Inhibition of eukaryotic translation elongation by cycloheximide and lactimidomycin

Khan Mohammad Golam Maola

Both Cycloheximide and Lactimidomycin are naturally occurring compounds that inhibit eukaryotic translation at the elongation stage. Cycloheximide is well known inhibitor for translation, whereas lactimidomycin was reported as translation inhibitor by the authors. They carried out a systematic comparative study of the mechanism of action of these two inhibitors. They found that both of the inhibitors occupy the same binding site in the large ribosomal subunit. However, they differ in binding affinity and also in the translocation step of the codons. Thus they found lactimidomycin as more potent inhibitor of eukaryotic translation elongation.

Article

Inhibition of eukaryotic translation elongation by cycloheximide and lactimidomycin

Tilman Schneider-Poetsch, Jianhua Ju, Daniel EEyler, Yongjun Dang, Shridhar Bhat, William C Merrick, Rachel Green, Ben Shen & Jun O Liu
(Dept. of Pharmacology and Molecular Sciences, The Johns Hopkins University School of Medicine)
Nature Chemical Biology 6, 209 – 217, June 15, 2010

Summary: Although the protein synthesis inhibitor cycloheximide (CHX) has been known for decades, its precise mechanism of action remains incompletely understood. The glutarimide portion of CHX is seen in a family of structurally related natural products including migrastatin, isomigrastatin and lactimidomycin (LTM). We found that LTM, isomigrastatin and analogs have a potent antiproliferative effect on tumor cell lines and selectively inhibit translation. A systematic comparative study of the effects of CHX and LTM on protein synthesis revealed both similarities and differences between the two inhibitors. Both LTM and CHX were found to block the translocation step in elongation. Footprinting experiments revealed protection of a single cytidine nucleotide (C3993) in the E-site of the 60S ribosomal subunit, thus defining a common binding pocket for the two inhibitors in the ribosome. These results shed new light on the molecular mechanism of inhibition of translation elongation by both CHX and LTM.

Reference:

1. Schneider-Poetsch, T., Usui, T., Kaida, D., and Yoshida, M. (2010) Garbled messages and corrupted translations, *Nat Chem Biol 6*, 189-198.