# Researcher wins NIH grant to study molecular components of disease

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A University of Chicago researcher is among the first to win a new award from the National Institute of Health aimed at supporting research that "has the potential to transform the way we think about and conduct science," according to NIH Director Francis Collins.

Shohei Koide, Associate Professor in Biochemistry and Molecular Biology, won an NIH Transformative R01 (T-R01) Award, which comes with a five-year, $2.8 million grant, to develop an innovative protein-capture technology with high levels of fidelity and predictability.

"Our work represents a paradigm shift in protein-capture reagents, which are essential for delineating the molecular mechanisms of diseases, detecting and characterizing cellular abnormalities, and characterizing the biological effects of drugs," Koide said.

Protein-capture reagents are molecules (most often antibodies) that allow researchers to detect and/or isolate proteins in a sample. Because human cells contain tens of thousands of different kinds of proteins, and bacteria and viruses have their own sets of proteins, there are millions of proteins in nature. To be useful, protein-capture reagents must be able to catch miniscule amounts of the protein of interest—but not others. In addition to high selectivity and sensitivity to the target molecule, a protein-capture reagent should be easy to generate and handle.

"The current shortage of high-quality protein-capture reagents presents a major bottleneck in many areas of biomedical sciences," Koide said. "This project will establish a new approach to generating protein-capture reagents that are high performance and easy to produce. It will fill a major void in available molecular tools and impact virtually all areas of molecular biomedical science, medical diagnosis and drug development."

Each protein molecule is comprised of hundreds of 20 different amino-acid building blocks that are connected one after another in the order programmed by the genome. Koide's new technology, called C-clamping, aims to develop reagents that find the right protein by reading only the last eight letters of the protein sequence.

"The term 'C-clamp' comes from the protein tail, which is called a C-terminus," Koide said. "Each protein has a tail, and virtually every protein has a unique combination of amino acids within this short tail that can be distinguished with high efficiency by C-clamping. In contrast, currently available protein-capture reagents try to read the entire protein sequence so they are overwhelmed by the long sequences.

"Our proof-of-concept experiments have been successful, and C-clamping has enormous potential," he added.

The T-R01 Award is a new part of the NIH Common Fund's Roadmap for Medical Research program enacted by Congress in 2006. The other Roadmap for Medical Research Awards are the Pioneer Award and the New Innovator Award.

The T-R01 Award provides a new opportunity for scientist that is unmatched by any other NIH program. Since the funding limit is so high (up to $25 million for five years) and preliminary results are not required, scientists are free to propose bold ideas that may require significant resources to pursue. This year, NIH awarded 42 T-R01 awards totaling $30 million.

"Competition for the awards was fierce, and standards were very high," Collins said. "These projects tend to be inherently risky, but if successful can profoundly impact a broad area of biomedical research."

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