Swarnajayanti Fellow may provide new genetic treatment for thalassemia, duchenne muscular dystrophy, haemophilia

Duchenne Muscular Dystrophy, a severe type of muscle weakness that usually begins at an early age and worsens quickly, may soon have a new strategy of treatment through genetic regulation.

There is no known cure for duchenne muscular dystrophy. Treatments usually aim to control symptoms to improve quality of life.

Sandeep Eswarappa, Assistant Professor Indian Institute of Science (IISc), Bengaluru one of the 21 recipients of this year's Swarnajayanti Fellowship of the Department of Science and Technology (DST), Government of India proposes to supress the disease-causing premature stop codon or the genetic process that initiates these diseases. He is trying to bring about the suppression through translational readthrough, a gene regulatory principle found in humans, yeasts, bacteria and drosophila which takes place with the variation of the genetic code.

Prof. Sandeep's group has been developing strategies to induce translational readthrough across genetic diseases caused by non-sense mutations --a change in DNA that causes a protein to terminate or end its translation earlier than expected. They were successful in achieving this *in vitro* in case of thalassemia and are working on other disease models. This research work has been published in the scientific journal *'Biochemistry'* recently. With the Swarna Jayanti fellowship, they will extend it to Duchenne muscular dystrophy. If successful, this project may lead to novel therapeutics for the treatment of genetic diseases like thalassemia, Duchenne muscular dystrophy, haemophilia.

In case of any protein formation genetic information present in the genome is first transcribed into an mRNA, which in turn is translated into a protein. Protein synthesis or translation is executed by macromolecular machinery called ribosomes. Ribosomes start this process at a specific location on an mRNA called ‘start codon’ and terminate at a stop signal called ‘stop codon’. In case of diseases with nonsense mutations, such mutations result in premature stop signal in mRNA often resulting in non-functional truncated protein

Prof. Sandeep Eswarappa’s laboratory at IISc has shown that in certain mRNAs, under certain conditions, translating ribosomes misread the stop signal and continue till they encounter another stop signal. In this translational readthrough process, a longer protein is synthesized with an extension. This extension might change the properties of the protein. The experiments carried out by his group have revealed that such long proteins can have different localization, stability and function.

“The knowledge we have already gained from our experiment have opened an unexpected avenue to treat genetic diseases caused by non-sense mutations like Duchenne muscular dystrophy, haemophilia and so on,” said Prof. Sandeep.

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