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ARRTI researcher earns \$642,600 CIHR grant to investigate complex process of ribosome formation

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Understanding one of the fundamental building blocks of life may also hold the key to unlocking new targets for the treatment of cancer. The University of Lethbridge's Dr. Ute Kothe and her team will look to unravel the complex process of forming ribosomes, the body's protein factories, through RNA research in a new five-year project that has received \$642,600 in funding from the Canadian Institutes for Health Research (CIHR).



Identifying Critical RNA-RNA Interactions during Ribosome Biogenesis is the title of the project that will be based at the U of L and within the Alberta RNA Research and Training Institute (ARRTI), but also include collaborators at the Universities of Sherbrooke and McGill University in Quebec, as well as three German institutions.

“What excites me about this project is the intersection between it being medically important and also fundamentally important to understanding life. If you don't understand life, you cannot develop new therapeutic strategies,” says Kothe, a professor of biochemistry in the Department of Chemistry & Biochemistry and Board of Governors Teaching Chair.

The CIHR grant has been close to a decade in the making. Kothe has revised and resubmitted her application multiple times over the years, indicating the competitive

nature of these grants. By earning this funding, she is among the top 10 per cent of biomedical researchers in Canada. The grant also illustrates the growth and impact of biomedical research at the University, and in particular ARRTI, as Kothe is the first of the research group to secure a CIHR Project Grant since ARRTI's inception in 2012.

"This important CIHR grant will support Dr. Kothe in making foundational advances in our understanding of cancer cells and cancer treatment," says Dr. Robert Wood, vice-president (research). "The U of L was recently named second in the country in our category in the Maclean's rankings. The groundbreaking research being conducted by stellar colleagues such as Dr. Kothe is a major driver of this strong reputational standing."

Kothe believes wholeheartedly in how this research can add to the body of knowledge around forming a complex biological machine, which is the prerequisite to better understanding cancer cell division and tumor growth.

"This study is a great example of how the University of Lethbridge is contributing to biomedical research in Canada, and also illustrates the important link between fundamental and biomedical research — one doesn't work without the other," she says. "RNA research and cancer research go hand-in-hand and this is the strength we can build upon here in Lethbridge with ARRTI."

All cancer types share a need for increased protein production to enable rapid cell divisions and tumor growth. Accordingly, all cancer cells are characterized by an enhanced production of protein factories called ribosomes and by an enlarged cellular compartment, where ribosomes are assembled.

"Cancer cells need the most proteins because they grow so rapidly. If a tumor wants to grow, it needs proteins, and cancer cells are smart — they have found a way to make more ribosomes, to make more protein machines, and that's how they can outcompete all the other cells," says Kothe.

Therefore, inhibiting ribosome formation is a promising future therapeutic strategy in cancer treatment. However, it is currently impossible to target this pathway because there is a fundamental lack of understanding ribosome formation. Kothe's research aims to close this knowledge gap, thereby opening a new avenue for impairing assembly of protein factories in cancer.

"Ribosomes consist predominantly of RNA, a sister molecule of DNA," says Kothe. "Critical steps during ribosome formation constitute the chemical modification and three-dimensional folding of ribosomal RNA. Interestingly, these steps are mediated by other small RNAs in the cell. Our long-term goal is to inhibit these interactions between small RNAs and ribosomal RNAs thereby depriving cancer cells of protein factories."

That the grant stretches over five years affords an excellent opportunity for students to participate in the research work.

“This research grant opens training and employment opportunities for different researchers ranging from post-doctoral researchers who already have their PhD, as well as a couple of PhD and master’s students,” says Kothe, who plans to send students to Quebec and Germany to work with their collaborators as the study progresses. “I also think it’s important we include our undergraduate students in the research. It is one of our particular strengths at the U of L that we train them early and they get experience that really sets them up to go anywhere they want in the world.”

Kothe is enthused to get started and eager to unlock the mysteries of RNA in forming the body’s protein factories as the prerequisite for future RNA-targeted cancer therapeutics.

“RNA is an awesome drug target, so once we understand ribosome formation and the role of RNA in this process, we are one important step closer to targeting and inhibiting it in cancer. This should be a much more feasible treatment method than any other types of drugs.”

To view online: <https://www.uleth.ca/unews/article/arri-researcher-earns-642600-cihr-grant-investigate-complex-process-ribosome-formation>

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