Testing a Novel RNAP I Inhibitor CX5461 that is Highly Specific to Cancer Cell: Effect upon r-genes Transcription and rRNA Processing Nucleolar Factors (UBF, Fibrillarin, B23)

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Summary

This work represents the initial step of common project (in collaboration with Laboratory MEDyC, URCA) targeted on the effect of novel highly specific antitumor compound CX5461 upon r-genes transcription and rRNA processing nucleolar factors UBF, Fibrillarin and B23. Meanwhile, the enhanced interest to this drug is stipulated by its high specifity to malignant tumor cells. Particularly, CX5461 blocks RNAP I activity only in tumor cells having no influence on normal ones. Thus the high efficiency of this drug for clinical application is obvious.

To address the question how specific nucleolar proteins respond to inhibitory action of CX5461 we resort to time-lapse laser confocal microscopy. Our survey was focused on 3D relocalization and 4D dynamics of nucleolar protein factors UBF, Fibrillarin and B23 within nucleolar volume of living He-La culture cells during 16 h of action of CX5461. Tracing behavior of proteins constituting the RNAP I transcription and processing machineries we registered that pattern of the 3D reorganization and 4D dynamics induced by this drug substantially differs from those caused by other RNAP I inhibitors, the widely used and clinically well approved Actinomycin D (AmD) in particular. For example, we noted especially sharp differences observing the behavior of Fibrillarin. Moreover, in overnight experiments we found that CX5461 is less cytotoxic then AmD.