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Putative t-RNA dihydrouridine synthase from Saccharomyces cerevisae (MTCC-181) as a biomarker for malignant cells

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Using comparative genomics and computational methods, we have identified the structural & functional aspect of a putative t-RNA dihydrouridine synthase encoding gene of Saccharomyces cerevisae (MTCC-181) by homology modeling approach. Dihydrouridine synthases (DUSs, EC 1.3.1.91) are flavin-dependent enzymes that catalyze site-specific reduction of uracils in tRNAs. A putative protein of 668 amino acids was analyzed. It contains 12-FMN-binding conserve domain on the active site, characteristics of DUS_like_FMN super-family (cd02801, E-value=3.21e-63) which catalyzes the reduction of the 5, 6-double bond of a uridine residue on tRNA. Four catalytic residues 386 (Cys), 428 (Arg), 457 (His) and 459 (Arg) were found on the DUS-like conserved domain (294-557), among which an active site cysteine is important for catalysis, likely through the protonation of uracil during tRNA reduction. The protein have multi-domains with high similarity to COG0042 (CDD, 284-597); a tRNA-dihydrouridine synthase (E-value=1.07e-62) and TIM barrel superfamily (cl09108, 296-550, E-value=3.83-20) which share a structurally conserved phosphate binding motif and in general have an eight β/α closed barrel structure. The structure of an FMN-binding α/β-barrel also has significant similarity to dihydroorotate dehydrogenases and dihydropyrimidine dehydrogenases. Three dimensional (3D) structure was constructed by modeller 9v7 modeling software by using the 1VHN (4.4e-15 & similarity =76%) as a template. Binding of substrate (uracil-t-RNA) and acceptor molecules (NADPH and FMN) were confirmed by Autodock 4.2.

Dihydrouridine modification of tRNA is widely observed in prokaryotes and eukaryotes. Most dihydrouridines occurs in specific positions in the D-loop of t-RNAs. The role of dihydrouridine synthase in oxidation of uracil bound t-RNA to tRNA-dihydrouridine by simultaneous reduction of acceptor molecule like NADPH and FMN were confirmed by enzymatic assay. Increase in tRNA dihydrouridine synthase activity was detected in human lung carcinoma cells (ATCC Number-TCP-1016) as compare to normal tissue. It is likely that different family members have different substrate specificities, which may overlap. Abundance of dihydrouridine is linked to pulmonary carcinoma. It was observed that hypermodified t-RNA-dihydrouridine has a specific functional role for growth of cancer cells, through the complex of tRNA-DUS protein combined with aminoacyl tRNA synthetase. This complex is a strong therapeutic target for new anticancer drugs.

Biography

Parul Aggarwal Pruthi has done her Ph.D in 1998 from IMTECH Chandigarh and was Post-Doc fellow in Indiana University Purdue University, Indiana Polis (IUPUI). Presently she is working as Scientist (DBT Biocare Program), Department of Biotechnology, IIT Roorkee. Dr. Parul has several publications in reputed journal and many international and national conferences.

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Isolation and characterization of arsenic resistance bacteria and their bioremediation implication

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Arsenic is naturally occurring element that is widely distributed in the earth's crust. Living organisms, both on land and in water, react in a variety of ways to Arsenic exposure. The effect depends on the chemical form of Arsenic, the nature of the surrounding environment and their own particular biological sensitivity. West Bengal and Bangladesh are highly Arsenic contaminated areas which can cause rapid poisoning, developing pigment spot in the skin and damage to red blood cells, bone marrow, livers, nerves and brains. Hence, it should be clean up by the process of bioremediation. There are number of strains of bacteria which can help in this process. Some bacteria isolated from soil such as Escherchia coli, Pseudomonas spp., Bacillus spp., Staphlococcus spp., Acidithiobacillus spp., Shewanella spp have ability to accumulate Arsenic metal. Out of which, P. vittata which is isolated from rhizosphere, can tolerate the high availability of Arsenic.

Keywords: Arsenic, bioremediation, Escherchia coli, Pseudomonas spp.

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