# Genes – protein – performance

**DR PETER KOEPPEL** PROVIDES US WITH A COMPREHENSIVE VIEW OF GENETIC REPLICATION AND EXPRESSION: HOW DOES CELL DIFFERENTIATION OCCUR; HOW DOES CELLULAR RECOVERY OCCUR AFTER TRAINING; AND WHAT ROLE DO NUCLEOTIDES HAVE IN THESE PROCESSES?

We take it for granted that our body can fulfil all the tasks that we want it to; from eating, to communicating, to performing extreme sport. All of these activities need a huge variety of specialised cells, which must be able to communicate and work perfectly together, at least most of the time. We rarely appreciate what it means for the body to adapt to the rapid changes of the environment, as well as increasing daily demands. Today, we are able to travel from an arctic to a tropical environment in less than a day, and we expect our body to adapt without problems. We really do not realise how many cells need to change their functions in order to maintain the integrity of the body under such exacting conditions.

Sport activities lead to even greater changes in the body. High intensity sport puts an enormous demand on the body and leads to big changes in the function of some cells. Surprisingly, the body is able to cope with all these demands, despite the fact that all cells carry the same genetic information. All the cells of the body actually have the same set of genes, but even so, the function of the cells in the different organs are so diverse. For example, the actions of a liver cell are totally different from a cell of the eye, or a brain cell, or indeed the stomach.

All the different types of cells originate from one single, fertilised cell. How is it possible that from one single cell, such a variety of cells can develop, even though they all have the same set of genes? What are

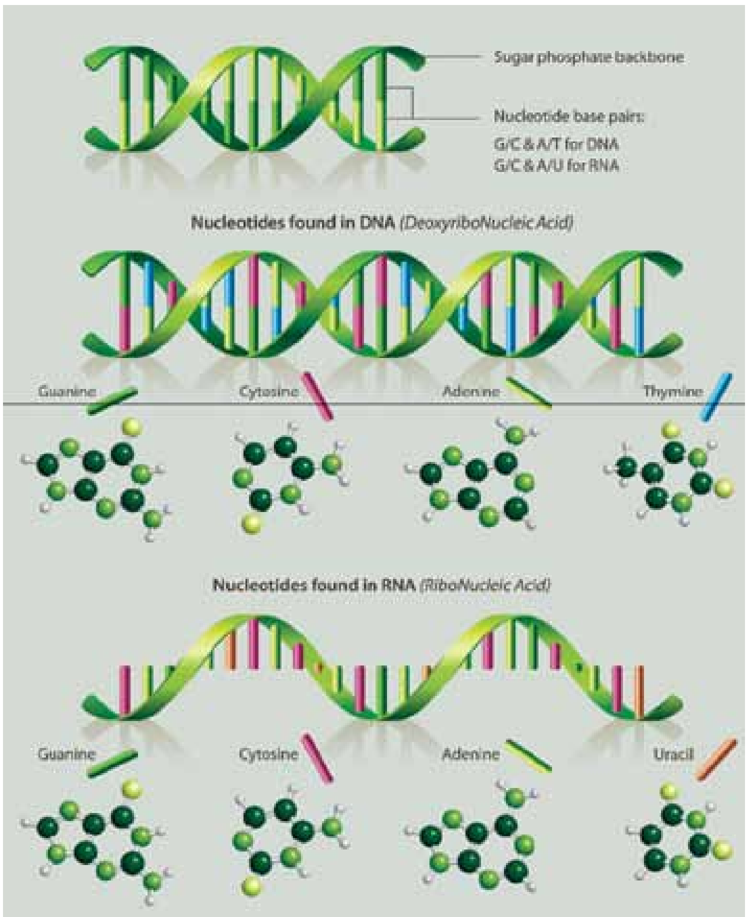


**Figure 1 – Structure of DNA and RNA**

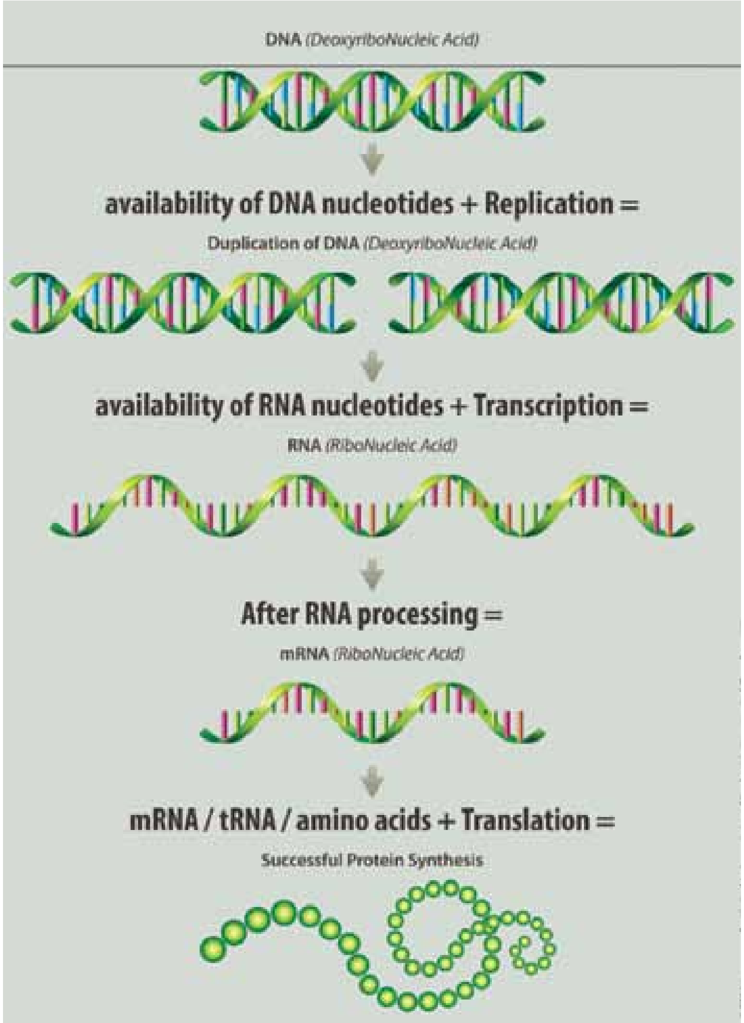


**Figure 2 – Transcription of DNA to RNA and translation to proteins**

**"During times of heavy exercise or permanent stress, the body produces stress hormones, which are able to switch off some genes that produce antibodies. This consequently leads to lower antibody titres and a suppressed immune system."**

the steps in the development of an embryo, which leads to a functional body with all the different organs? What kind of mechanism is behind this process, leading to the variation in the function of the cells?

## DNA, the genetic blueprint

You've probably heard that DNA is the blueprint for lifelife; the plan of the body. But how is it built up? As shown in Figure 1, the DNA molecule is a twisted, ladder-like double helix built from blocks called nucleotides. There are four types of DNA nucleotides; Adenine (A), Cytosine (C), Guanine (G) and Thymine (T).

The single strand of DNA in each cell is made of three billion nucleotides, containing the information to build the entire body. The sequence of the four bases determines the genetic code. If the DNA is the factory, producing everything that a cell requires to function, what gives the instructions for each bit? The answer is our genes.

The DNA strand is subdivided into segments called genes (1). A gene is a distinct section of DNA that determines something about who you are. Genes vary in size; from just a few thousand pairs of nucleotide bases to over two million base pairs. These three billion nucleotide pairs in the DNA strand carry around 23 000 genes (2).

This still does not explain how the cells of the various organs can perform such different functions. The answer lies in the understanding that genes in a cell can be switched on or off. During the development of the embryo, some genes in certain cells are definitively inactivated, whereas others remain active. By enabling only a certain number of genes to be expressed within a specific cell, it is in this way that the functions of the cells in different organs are differentiated and controlled (3).

Genes and the function of their protein products are regulated within a highly complex cellular system; each cell interacts with hundreds of neighbouring cells, all communicating closely with one another and influencing each other's structure and function.

## Genetic expression

When genes are expressed, a series of steps are initiated within the nucleus of the cell that leads to the synthesis of new proteins. These proteins may be enzymes (catalysts for metabolic and other cellular activity), structural proteins (important for the physical integrity of the cell) or receptors (proteins that interact with, among other things, hormones to induce changes in cell activity). Regulation of the expression of a particular gene is influenced by many different factors (4), all of which determine the health and viability of the cell and its flexibility in responding to challenges: these include both internal (e.g. nutritional and hormonal) (5) and external (e.g. environmental and chemical) factors (6).

As shown in Figure 2, the first step in the whole process of protein synthesis is the transcription of the information from DNA to RNA. The basic constituents of RNA are the same nucleotides as in DNA, apart from Thymine, which is replaced by Uracil (see Figure 1). The nucleotide sequence on a specific RNA is an exact copy of the nucleotide sequence on DNA.

External factors can trigger a positive or negative regulation of genes. A positive regulation leads to a greater production of proteins, and a negative regulation leads to lower protein production. Typical examples for humans are viral infections: some viruses can activate an immune response, whereas other viruses act in an immunosuppressive way (7).

## The function of nucleotides

The primary purpose of nucleotides is to store genetic information. The ▶

speed of cell multiplication is largely dependent on the speed in which the genetic information is doubled. A lack of nucleotides will lead to a very slow cell multiplication. Dietary nucleotides are therefore essential for triggering the speed of cell multiplication. This is very important, for example, in wound healing or in proliferation of muscle cells. But they are also very important in the oxygen supply in the body: as shown in Table 1, tests with a product based on purified nucleotides (Nucell®) have shown that increased intakes of dietary nucleotides leads to an increased production of red blood cells, and therefore to a greater uptake and transport of oxygen in the body.

As a consequence of increased oxygen levels, glucose can be more efficiently metabolised, more energy can be produced, and the build-up of lactate in the blood of athletes supplemented with dietary nucleotides is lower than that of non-supplemented athletes.

Additionally, nucleotides are the basic constituents of RNA, and contribute through multiple steps to protein generation in cells. Since protein synthesis is partially the result of nucleotides, and proteins make up the structure and function of cells, nucleotides are proven to be important for maintaining cell and tissue health. An inability to generate new DNA and RNA, due to a lack of readily available nucleotides, can lead to tissue damage and disease.

During times of heavy exercise or permanent stress, the body produces stress hormones (e.g. cortisol), which are able to switch off some genes that produce antibodies. This consequently leads to lower antibody titres and a suppressed immune system (8,9,10). The athlete is not likely to notice this happening during training because during exercise or stress, the body is protected by the high cell metabolism and can still function normally. Infections or breakdown in physiological function occur mostly as soon as the stress or the exercise ends, which is when the protection provided by the high metabolism is over. In such situations, it is of utmost importance that the immune system recovers as quickly as possible.

The trial in Table 2 shows the effect of nucleotide supplementation on the formation of immunoglobulin G after stimulation with LPS. LPS (Lipopolysaccharide) is a cell wall constituent of some bacteria, and has a high immune-stimulating effect (11).

This trial clearly shows that the antibody production after supplementation of nucleotides was higher and faster. In the test group, the increase of antibody titre after two hours (+17.9) was higher than in the control after eight hours (+14.6). Therefore, the reconstitution of the weak immune system during and after exercise and stress is significantly improved by supplementing a specific nucleotide product, where nucleotides are presented in their pure form.

This is only one example of how nucleotides can increase protein production. Nutrition research in the past concentrated mainly on the effects and rectification of nutrient deficiencies and consequent impairment on health and performance (12,13,14). But, an increasing number of study findings prove that particular nutrients have the ability to interact and modulate the expression of genes (5,14).

Most athletes concentrate on the intake of amino acid supplements to obtain consistent maximum performance levels. This is because it is well-known that amino acids are the basic building blocks of protein. As mentioned, the first step of the protein synthesis is the transcription from the DNA to the RNA. A lack of any of the five nucleotides required will delay this step, and the protein formation is blocked, even in the presence of a surplus of amino acids (16,17,18).

Taking into account the explanation above, athletes should seriously consider a combination of supplements; namely a good nucleotide supplement, along with their regular protein and amino acid intakes (19,20).

Sports nutritionists often take note of developments in infant formulas. It is ironic that one of the intrinsic components of an infant formula, purified nucleotides, remain largely unconsidered by sports nutritionists and athletes alike, and until recently were a long forgotten class of nutrient in the elite sports menu plan. FSN

| Parameter | Duration fed | Not supplemented | Supplemented |
|---|---|---|---|
| RBC ($10^6$/ml) | 0 day | 4.69 | 5.04 |
| | 6 weeks | 5.26 | 5.01 |
| | 4 months | 5.69 | 6.37 |
| HGB (g/dl) | 0 day | 6.79 | 7.50 |
| | 6 weeks | 7.14 | 7.25 |
| | 4 months | 7.10 | 9.07 |

**Table 1 – Erythrocyte counts (RBC) and Haemoglobin (HGB) in athletes with or without nucleotide supplementation.**

| Measurement | Stimulation | Control | Nucleotide supplemented |
|---|---|---|---|
| Immunglobulin G (IgG; mg/ml) | Pre - LPS | 27.3 | 30.0 |
| | 1 h post LPS | 27.9 | 34.1 |
| | 2 h post LPS | 29.8 | 47.9 |
| | 8 h post LPS | 41.9 | 67.4 |
| | | ***+14.6*** | ***+37.4*** |

**Table 2 – Formation of immunoglobulin G after stimulation with LPS in athletes with or without nucleotide supplementation.**


## About the author

**Dr Peter Koeppel** has a PhD in biochemistry and immunology. He was trained in biochemistry, with a special interest in clinical immunology at the Institute of Virology at the University of Zürich. He then worked as a researcher in osteoarthritis and osteoporosis in a pharmaceutical company in Basel. Since 1989 he has been involved in producing special additives for human nutrition for ProBio Ltd, laterally becoming the managing director of this company in the year 2000.



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