MECHANICAL WONDER

Dr. James Anderson decodes an RNA process essential for cell survival

He might be examining molecules, but Dr. James Anderson is moving mountains.

The role of ribonucleic acid in protein synthesis is vital to all living things, and while scientists have studied RNA for more than a century, they are still unraveling clues to the mysterious building blocks of life.

Anderson, associate professor of biological sciences, recently discovered a particularly important clue: an RNA process that is essential for cell survival. In what has been lauded as a "landmark discovery" by colleagues around the globe, Anderson's development laid the groundwork for what is sure to be a cascade of follow-up projects by others in his field. It's a critical first step that could lead to breakthroughs in the treatment and prevention of disease.

Anderson has always been passionate about basic science, and he loves when his research becomes the pebble that produces a ripple effect.

"There will certainly be applications to medicine and disease. We just don't know what they are yet," he points out. "What's exciting to me is how that will unfold."

Anderson, whose work is supported by the largest, most prestigious grant program of the National Institutes of Health, was curious about how RNA molecules work together to assemble proteins with the correct sequence of amino acids. When a cell functions properly, transfer RNA (tRNA) molecules do this without fail. If one of the tRNA molecules is faulty, the cell recognizes it and either repairs or destroys the molecule before it synthesizes the proteins incorrectly. In simple terms, cells operate like a factory, with the foreman identifying faulty parts and either fixing or replacing them.

Those exquisitely programmed cellular machines are crucial to sustaining life — after all, improper protein synthesis is the root of many genetic diseases. By understanding how correctly functioning cells identify and then repair or destroy defective tRNA molecules, scientists could better identify and ultimately prevent the earliest stages of disease.

By applying the principles of genetics to bread yeast, Anderson was able to identify the molecular pathway responsible for the degradation of tRNA. "We've known that when RNA is non-functioning, it is recognized in such a way that it becomes a target for elimination," he says. "Until now, though, we didn't know *how* it was recognized."

During normal synthesis, a certain protein group modifies the RNA molecule by adding to it a carbon-hydrogen compound known as a "methyl group." The addition of this methyl group allows RNA to function properly during synthesis; without it, the RNA is defective.

"Genetics revealed that a defective tRNA molecule is recognized by a completely different protein group," Anderson says. "We discovered that a particular protein group adds a 'tail' of nucleotides to the tRNA. It is

that tail that signals to the cell that the tRNA is faulty."

Anderson notes that HIV — the virus that causes AIDS — utilizes RNA to capitalize on cells' own components and compromise the body's immune system. While his discovery in yeast may not provide direct answers for curing this deadly disease in humans, understanding how cells deal with faulty RNA molecules during protein synthesis could ultimately reveal how the virus turns the human body against itself.

Just as RNA and other genetic materials are the foundation for all living things, basic science like Anderson's work is the cornerstone of practical research and developments in medicine, genetics and other applied sciences.

No one, including Anderson, knows how his research will be ultimately applied. And that's OK with him.

Says Anderson, "I want my research to provide opportunities and resources for other scientists."

Illustration by Tom White