Review Article

Creating Genetic System

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Along with RNA and proteins, DNA is one of the three major macromolecules that are essential for all known forms of life. DNA is a long polymer of two helical chains, each measuring 2.2-2.6 nanometers (nm) and one nucleotide unit measuring 0.33 nm long. Although individual repeating unit is very small, DNA polymer, containing millions of nucleotides (approximately 220 million base pairing long (1,2). As described by Watson and Crick (3), DNA has a molecular structure. In reductionist sense, DNA can be described as two antiparallel strands; each strand is assembled from four different nucleotide building blocks, which are themselves assembled from sugar, phosphate, and nucleobases. These are in turn assembled from carbon, nitrogen, oxygen, phosphorous , and hydrogen atoms. In Watson and Crick model, nucleotide pairs contribute independently to the stability of the duplex, DNA duplexes can be designed with considerable success by applying just two rules: Adenosine pairs with Thymine, and Guanine pairs with Cytosine. A second order model does very well by adding only the effect of adjacent base pair into the calculation (4). Although some diversity in nucleic acid structure and function is not captured by such simple rulesATCG (5,6,7). The role of DNA backbone in molecular recognition was known since 1980s, some synthetic biologists began to wonder whether DNA and RNA were only molecular structures that could support genetics on earth or elsewhere (8, 9, and 10). Other biologists, seeking technological goals attempted to replace molecules in the DNA structure to create analogues that would, for example, passively enter cells but could still support the « A pairs with T, G pairs with C» rule, with the aim of disrupting the performance of intracellular nucleic acids in sequences-specific «antisense» (11). It is realized that both phosphate and ribose have an important role in, the molecular recognition that is central to genetics. In particular, a genetic molecule must be able to suffer change (mutation) without markedly changing its overall physical properties. Again this feature is infrequent in chemical systems (in proteins, for example). But because charge dominates the physical properties of a molecule, a repeating charge should allow appendages (thenucleobases, in the case of DNA and RNA) to be replaced without changing the dominant behavior of a genetic system . This had led to the suggestion that the repeating charge may be universal feature of genetic molecules that work in water (12).Furthermore, the discovery that ribose was one of the better backbone sugars for supporting molecular recognition (11,13) had implications for the origin of life on earth . Miller (cf. 14) had commented that because of the ease with which ribose decomposes as a sugar on heating, ribose could not have supported the first genetic system on earth. The result from the synthesis which indicated that ribose is especially good for genetics, drove efforts to find prebiotic routes to ribose that would overcome its intrinsic instability (15,16).The Watson-Crick pairing rules arise from the rules as chemical complementarity . The first, size complementarity, pairs large purines with small pyrimidines. The second, hydrogen bonding complementarity, pairs hydrogen bond donors from one nucleobase with hydrogen bond acceptors from the other.If nucleobase pairing were indeed so simple it should be possible to move atoms around within the nucleobase to synthesize unnatural nucleobases that would still pair following rules of size and hydrogen bonding complementarity but differently from the natural nucleobases. Induced by shuffling the hydrogen-bond donating and accepting groups, one can easily generate eight and/or twelve additional synthetic nucleobase(17) ,forming more additional base pairs. Therefore, extended Watson-Crick model (rules) is possible.Because it provides rule-based molecular recognition that is orthogonal to the recognition provided by natural DNA, this synthetic genetic system is found today in the clinic. As part of the Boyer VERSANT branched DNA diagnostic assay(18), synthetic biology helps to manage the care of approximately 400,000 patients infected with HIV and hepatitis viruses each year(19,20 . The synthetic biology of nucleic acids is successful because the repeating charge in the backbone enables the nucleotide parts to be exchanged independently. Proteins unfortunately do not have a repeating charge, engineering them has therefore been more difficult. Proposals to engineer proteins, for

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which the interchangeable unit is the amino acid, is as old as recombinant DNA technology (21,22). The twenty years of experience shown that the behavior of a protein is not a simple combination of independent contributions from the constituent amino acids (17).

The archetypal example of modularity in evolution is found in genetic regulatory and signaling pathways. Here, combinations of proteins (receptors) often function as molecular switches (ligand binding, chemical reaction), or the movement of compounds into new locations. one goal of synthetic biology is to take the proteins themselves as building modules and synthesize artificial regulatory circuits. Synthetic genetic system that resemble natural DNA in many ways, but have independently a number of replicating nucleotide « letters» in their genetic «alphabet» (24). Scientists create artificial genetic material XNA, that can store information and evolve over generations in similar way to DNA; a fact expected to drive research in medicine and biotechnology, and shed light on how molecules first replicated and assembled into life billions of years ago (23). Researchers of the molecular biology center (MRC), in Cambridge, developed chemical procedures to turn DNA and RNA into chemical cousin , the chemical basis for known life, into six alternative genetic polymers called XNAs. The process swaps the deoxyribose and ribose (the «d» and «r» in DNA and RNA) from the molecules. It was found that the XNAs could form the double helix in a similar way to the natural genetic material and showed a description how they caused one of the XNAs to stick to a protein, an ability that might mean the polymers could deployed as drugs working like antibodies. In DNA and RNA, replication is facilitated by molecules called polymerases. Using a crafty genetic engineering technique called compartmentalized self-tagging (or «CST»), the team designed special polymerases that could only synthesize XNA from a DNA template, but actually copy XNA back into DNA. (24).Gene and genome synthesis that is , constructing long stretches of DNA from constituent chemicals, provides scientists with new and unparalleled capabilities both forunderstanding biology and for using it for benefical purposes. But along with new capabilities come new risks. Synthetic genomics combine methods for the chemical synthesis of DNA with the computational technique to design it. these methods allow scientists to construct a genetic material that would be impossible or impractical to produce using more conventional biotechnological approaches(25). Ibrahim(26), introduced the two terms methylome and methylomics which are derived from the established scientific terms genome and genomics. These might be useful and could be used to explain various issues related to specific regions in the DNA sequence and chromosomes of eukaryotic organisms which contain the fifth base. A recent article on the subject of synthetic biology was given by Zahid (27).

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