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## Mass Spectrometric identification of a ribosomal protein promotor of cancer, targeted by anticancer drugs

Increasing evidence points to a connection between protein synthesis and cancer cells growth. For example, cycloheximide that had been shown to be a strong inhibitor of eucaryotic translation, was also shown to inhibit cancer cells growth in vitro and in vivo, suggesting that this translation inhibitor may serve as lead in the development of new cancer therapeutics. Here, by combining affinity labeling studies and mass spectrometric analyses on human 80S or E. coli 70S ribosomes, we have identified the ribosomal proteins (rPs) targeted by the small-molecule inhibitors of translation. These are rP-eL42 of human 80S ribosomes and rPbL12 of E. coli 70S ribosomes. We have recently demonstrated that these rPs assist catalysis of peptide bond formation at the elongation step of translation. The human rP-eL42 was previously shown to be overexpressed in human hepatocellular carcinoma (HCC) as well as in several human tumor cell-lines, while an increased exposure of intestine to bacterial rPbL12 was previously observed in colorectal cancer patients. It is generally accepted that ribosomal protein overexpression might promote tumorigenesis by interactions with the p53 tumor suppressor pathway, and that these overexpressed proteins could represent targets for cancer therapy. Therefore, we have designed anticancer drugs analogous to cycloheximide capable of targeting rPs eL42 and bL12 in order to block the hyper-proliferation of tumor cells by reducing the rate of protein synthesis. These molecules are thiosemicarbazones, two of which having a potent antiproliferative effect on tumor cell lines and selectively inhibiting translation. They are now ready to undergo clinical trials.

### Speaker Biography

Codjo Hountondji is distinguished professor at Sorbonne University (Campus Pierre et Marie Curie, Jussieu, Paris) where he has been teaching biochemistry and molecular Biology for 35 years. He is currently director of the research Group "Enzymology of RNA". He has served as assistant professor of Biochemistry at the University Paris XI (Orsay) 1982-1986. At the University Pierre et Marie Curie (Paris), he has served as chair of the division (department of biochemistry and molecular biology 2010-2014). He has been a visiting scientist at Penn State University School of Medicine in Philadelphia in 1981-1982. He published more than 40 research papers and articles in international journals. He supervised numerous master and PhD students for their research projects. His career research focus has been on the mechanism of the translation process. His current research interest concerns a "Targeted molecular therapy of cancer: Structure-assisted design of anticancer drugs targeting the ribosomes in cancer cells".

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