University of Lethbridge

NEWS RELEASE

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New possibilities for therapeutic interventions revealed in collaborative study

Many medications on the market today target disease-related proteins, but a new study by scientists from Massachusetts General Hospital (Harvard Medical School), Merck Research Laboratories and the University of Lethbridge has shown that small-molecule drugs can target non-coding RNA (ribonucleic acid), thereby expanding the possibilities for therapeutic interventions in many diseases.

"This work opens up the possibilities of developing drugs that can target RNAs that are involved with many diseases," says Dr. Trushar Patel, Canada Research Chair in RNA and Protein Biophysics.

In our bodies, DNA is transcribed or copied into coding RNAs, which in turn are translated into proteins that are the workhorses of a living system. However, most RNA is noncoding and scientists are learning about the critical role it plays in controlling systems. On a normal day, these nucleic acids provide cell maintenance and cell differentiation, but if they go rogue, they can play a major role in diseases such as cancer.

Developing therapeutics against noncoding RNAs is very challenging, primarily because of their flexible shapes. Proteins usually have stable shapes and charged regions, meaning drugs can easily bind to proteins as a result. However, scientists know some regions of RNA have more stable shapes; the challenge is to find those regions.

After investigating thousands of small molecule compounds, the scientists at Harvard and Merck found one that binds to a specific noncoding RNA. To find out more about how the small molecule affects the RNA structure, the group turned to ULethbridge's Dr. Trushar Patel, Tyler Mrozowich, a PhD student supported by NSERC, and Dr. Maulik Badmalia, a post-doctoral researcher supported by Alberta Innovates.

“We collaborated because we wanted to know what it looks like,” says Mrozowich. “Our lab specializes in visualizing these RNA molecules in solution. Our contribution was the visualization of this extremely important RNA element and we do this primarily through a technique called small-angle X-ray scattering.”
“This is one of the first examples of showing that RNA can be targeted for drug discovery, unlike traditional approaches where proteins have been targeted. This is a revolution in a way,” says Patel. “The second significant item is that we used a combination of various methods to come up with the full story.”

The methods used in this study could be applied in future studies to identify other drugs that target RNA.

“Essentially, the results of this study can also be translated as providing a platform for exploring new avenues for developing therapeutics in which RNA is involved,” says Badmalia.

The collaboration came about as a result of Mrozowich’s and Patel’s previous work with Dr. Karissa Sanbonmatsu (published in Nature Communications) at the Los Alamos National Laboratory, who also works with Harvard Medical School. The study was recently published in Nature, a leading science journal that has been in existence since 1869.

This news release can be found online at new possibilities for therapeutic interventions.

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