An energetic view of nucleotides

Dr Peter Koeppel has written on his specialist topic of nucleotides several times for this publication before, but due to the ubiquitous physiological effects of these nutrients, each article is completely different. This time, he explores the contribution of nucleotides to the body's production of ATP.

Our body is a finely tuned machine and like all machines, it needs fuel. Our ability to run, bicycle, ski, swim, and row depends on the capacity of the body to extract energy from ingested food. The more efficiently the body can extract nutrients from food, the more energy it has at its disposal for the daily activities. This article shows you which organs, cells and organelles are involved in the energy generation and how nucleotides are involved in these processes.

Which organs, cells, enzymes and metabolic pathways of the body are involved in energy exploitation?

Food passes from the mouth to the stomach and intestine. At first, it is mechanically broken down and then digested through the action of enzymes. These enzymes are produced in the mouth, in the stomach and in the intestine. The biggest gland that produces digestive enzymes is the pancreas, which secretes enzymes for the small intestine. These enzymes break down protein, fat and carbohydrates into single amino acids, fatty acids and single sugars. The resultant single nutrients are then absorbed in the body through the intestinal wall and transported in the blood to the liver – here, a further processing of the nutrients takes place. Toxic substances are inactivated and excreted. The nutrients leave the liver via the blood stream and reach the different organs, and the cells of these organs absorb the nutrients as required. Within the cells, the important process of gaining the usable energy takes place in our mitochondria, where the transformation of glucose and fat into the usable form of energy, ATP, takes place. The mitochondria are the most important organelle in the cell for this energy production. In fact, they are the primary source of energy for your body.

What is the role of nucleotides in the extraction and supply of energy from food?

In the body, nucleotides rank as important molecules, such as proteins, fats, carbohydrates, minerals, vitamins and trace elements, but they are the least known or understood (1). Some people may be familiar with nucleotides in the context of genetic engineering, whereas others may know that nucleotides are the basic molecules of DNA, the genetic code of our body. But, all the other important functions of nucleotides are only recognised by specialists. Nucleotides are also required for:

- Protein synthesis.
- The coenzymes NAD(P)+, FAD, CoA etc.
- Metabolic regulation – intermediates in cellular communication.
- Activated intermediates in many biosynthesis – e.g. UDP-glucose → glycogen; CDP-diacylglycerol → phosphoglycerides; S-adenosylmethionine as a methyl donor.
- Energy supply for the body.

This article concentrates on highlighting the effect of nucleotides on the energy supply to the body. First of all, the body needs to convert food and deliver the simple nutrients.

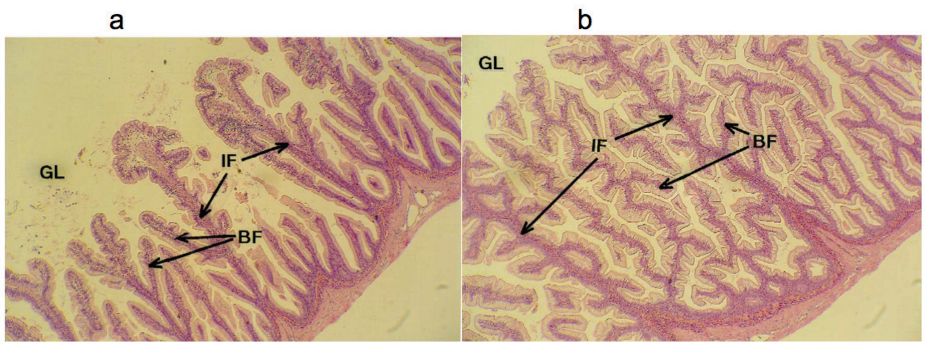


Figure 1 – Histological appearance of the distal intestine: a) control diet and (b) nucleotide diet.

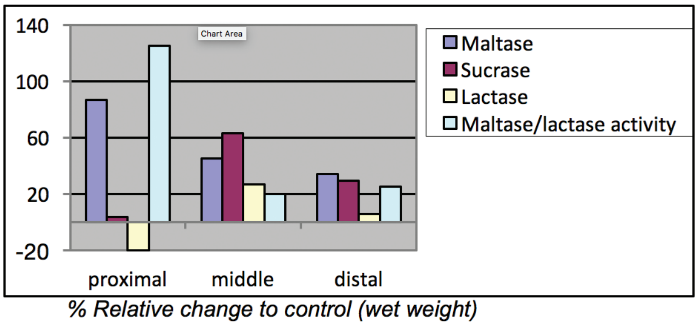


Figure 2 – Percentage change in brush border enzymes with nucleotide supplementation

The effects of nucleotides start in the mouth: in the mouth and later in the small intestine, digestive enzymes are secreted to break down nutrients, making them ready for absorption in the small intestine (2). It has been shown that the oral supplementation of nucleotides can enhance the formation of digestive enzymes (3, 4). As most of the enzymes are proteins, the code for these proteins is stored on the DNA in the cells. The translation and transcription from the genes into a protein needs several nucleotide components. All in all, five different nucleotide components are involved in this protein synthesis.

Additionally, supplementation of dietary nucleotides changes the gut flora (5) – by facilitating cellular regeneration, the number of bifidobacteria species is increased, leading to a lower pH in the intestine. As many of the important enzymes show their optimal activity in a low pH, the digestion of nutrients is therefore improved.

The next step is the absorption of the digested nutrients, which depends largely on the surface area of the small intestine. The average surface area of the small intestine is around 30 square metres. As illustrated in Figure 1, trials have shown that the surface area increases around 18 – 20 per cent after supplementation of nucleotides, leading to a greater area for absorption (6) – this leads to the body being better supplied with nutrients and energy. The supplemented nucleotides ensure adequate levels are available in the nucleotide pool in the crypt at the base of the villi, enabling the efficient cellular regeneration of epithelial cells.

All these positive physiological effects of nucleotides secure a better utilisation of the nutrients from our daily food, leading to a better supply of energy sources for the body. The most important sources of energy are:

- **Carbohydrates:** the fuel for muscles, nerves and brain.
- **Fats:** important for padding the inner organs and for the production of the elastic mantle of the cells.
- **Proteins:** for the production of muscles, skin, hormones and immune cells.

How is the digestion of carbohydrates the main energy source for the body?

The digestible carbohydrates, e.g. starch, are broken into simpler molecules by the enzymes in the saliva, in the juice produced by the pancreas, and in the lining of the small intestine. Starch is digested in two steps: firstly, salivary amylase in our mouth and pancreatic juice (containing dextrinase, glucoamylase and pancreatic amylase) break the starch into molecules called maltose; then an enzyme in the lining of the small intestine (maltase) splits the maltose into glucose molecules that can be absorbed into the blood. As shown in Figure 2, the activity of maltose is significantly increased by dietary nucleotides. The activity of brush border enzymes (maltase, sucrase and lactase) is improved after supplementation of nucleotides in different part of the small intestine (7).

Once absorbed, glucose is carried through the bloodstream to the liver, where it is stored or used to provide energy for the functioning and work activities of the body. It is further transported in the blood to the different organs, where it finally reaches the individual cells. Within the cells, glucose is oxidised in small steps to carbon dioxide (CO_2) and water, producing adenosine triphosphate (ATP) and other activated energy carriers. ATP can then be used for energy consuming processes in the body. It is also important to note that ATP is a nucleotide, which is an often over-looked fact.

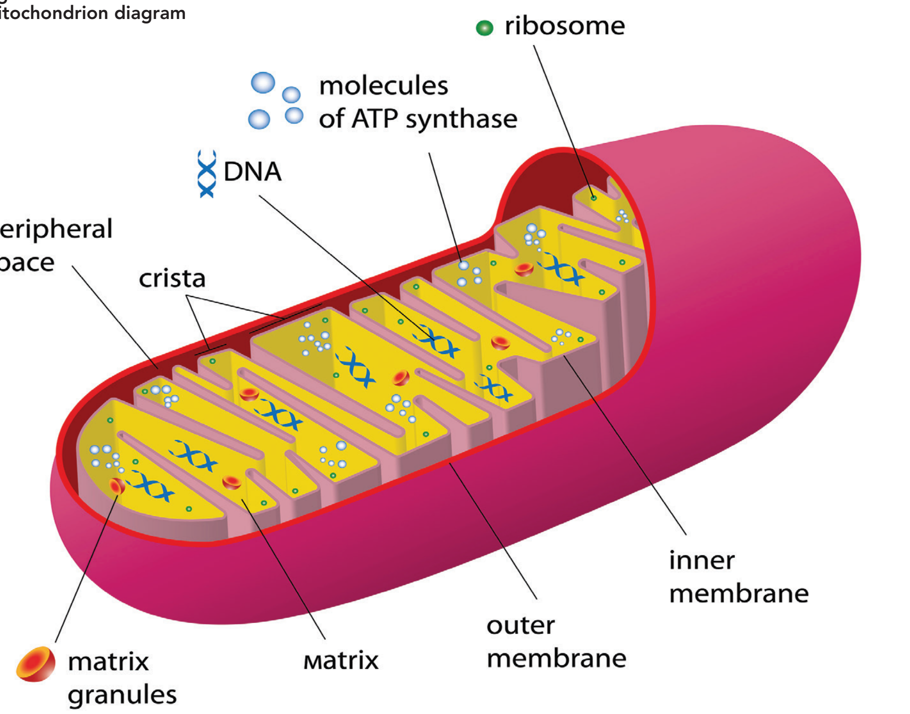
Glycolysis takes place in the cytosol, where glucose is broken down into pyruvate (8). This anaerobic process produces two ATP molecules and does not need oxygen. The following step of degradation (the aerobic respiration), in which the pyruvate is degraded to CO_2 and water, is oxygen dependent and happens in the mitochondria, producing 34 ATP molecules.

The amount of ATP that can be generated by the degradation of glucose is therefore highly dependent on the available oxygen. In an anaerobic situation, only a small part of the energy in glucose can be utilised. It is therefore important that the oxygen supply of the cells in the body is guaranteed – this is dependent on the number of red blood cells and haemoglobin in the body. It has been shown that the number of both red blood cells and haemoglobin is increased by supplementation of dietary nucleotides. During heavy physical exertion, with nucleotide supplementation the cells can stay longer in an aerobic state and are therefore able to produce more energy. In trials with racing horses, it could be shown that the uptake of oxygen and the expiration of CO_2 was increased, leading to a lower formation of lactate in the muscle (9).

Why are mitochondria so important for energy production?

Each cell contains around one billion ATP molecules. If needed, each ATP can be broken down to ADP and recycled three times per ➤

Figure 3 – Animal mitochondrion diagram



minute. This is only possible if the cell is healthy and enough oxygen is supplied. If not, energy supply is not only lacking for the muscle, but also for the production of proteins, hormones and enzymes. A large amount of ATP must be produced by the mitochondria every second of every day because ATP cannot be stored. This function is therefore so vitally important that mitochondria can take up as much as 25 per cent of the cell volume.

The average cell uses 10 billion ATP per day, which translates to the typical adult needing 3.0×10^{25} ATP. To accomplish this amazing performance, each ATP needs to be recycled from ADP 1000 times per day. Because the body cannot store ATP, the mitochondria must function consistently all the time.

Cells contain from 2 to over 2500 mitochondria (10). They're particularly important for your brain and muscles because they consume larger amounts of energy than other organs. In highly active muscle cells, the number of mitochondria can reach more than 5000. Mitochondria can multiple within the cells independently as they have their own DNA, the so-called mitochondrial DNA (mtDNA) (11). This mtDNA is typically a small circular double-stranded DNA molecule that encodes for a number of proteins and RNA, involved primarily in cellular respiration and cell reproduction. Compared to cell coding genes, mitochondrial DNA evolves about 10 times more quickly, allowing changes to be seen in a relatively short time. But, the speed and the degree of multiplication again are dependent on available nucleotides. Mainly under physical effort, the number of mitochondria in the muscle must increase quickly and therefore the need for supplementation of nucleotides also increases.

How is the energy used in the body?

- About 50 per cent of the ingested energy is transformed into heat.
- A small part is used for the excretion and repelling of dead cells.
- A big proportion is needed for the digestion of food.
- The rest is used to produce energy for the heart, for breathing and all physical activities.

The prime reason cells lose their energy-producing ability is that the powerhouses of the cells, the mitochondria, become dysfunctional due to nutritional deficiencies. Every organ, from the heart to the kidneys to the skin, every process in the body, from walking to breathing to immune function to vision, is driven by energy produced in the cell's mitochondria.

What are the outcomes of increased energy production in athletes?

In a trial, the peak force levels were analysed in a double blind, placebo controlled, cross over test after acute heavy resistance exercise (12). Ten male athletes underwent two supplementation and testing cycles, which were separated by a one-week washout period. The two treatment cycles consisted of a nucleotide or placebo supplement, with cycle order randomised and balanced.

As shown in Figure 4, the most important outcome of the study was that nucleotide supplementation increased the peak force in the back squat isometric force test immediately after the exercise and at 24, 48 and 72 hours later. The isometric force in supplemented athletes did not change after an acute heavy resistance exercise, whereas in non-supplemented athletes, the peak force was significantly reduced and they required 48 hours for full recovery.

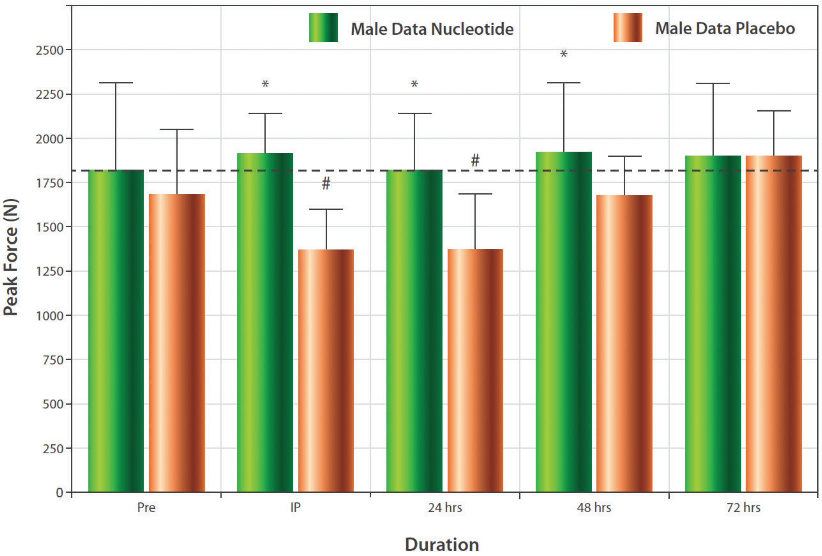


Figure 4 – Peak force in a back squat isometric force test with nucleotide versus placebo supplementation

In ongoing trails at Liverpool University, improved cardiovascular function was shown by reduced submaximal heart rates (164 beats versus 174 beats in the placebo trial) after the intake of a nucleotide supplement. Additionally, improvement in performance was shown by a faster sprint time over 35 meters (placebo 7.06 seconds vs. nucleotide 6.60 seconds).

Summary

Dietary nucleotides are needed for the entire process of generating energy from our food:

- Starting with increased production of enzymes in the mouth, the stomach and the small intestine – this ensures a full breakdown of food into absorbable nutrients, e.g. glucose.
- Next, the supplementary nucleotides improve gut flora.
- The increase of the inner surface area of the gut, which means that more of the digested nutrients can be absorbed.
- The improved functioning of the liver, where more nutrients are delivered into the blood stream.
- The improved supply of oxygen through an increased number of red blood cells.
- All this leads to a quicker and increased production of ATP, since there is a higher number of mitochondria in the cells. **fsn**

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PETER KOEPPEL, PKN AG, Switzerland 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. As managing director of Chemoforma Ltd and Pro Bio Ltd in Switzerland, Dr Köppel has, for over 20 years, led research and production of special nucleotide ingredients for both animal and human nutrition. This has led him to being seen as one of the world's foremost experts on nucleotides for health and performance. www.nucleotidenutrition.com

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