Over the last three decades, Ratmir Derda spent many of his waking hours studying how and why certain molecules interact. Now, what started as an interest in basic science is changing the way researchers develop drugs to treat life-threatening illnesses.

Ukrainian-born Derda studied applied physics and mathematics, and biophysics as an undergraduate student in Russia, then moved to the United States to study organic chemistry for his PhD. For a decade, he has run his own lab in the U of A's Faculty of Science. He specializes in researching the space where chemistry, physics and biology connect.

In time, he became convinced that treatments for diseases lay in better understanding how ligands, the molecules that bind to receptors on other cells, interact with genes and proteins associated with different diseases.

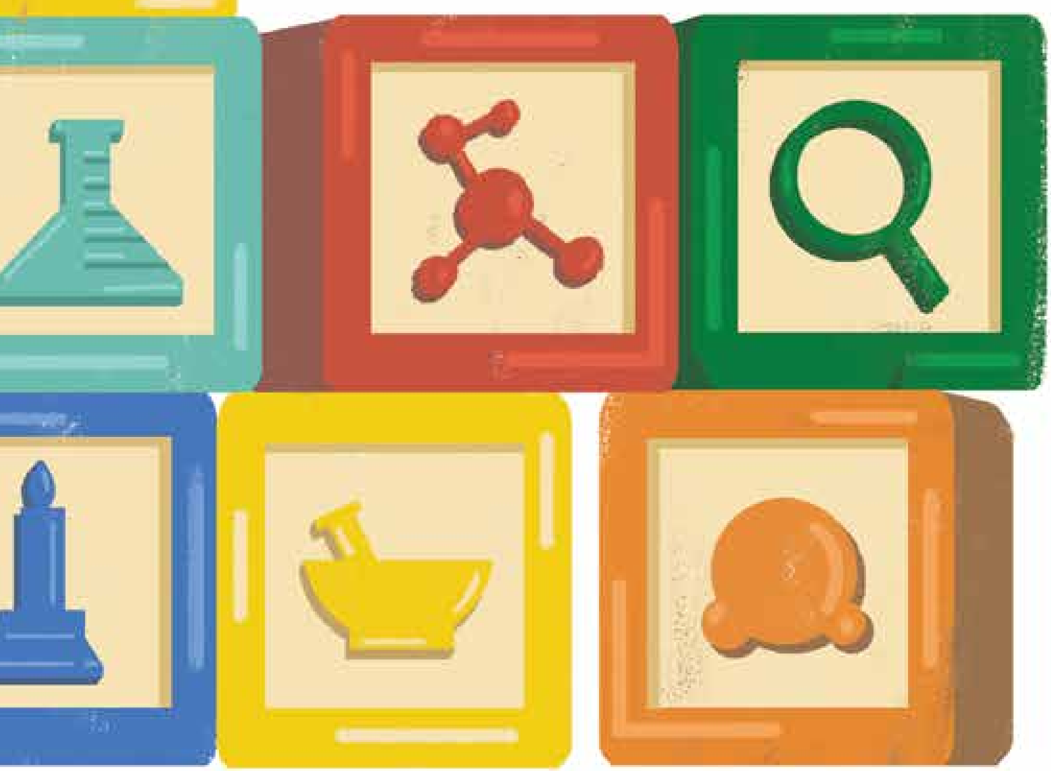
The theory behind ligand drug-delivery systems, which Derda and others have been researching for years, goes like this: ligands can deliver drugs directly to diseased cells by binding to them, targeting the cells where drugs can work most effectively. The result holds the promise of fewer side effects from treatment, more purposeful drug delivery and a speedier timeline for drug development.

But it took years of basic research to get there. It meant going down rabbit holes to ask fundamental questions, like: "How can we encode and mine and search in the space of molecules, for no reason whatsoever, other than to be able to search in this space of molecules?" says Derda.

There are many kinds of targeting ligands: antibodies, aptamers, small molecules and peptides. Of these, Derda believes that peptide ligands are particularly promising. They're larger than other ligands, so better for binding to receptors. They're easily synthesized, making them a convenient and economic option.

In his lab, Derda and colleagues created a proprietary technology to build a massive library of billions of molecules. And they developed a method to scroll through this library using artificial intelligence, looking for ligands that are suitable for binding to receptors associated with specific diseases.

Derda regularly published his research and presented at meetings where he knew representatives from the pharmaceutical industry were listening. He figured it was a matter of time before someone from industry approached him about translating his work from academia into real-life solutions. "You don't necessarily try to sell your work like a pack of knives on TV, but you imply some translational practical value in it



and kind of seed that thought in somebody's brain," says Derda.

In 2015, it worked. One company reached out, and then another; neither can be identified due to non-disclosure agreements. They asked Derda to search through his genetically encoded libraries to identify functional ligands for receptors involved in specific diseases.

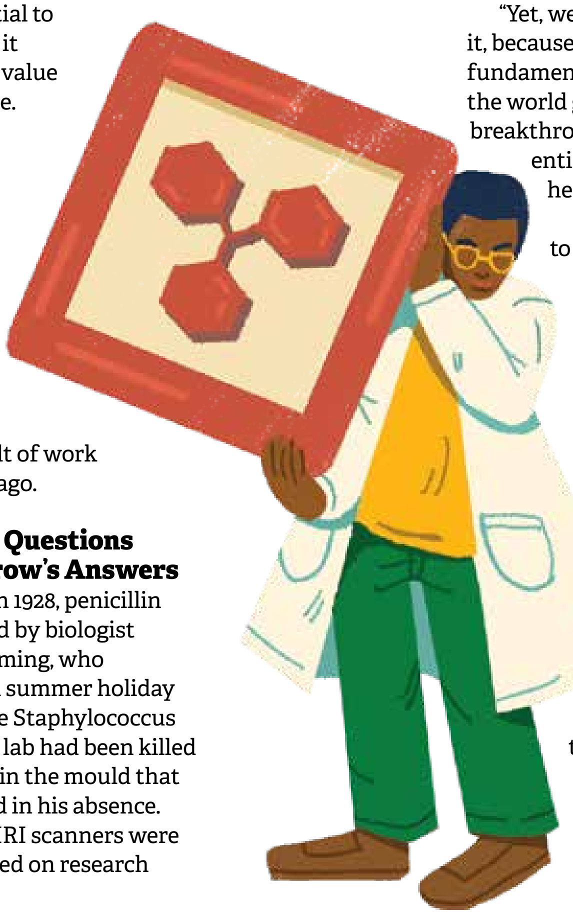
What's more, Derda can do this very quickly — repurposing tools used in genomics, like next-generation sequencing and data mining, to analyze mixtures of small ligands to find suitable targets within a matter of hours.

In 2017, Derda, working with the Canadian Glycomics Network (GlycoNet) and the former Alberta Glycomics Centre, launched 48Hour Discovery, a commercially available service to screen billions of molecules simultaneously in a single test tube and get results in 48 hours. Over the last five years, 48Hour Discovery has worked with five leading global pharmaceutical companies on multiple contracts. (Derda is now a member of the new Glycomics Institute of Alberta.)

"It's really a vision of how drug discovery should be done. It's a proposal that discovery of drugs should not take them more than two business days," says Derda.

Derda's work at 48Hour Discovery has the potential to save lives, and it illustrates the value of basic science. The company is among countless examples of basic science helping to solve pressing problems of the time.

His work at 48Hour Discovery has the potential to save lives, and it illustrates the value of basic science. The company is illustrative of countless examples of basic science helping to solve pressing problems. These solutions are often the result of work initiated long ago.



Yesterday's Questions Are Tomorrow's Answers

For instance, in 1928, penicillin was discovered by biologist Alexander Fleming, who returned from summer holiday to find that the Staphylococcus colonies in his lab had been killed by something in the mould that had taken hold in his absence. In the 1970s, MRI scanners were developed based on research done years earlier by physicists studying how electrons and atoms respond to magnetism.

In 2016, the Laser Interferometer Gravitational-Wave Observatory, known as LIGO, picked up the collision of gravitational waves of two black holes 1.3 billion light-years away. Albert Einstein had predicted these waves a century prior, but this was the first confirmation of their existence. The same technology has now been adapted for commercial manufacturing, notably in optics.

Basic research is curiosity-driven and its short-term results aren't immediately obvious. At least that's what L. Rafael Reif, then-president of the Massachusetts Institute of Technology, wrote in a 2017 editorial in Foreign Affairs, the year after the LIGO finding. It often takes decades for basic science to yield practical applications.

"Yet, we cannot do without it, because it is from such fundamental explorations that the world gets the startling breakthroughs that create entirely new industries," he continued.

It's these attempts to expand knowledge that lead to powerful new products and businesses, generate jobs and inspire innovation, he wrote.

Consider the mRNA vaccines for COVID-19: in the late 1980s, two scientists at the University of Pennsylvania, Katalin Karikó and Drew Weissman, pioneered the mRNA technology that is the backbone of these new vaccines. The companies Pfizer, where Karikó now works, and Moderna launched the world's first mRNA vaccines for COVID-19 in the late fall of 2020, a lightning-quick pace compared to earlier vaccines. They were successful because of the basic science that had been in development by scientists working in universities over decades.

The Search for Cheaper Lithium

In Canada, this pattern is playing out across industries. Daniel Alessi, a geochemist and professor of Earth and Atmospheric Sciences, is revolutionizing the extraction of lithium, setting the province up to be a critical player in a green energy revolution.

Demand for lithium has been rising sharply over the last decade, driven by the growing need for lithium-ion batteries for electric vehicles and large-scale renewable energy storage. Lithium's cost is also skyrocketing: it has increased nearly 900 per cent since January 2020, a rate almost 10 times that of other critical raw materials in batteries like cobalt and nickel, according to Benchmark Mineral Intelligence, a research firm. This trend is expected to continue well into the future, with demand predicted to grow nearly eightfold by 2030.

Today, we mine lithium primarily in two ways. The most common is through salars, the lithium-rich, salt-encrusted depressions on the basins of evaporated lakes that are found mostly in Argentina, Bolivia and Chile. This method of lithium extraction is cheap and efficient but environmentally intrusive. In order to glean lithium from the salars, extractors draw in groundwater from the surrounding areas, which are often places where water is scarce. Lithium is also sourced through hardrock mines, but these mines leave scars on the landscape and require vast amounts of energy. Estimates suggest that about 15 tonnes of CO_2 are released into the atmosphere for every tonne of lithium extracted from hardrock mines.

There is potential for a third way with a smaller environmental footprint. In this scenario, Alberta could be a key player. Most oil and gas wells in Alberta produce saline water, or brine. This brine is five to 10 times saltier than seawater and, among its components, is a bit of lithium: about 50 to 100 parts per million, which is between five and 10 percent of the lithium concentration in salars. Companies face an enormous technological challenge in separating the lithium from other components in the brine.

"It's a needle in a haystack problem," explains Alessi, who holds the Encana Endowed Chair in Water Resources.

In 2016, Alessi's lab was approached by E3 Metals Corp. (now E3 Lithium) about developing a technology to help extract and separate lithium from oilfield brines in Alberta.

With his colleague Salman Safari, Alessi worked on three grants from the Natural Sciences and Engineering Research Council of Canada to develop a technology that would use basic science principles to understand the materials in the brine and find solutions for how to separate the lithium from other components.

In 2019, Safari and Alessi founded their own company, Recion Technologies, Inc., to

Resistant Questions

Basic science is everywhere across the Faculty of Science.
For example, at the Charlebois Lab, researchers are asking big questions about the intersection of antimicrobial resistance, bioelectromagnetics and biophysics. Their research exists at the interface of physics and biology and aims to make fundamental advances in our understanding of living systems. They use quantitative mathematical, computational, and machine learning models to perform experiments on genetically engineered and pathogenic yeasts. The team works in the Charlebois biosafety level two biophysics-microbiology laboratory in the Centennial Center for Interdisciplinary Science.They want to apply this knowledge to the growing problem of antimicrobial drug resistance.

develop technology to extract, purify and produce lithium products from lithium-bearing saline waters in Western Canada — addressing what they see as the stumbling blocks in the current technology.

"The biggest positive impact is that we're enabling the lithium-ion battery industry and, ultimately, the green energy revolution," Alessi says. Unlike lithium extraction from salars, he describes his technique as low impact and non-toxic.

Alberta is home to hundreds of thousands of oil and gas wells, many of which produce brine as part of the oil and gas extraction process. The brine could be repurposed for lithium extraction, providing another income stream to oil and gas producers, he says.

"It's potentially not only a cost offset, but the environmental impact is leveraging the infrastructure that's already here in Western Canada. It's a nice positive side activity for the oil and gas industry," Alessi says. "Or potentially an industry in its own right."

Big AI Serves Smaller Communities

In health care, basic science research at the U of A has led to changes in the way that life-threatening cardiovascular conditions are detected.

As undergraduates, Talwinder Punni, '16 BSc, and Esmat Naikyar worked on developing deep neural networks — an advanced version of artificial intelligence — as part of the U of A's Precision Health program. Precision Health, a collaboration between different departments including health and computer sciences, uses advanced computer technology to help understand, diagnose and treat disease.

Through their work, Punni and Naikyar saw a role for AI in remotely diagnosing medical conditions in patients, particularly those in small communities away from large medical centres.

In Canada, rural populations do not have equitable access to health care services: one in five Canadians lives far from a major city, but only eight per cent of the country's doctors work in these places.

In 2020, Punni and Naikyar co-founded Naiad Lab Inc., a spinoff that grew from their research. Today, the company is focused on developing products to improve early detection of cardiovascular disease. To reduce cardiovascular fatalities (the No.1 cause of death globally, according to the WHO), health care providers need to detect early warning signs of cardiovascular disease and intervene, explained Punni. "Detection is the only real solution," she said. But traditional ECGs can miss cardiovascular disease in early stages, and reading ECGs is a time-consuming process.

Naiad Labs used real-life data from a growing dataset of 300,000 electrocardiogram recordings to train algorithms to detect cardiovascular abnormalities in early stages and flag patients who may benefit from intervention.

Naiad's first product, Naiad DETECT, offers subscribers an automated analysis of ECGs in order to accelerate early diagnosis of cardiovascular diseases. DETECT works with all 12-lead ECG devices, regardless of manufacturer. The company is currently in partnership in Canada with TeleMED, through its flagship application, ViTELflo. and is working with virtual telehealth companies in India.

Make Room for Questions

Scientists point out that the business world moves at a rate far quicker than basic science. The timelines are tighter; the goals more specific. It means less time to carry out exploratory research, that valuable act of looking for answers to satisfy curiosity rather than addressing a specific need of business or government.

And that, says Derda, is exactly why basic science is so vital.

"If we only rely on commercial entities to provide breakthroughs, those breakthroughs usually involve optimization and tightening up of something that already exists," he says. "Discovering something completely unexpected or something brand new is almost impossible (in the commercial space)."

He plans to continue pursuing answers to fundamental questions in the lab, while working with industry. It's in the lab where the most pressing problems of the future are already in the process of being solved.

"I think that work is already being done. It just might not be recognized or elevated to the front pages yet," he says. ■