2012

Synthetically Altering the Genetic Code

Chante Terrel Biological Sciences Junior Department of Microbiology and Molecular Genetics, Oklahoma State University, Stillwater, OK 74078, USA

Key Words: Genetic code, tRNA, proteins

All organisms on earth have the same genetic code. They all have the same twenty proteins that are formed from the same amino acids that are derived from the same nucleotides and they all perform these operations in a very similar manner. These twenty proteins are used to provide energy for almost every cellular process that takes place within an organism. Although seemingly impossible, scientific advances have discovered a way to insert synthetic proteins into tRNAs *in vitro*. With these advances scientists are able to go beyond the normal twenty proteins in order to discover more about the genome of both prokaryotic and eukaryotic cells.

Introduction

Proteins are one of the most important macromolecule in the success of cells. They have many functions within the cell. For example, there are structural proteins to provide mechanical support for cells and tissues, motor proteins that generate movement in cells and tissues, receptor proteins to detect signals and transmit them to the cell's response apparatus, storage proteins to store small molecules, signal proteins that carry signals from cell to cell, transport proteins that carry small molecules, gene regulatory proteins that bind to DNA to switch them on or off when necessary and there are also special-purpose proteins that have a wide range of functions. Proteins are made up of one or more chains of amino acids known as polypeptides. Amino acids are composed of nucleotide triplets called codons which are linked together by peptide bonds. Each amino acid chain is folded into a three dimensional shape thus giving each protein their own unique shape. If the proteins are not able to function properly, the necessary cellular functions are impossible. Proteins are required for a majority of work in the cell.

Forty years ago, "*in vitro* polyester synthesis was demonstrated through the chemical modification of tyrosine (a nonessential amino acid produced from phenylalanine that is an important building block of neurotransmitters) on a tRNA". Altering of proteins is so difficult is because they are restricted to the rearrangement of the nucleotides to form something other than one of the already known twenty amino acids that make up the twenty types of proteins. By altering the nucleotides they could alter protein translation to produce synthetic polymers thus completely altering the entire genome. These processes of synthesizing amino acid sequences, proteins and the entire genome it would help to further the understanding of the functions and make-up of proteins.

Recent Progress

Scientists have been able to inject "chemically aminoacylated orthogonal tRNA" that they have compiled to recognize an amber codon which allows to them to understand the function of membrane proteins by encompassing synthetic amino acids. They have used "the pyrrolysyl-tRNA synthetase-tRNA pairs from Methanosarcina species [that] can be used to incorporate unnatural amino acids into protein in bacteria, yeast, mammalian cells, and even a whole animal, the worm Caenorhabditis elegans" (Chin, 2012). This gives scientists hope that it will lead to discoveries in other seemingly impossible areas of molecular biology. In order to insert these synthetic amino acids properly, scientists have learned that they must also insert blank codons. These blank codons work by reducing the "codons that encode all 20 amino acids and deleting the endogenous tRNAs that decode the replaced codons" (Chin, 2012). Although, scientists believe that the number of blank codons that can be inserted is limited because of the wobble pairing rules of tRNA. Quadruplet codons are inserted because of the restrictions. The blank codon approach "has been used to genetically direct the formation of a nanoscale redox-insensitive cross-link" (Chin, 2012) that could possibly lead to stabilized protein therapeutics and by inserting blank codons may provide the evidence for the processes that are "evolutionarily embedded in natural codon usage" (Chin, 2011). In the last eight years, Chin and colleagues have programmed protein translation for purposes such as synthesis of new polymers, to get new insight of their biological functions and with the development of "photochemical genetic" (Chin, 2011) methods they are able to control the activity of proteins in living cells that provide an understanding of biological processes that are mostly only known from in *vitro* testing. In order to completely synthesize polymers by inserting new amino acids into proteins Chin and his colleagues had to overcome three different issues. One being attaching a new amino acid to a new tRNA in a precise manner, then they needed a codon they could incorporate with the new amino acid and they had to make alterations to the translational machinery of the ribosome. These tests have been performed in vitro and in vivo in yeast, E. coli and mammalian cells.

Discussion

These advances are giving rise to new information; they are also giving rise to new questions as well. By integrating synthetic amino acids in order to produce synthetic proteins and synthesizing the ribosome, scientists have uncovered details about the biological processes involved with nucleotides, amino acids, proteins, and ribosomes and about their functions within a cell. By altering amino acid sequences scientists could ultimately add blank codons or other synthesized codons to possibly fix mutations. Since most mutations within the ribosome are dominant, negative or lethal, a synthetic ribosome aids in the reduction and possibly even the elimination of those mutations. These types of advances show how great of importance proteins actually play in our essential cellular functions.

All organisms are constantly evolving in order to enhance their fitness. If scientists continuously keep injecting the same synthetic material into cells perhaps the organism would eventually adapt to them and, if they are beneficial proteins, begin to produce them naturally. If the synthetic materials being injected are not beneficial or harmful there is still a chance that the organism would produce it but if it is harmful the organism will build up immunity to it over time. To build up their immunity to the harmful material they could produce a small amount of it.

When scientists are able to synthetically alter a human's genome, they will eventually be able to alter

phenotypes. Parents will one day be able to choose the hair color, eye color, physical fitness, and etc. The downside to being able to choose everything about phenotypic expression of future offspring is that it is human nature to want the best and to want your offspring to succeed. If every person is altering their offspring to be the best athlete and the smartest student and the most handsome, every person would ultimately be the same. This would encourage the process of natural selection to evolve into an individual with a higher fitness than the rest, basically starting the whole life process over again. If the already altered genes started to evolve and alter themselves scientists would have to start from scratch trying to figure out how to then alter those new versions of the genes. This would happen over hundreds or thousands of years but all the work that had been to done to discover how to synthetically alter a genome would now be irrelevant. It would simply be a building block for teaching, a way for the new scientists working on this same issue to learn what not to do and what could possibly jump start their research.

Scientific advantages provide insight to the processes that make it possible for organisms to survive. Proteins are one of the most important macromolecules that an organism needs to survive. If scientists are able to successfully alter a genome by inserting synthetic amino acid sequences it could open up doors to things never thought possible and scientists are well on their way to this great success.

References

- Chin, J.W., 2012, Reprogramming the genetic code, *Science*, v. 336, no. 6080, p. 428-429.
- Chin, J.W., 2011, Reprogramming the genetic code, *The EMBO Journal*, v. 30, p. 2312–2324.
- Wang, L., Schultz, P.G., Expanding the genetic code, *Angewandte chemie international edition*, v. 44, p 34-66.