

Nucleotides – the building blocks of life

IN THESE DAYS OF GENETIC UNDERSTANDING, WE ARE INTERESTED IN FAVOURABLE GENETIC EXPRESSIONS. **Dr Koepfel discusses the role of Nucleotides in our health.**

DNA is the substance inside each and every cell that carries our genetic blueprint. As shown by the characteristic double helix diagram in Figure 1 (see right), it is made from building blocks called nucleotides. There is a particular need for sufficiently available nucleotides in cells that divide often. This is the case for our immune cells, which have to divide rapidly in order to respond fast enough to an infection. But also the cells lining our digestive tract, called intestinal villi, are frequently replaced and are in need of nucleotides for repair. The body is able to recycle old nucleotides from worn out cells (the salvage pathway) or to make new nucleotides (by de novo synthesis) from sources such as glucose and glutamine. However, this process is not very energy-efficient; it's time-consuming and metabolically taxing. Thus, since the body has only a finite capacity to provide its own nucleotides, it is uniquely able to extract them from foods in our diet which contain them in substantial quantities.

Nucleotides and immunity

In order to stay healthy, it is crucial for our bodies to be able to rapidly respond to special needs and stressful circumstances. For example, when infected with the 'flu, millions of viruses invade our body: these need to be destroyed in order to regain normal health. It therefore becomes crucial that the body has the availability of sufficient nucleotides to rapidly and efficiently respond by producing enough new white blood cells to overcome the

infection. If the nucleotide supply is insufficient, the 'flu viruses will proliferate unhindered, which may lead to more severe symptoms and prolonged illness. Conversely, with enough nucleotides the infection can be quickly counteracted during its initial stages.

As with many other nutrients, the evidence of the effectiveness and importance of dietary nucleotides was first demonstrated in animal nutrition where they are widely used in fish, poultry, pigs, cattle and horses to enhance performance and to intensify and accelerate natural immune response. Nucleotides are not yet considered essential nutrients for humans, but stress, physical exertion, illness, poor diet and the excessive use of antibiotics and alcohol increase their need in order to facilitate timely and effective cell proliferation. Human breast milk is especially rich in nucleotides. Many infant formulas now contain them because studies have shown that babies fed nucleotide-supplemented infant formula experience better growth and development, maintain a healthier immune system, and have increased levels of beneficial intestinal bacteria which reduce gastrointestinal distress.

In adults, advantageous effects were found in markers of immune function: i.e. salivary immunoglobulin-A (sIgA), which is involved in the first defence against coughs and colds. From a more holistic point of view, it is interesting that both innate and acquired immunity need rapid and unhindered cell proliferation for proper functionality. Unfortunately, cells of the immune system lack the potential to synthesise nucleotides themselves. Other cells not capable

of producing sufficient amounts of nucleotides include gastrointestinal and blood cells. Importantly, nucleotides do not stimulate innate or acquired immunity, but rather provide the resource for unhindered cell proliferation, gene expression, and response to special environmental and physical challenges. Their universal use and fundamental functionality and efficacy in every living organism make nucleotides a valuable management tool for many stress- and health-related conditions.

Dietary and supplemental nucleotides

Nucleotides have also gained interest in the area of food allergies or sensitivities because the gut and the immune system are dependent on their ready supply to meet the rapid "turnover" of cells. Nucleotides modulate the expression of inflammatory reactions in the intestine. In infants, nucleotides boost the production of Immunoglobulins and increase the tolerance of food. Another outcome, and probably the most interesting one, is the improvement of gut health: nucleotides strikingly increase the length of intestinal villi (shown in Figure 2), the structures in our gut which constitute the enormous surface of our gastrointestinal tract. For instance, the incidence and duration of childhood diarrhoea is reduced when supplemental nucleotides are given. Improvements were also found in patients with irritable bowel syndrome (IBS), a very common gastrointestinal disease.

The problem is that foods rich in nucleotides are now rarely on our menu. Meat products from organs

Figure 1: Nucleotide structure within a DNA string

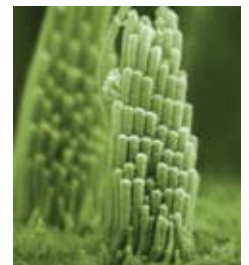
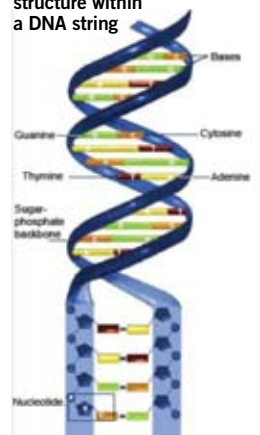


Figure 2: Intestinal Villi

“The problem is that foods rich in nucleotides are now rarely on our menu. Meat products from organs such as liver, kidney, intestines and lung are particularly rich sources of nucleotides, but are now rarely eaten.”

such as liver, kidney, intestines and lung are particularly rich sources of nucleotides, but are now rarely eaten. Modest vegetarian sources include yeast extract, mushrooms, broccoli and cauliflower. In the light of a widespread tendency to cut down on adequate animal-derived foods and the common low consumption of vegetables, it seems reasonable that our overall intake is substantially lower than in pre-industrialised times and populations where a hunter-gatherer-type diet was common. Adding nucleotide-rich foods or taking supplements derived from yeast may improve gut integrity, digestive processes and possibly diminish some food intolerances. It may also be relevant for patients of coeliac disease in helping speed up the recovery of the gut villi damaged by a gluten-containing diet.

There are a couple of contraindications for taking nucleotides as supplements; because of its purine content, people who are genetically predisposed to, have a history of, or suffer from gout are generally advised not to supplement nucleotides. Furthermore, the strong immune-enhancing effect prohibits the use of nucleotides for sufferers of auto-immune diseases and users of immune-repressive medications.

Nucleotides for athletes: improved recovery and muscle-to-fat ratio

Body tissue is constantly catabolised during training and competition and has to be rebuilt. Without prior physical training and concomitant tissue break-down, no muscle build-up, strength enhancement or performance improvements will occur. Furthermore, the more quickly cells are resynthesised after workouts, the faster and better will be the recovery. Tissues or cells with a high turnover rate such as the skin, gut-lining, white and red blood cells, as well as growing and recovery tissues, need a steady resynthesis of DNA

and high turnover rate of RNA. Particularly, in phases of intensive training, an additional supply of nucleotides through dietary intake is important. Nucleotides are essential for muscle function in different ways: besides protein synthesis, they improve oxygen transport and reduce the effects of lesions in the intestinal tract and muscles.

Hard physical training is a significant stress factor for athletes with various negative outcomes. For example, the levels of immunosuppressive substances like the stress hormone cortisol increase and thereby reduce the defence forces of our body. As a result, decreased levels of the important immunoglobulin sIgA have been found in athletes prone to physical stress. Nucleotide supplementation for 60 days significantly increased sIgA compared to a placebo. Additionally, in the liver and muscles, lower serum levels of stress indicators such as creatinase and lactate dehydrogenase were found after nucleotide supplementation versus the placebo, demonstrating improved recovery from physical stress.

Regarding lipoprotein metabolism, nucleotides are advantageous for endurance and strength athletes alike. Nucleotides are first transported to the liver where they promote the synthesis of protein instead of fatty acids, thereby optimising the muscle-to-fat ratio. This effect is not only significant for lean muscle build-up, but also for weight management. In conjunction with lipoprotein metabolism, effects of nucleotide supplementation have demonstrated increased levels of (good) HDL-cholesterol.

Dietary nucleotides offer pre-absorptive benefits in that they serve as fuel to the gut flora (e.g. bifidus bacteria), which improves intestinal health and nutrient absorption. Our gut is the organ with the highest immune capacity of the body. Therefore, a sufficient supply of nucleotides reduces the

incidence of intestinal infections. Improved gut health is positive on overall health in general. The absorption of all nutrients such as amino acids, minerals, vitamins and other micronutrients takes place in the gut.

NuCell@IM – a clinically tested nucleotide supplement

For the serious athlete, supplemental nucleotides may constitute the extra building blocks that are needed during times of extraordinary demand, such as during recovery from strenuous exercise or injury and as prophylaxis to prevent or overcome infections. Even the harmful effects on gut flora from antibiotics may be reversed more rapidly. In several studies*, supplemented nucleotides were shown to more rapidly restore reduced hematocrit values (red blood cell counts) which, in turn, improved oxygen supply and uptake.

One double-blind study demonstrated reduced cortisol values after 60 days of NuCell@IM supplementation compared to the placebo and pre-supplementation, along with improved sIgA levels. Cortisol is a stress marker and its reduction after physical exercise points to reduced exertion and improved recovery. Because cortisol is also a testosterone inhibitor, its reduction is also advantageous for protein synthesis and muscle build-up. As mentioned above, the increased sIgA values indicate a strengthening of the athletes' immunity. The measured differences on IgA and cortisol were highly significant ($p < 0.0001$) [1] and the results have been confirmed in another publication by the same authors (2).

An unpublished study done by McNaughton et al. with NuCell@IM found substantially enhanced (good) HDL-cholesterol of 15% vs. placebo and even a drop in the control group after supplementation for 60 days (see Figure 3). Additionally, slightly lower (bad) LDL-cholesterol levels were measured. Earlier studies on nucleotides

examined the influence on immunity with respect to cold and 'flu symptoms. NuCell@IM supplementation for 28 days reduced the symptoms of a common cold or flu infection or secondary infection: painful sinuses, earache, dry mouth, sore throat, muscle aches, and headache (3).

Much potential exists for the use of nucleotides in a sports person's supplement regime. By supporting a more rapid turnover of immune, digestive, muscle and blood cells, along with improving anabolic vs. catabolic drive, this "new" type of nutrient can be a real support to the training and recovery processes of a serious athlete. FSN

*Studies on nucleotides in athletes were undertaken at the University of Bath, with the supplement corresponding to NuCell@IM, manufactured by Swiss biochemical company Pro Bio Ltd.

REFERENCES

1. McNaughton et al (2006). The effects of a nucleotide supplement on salivary IgA and Cortisol after moderate endurance exercise. *J Sports Med Phys Fitness*. 46:84-89.
 2. McNaughton et al (2007). The effects of a nucleotide supplement on the immune and metabolic response to short term, high intensity exercise performance in trained male subjects. *J Sports Med Phys Fitness*. 47(1):112-118.
 3. Davidson et al (2002). A randomised, double-blind placebo-controlled Phase II exploratory trial to assess the effect of NuCell@IM supplementation on perceived symptoms of the common cold and markers of immune function. Queen Margaret University College, Dep. of Dietetics, Edinburgh, Scotland.
- Other Nucleotide studies:**
- Grimble, G.K. (1996) Why are dietary nucleotides essential nutrients? *British Journal of Nutrition*. 76:475-478.
 - Jyonouchi, H. (1994). Nucleotide Actions on Humoral Immune Responses. *Journal of Nutrition*. 124:138S-143S.
 - Uauy, R. (1994). Nonimmune System Response to Dietary Nucleotides. *Journal of Nutrition*. 124:157S-159S.
 - Van Buren C.T. (1994). The Role of Nucleotides in Adult Nutrition. *Journal of Nutrition*. 124:160S-164S.
 - Köppel, P. (2001). The Role of Nucleotides in the Body. Unpublished, Pro Bio, Switzerland.
 - Tanaka et al (1980). Improved Medium for Selective Isolation and Enumeration of Bifidobacterium. *Applied and Environmental Microbiology*. 40(5):866 ff.



About the author

Dr. Peter Koepel 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 year 2000.