Unnatural Amino Acids: An Attempt to Play God or a Breakthrough in Fighting Disease?

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Though it may sound as if humans have no business changing the natural genetic code, scientists modifying proteins that make up the human body are designing innovative treatments for a range of debilitating diseases, including Parkinson's, cancer, and HIV. The body naturally creates proteins from 20 different amino acid building blocks. Peter Schultz of the Scripps Research Institute found a way to introduce new building blocks to the genetic repertoire, allowing for new combinations of amino acids that create different proteins. Schultz made a flippant remark in a recent interview suggesting that these unnatural amino acids allowed him to play God, which sparked controversy regarding his financial support from the NIH. However, Schultz and other NIH-funded researchers are not using these new amino acids to design futuristic humans who can survive underwater or achieve immortality. Instead, they are using them to study naturally occurring systems and protect them from disease, fulfilling the NIH's mission: to "seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability."

Unnatural amino acids lead to better models of biological mechanisms. Dennis Dougherty and colleagues study Parkinson's disease, a neurodegenerative disorder that affects up to 1 million people in the United States and currently has no cure. Parkinson's patients suffer from decreased dopamine release in a region of the brain known as the substantia nigra, and Parkinson's therapies aim to increase the amount of dopamine in this region. Drugs that activate acetylcholine receptors, proteins which bind the neurotransmitter acetylcholine, can stimulate dopamine release. Two different categories of acetylcholine receptors exist in the body: the nicotinic receptors affected by Parkinson's and the muscarinic receptors involved in involuntary functions like heart rate. Drugs that bind to both types can have disastrous consequences. Dougherty and colleagues used unnatural amino acids to examine a complex molecular interaction unique to the nicotinic category of acetylcholine receptors. The unnatural amino acids allowed them to observe the effects of very subtle changes to the receptor so they could pinpoint the specific regions of the protein responsible for the molecular interaction and the efficacy of drug binding to the nicotinic receptor. The binding model created in this study will assist in the development of extremely specific drugs that target only the nicotinic acetylcholine receptor, leading to a possible cure for Parkinson's.

Other applications attempt to develop novel solutions for disease. Wang and colleagues used unnatural amino acids to exert control over the viability of the HIV-1 virus, which could lead to the development of an HIV vaccine to curb the worldwide AIDS epidemic. Schultz and colleagues have used unnatural amino acids in cancer treatment to synthesize antibodies that simultaneously target T cells, white blood cells essential to the body's immune response, and the toxins specific to cancerous tumors. Activating these targets at the same time directs the T cells to fight the cancer cells. Schultz has worked on antibodies for the treatment of breast cancer, prostate cancer, and acute myeloid leukemia. These researchers have no desire to play God. Instead, they seek to use unnatural amino

acids as new tools to understand and treat serious diseases. Their research serves each part of the NIH's mission, and continued funding can only lead to more precise, effective solutions for a variety of illnesses.

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