNAox is Lys-53 and Lys-65, respectively; (iii) the CCA-end of P-tRNA contacts both eL42 and the A-site bound translation termination factor eRF1 at the peptidyl transferase center, the active site of the human 80S ribosome; (iv) the residue of eRF1 cross-linked with tRNAox is Lys-197. Since previous studies had demonstrated that rP-eL42 is overexpressed in human hepatocellular carcinoma as well as in several human tumor cell-lines, while an increased exposure of intestine to bacterial bL12 was previously observed in colorectal cancer patients, our results suggest that the functional role of these rPs might be related to tumor cell proliferation. In addition, our results provide new insights into the mechanism of the peptidyl transfer reaction.

Biography

Codjo Hountondji has completed his PhD at the age of 30 years from University of Orsay (Paris 11, France). He is professor of Biochemistry and Molecular Biology at the University Pierre et Marie Curie (Paris 6, France) and director of a research team focusing on “the mechanism of peptide bond formation at the peptidyl transferase center, the active site of the ribosome” and on “the ribosome as a target for anti-cancer drugs”. He has published more than 40 papers in reputed journals.

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