Science and technology

Jewels in the junk http://www.economist.com/node/21589081/print

RNA may hold the answer to lifeôs great riddles

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In 2014 the Cinderella of genetics will come to the ball, as the acronym RNA enters the public consciousness in the way that DNA did two decades ago when the Human Genome Project was in full swing. That project, so hopeful at the time, is perceived by many to have ended in anticlimax. The cornucopia of medical advance it promised has not turned up. The reason for that failure is, in large measure, that geneticists did not then understand the importance of RNA, a molecule that was seen as a skivvy to its step-sisters, DNA and proteins. Now they have realised that RNA is actually the belle of the ball. To understand how genes work, and thus create those much-sought medical benefits, it is RNAôs role you have to disentangleð and that process will accelerate rapidly in 2014.

RNA is chemically similar to DNA; indeed, its molecules are made from DNA templates in the nucleus. The old view was that these molecules were merely the workforce that put proteins together. One sort carried the plan for a protein to a second lot which, in the form of a sub-cellular machine called a ribosome, read and interpreted that plan. A third sort picked up amino acids (the building-blocks of proteins) from the cellôs cytoplasm and delivered them to the ribosome for assembly.

Over the past few years it has emerged that these three types of RNA (mRNA, rRNA and tRNA) are not alone. There are also aRNA, lincRNA, miRNA, piRNA, siRNA , snRNA and many others; so many, indeed, that what they all do is not yet clear. What is clear is that the view prevailing during the genome projectð that the important bit of the genome is the 2% of it that encodes proteins, and that the other 98% is junkð is, itself, junk.

In fact, as RNAôs own, private genome project, ENCODE, reported in 2012, at least three-quarters of DNA, not just the protein-coding bit, can be copied into RNA. Moreover, a paper published in September 2013 showed there are 160,000 places in a human genome which look like starting-points for such copying. This suggests there are 160,000 genes. But the Human Genome Project showed that there are somewhat more than 20,000 protein-coding genes. Picking through the remaining 140,000ð in which RNA itself, rather than protein, is the active end-productð will be no mean feat.

The biggest job these non-protein-coding genes seem to be involved in is regulating how the whole genetic apparatus works. They do this in lots of ways. Some bind to mRNA and render it inactive, a process known as RNA interference. Some bind to stretches of DNA. Some alter the proteins that surround DNA so that entire genetic blocks cannot be read. And some glom onto other proteins, called transcription factors, that themselves would otherwise trigger the copying of genes. By these means, in ways whose details are just beginning to emerge, RNA controls what a cell does, and also what type of cell it is. It thus regulates how bodies workð and even how they develop from fertilised eggs into adults.

Magic and medicine

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This is, at last, beginning to shed light on disease. Non-coding genes are now known to be involved in many types of cancer, in several neurological problems (including Alzheimerôs disease, autism and schizophrenia), in heart disease and in diabetes. Such genes may account for the hitherto mysterious observation that many illnesses have a far larger hereditary component than can be accounted for by variations in protein-coding genes. It is possibleð probable, evenð that researchers who have been looking for this heritability in protein-coding genes have been looking in the wrong place.

Drug companies, not surprisingly, are interested in what may be a new category of chemical they can turn into something effective. RNA interference, in particular, is seen as a likely route. But even if RNA drugs prove elusive, better understanding of RNAôs role in disease should help the design of other therapies, delivering the promise made when the Human Genome Project started.

Nor is that the end of RNAôs new significance. For it might hold clues to the origin of life itself. The core of a ribosomeð the part that links amino acids togetherð is almost identical in all living creatures. Ada Yonath, of the Weizmann Institute in Israel, who discovered this, thinks the stable core must go back, if not to the origin of life, then close to it.

In effect, a ribosomeôs core is the oldest fossil aroundð and a living fossil at that, reproduced a zillion times a day in the cells of animals, plants, fungi and bacteria. If someone could work out how this piece of RNA first came into existence, it might explain how living things came to be. So 2014 could, just possibly, be the year when a bright biochemist has an ñahaò moment, and biologyôs greatest secret yields itself up.

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