Nucleotides – the forgotten nutrients.

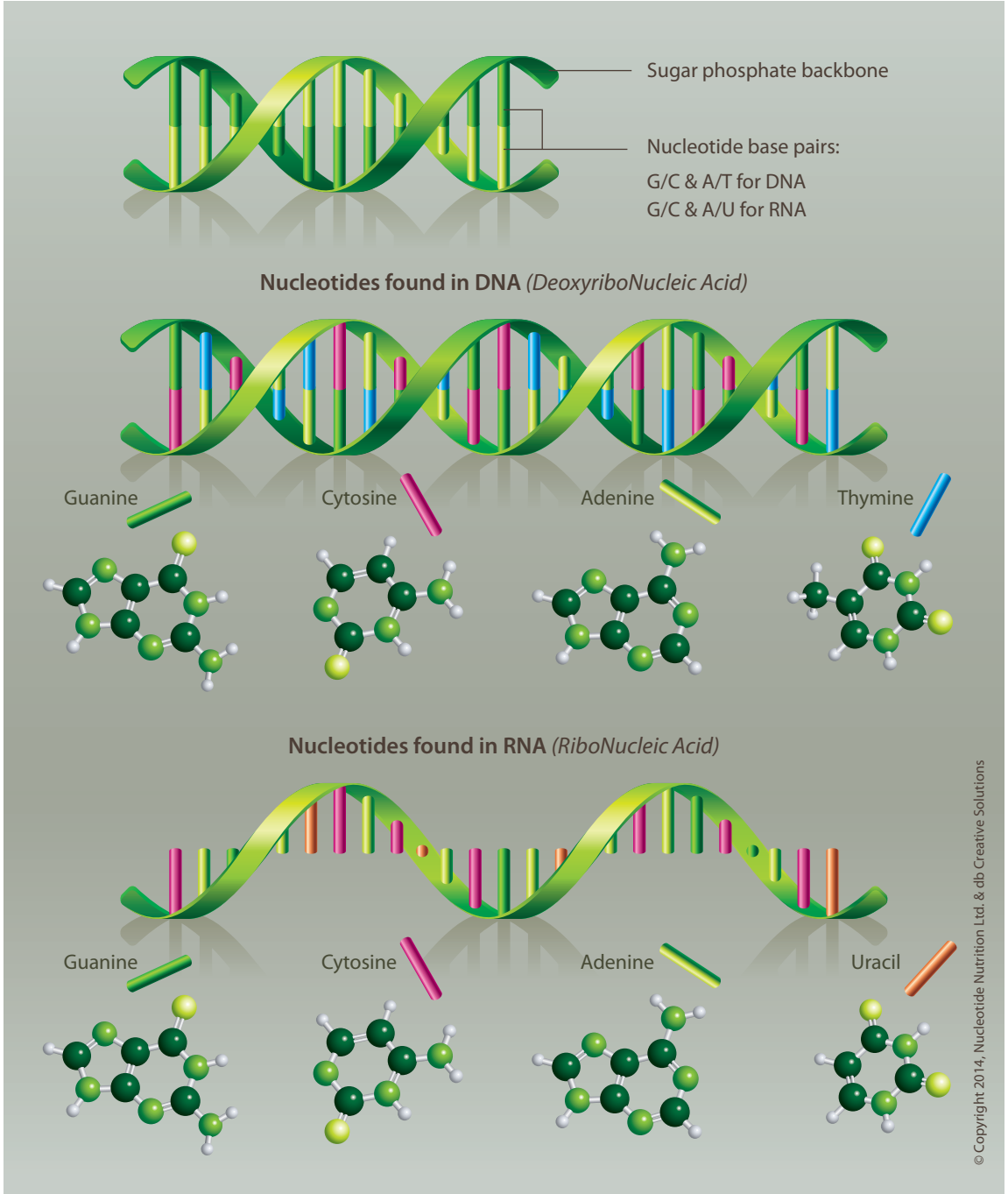
The science of nucleotides.

Produced by Nucleotide Nutrition Limited, UK
for the NTOI Conference (follow-up), Dublin 2019.

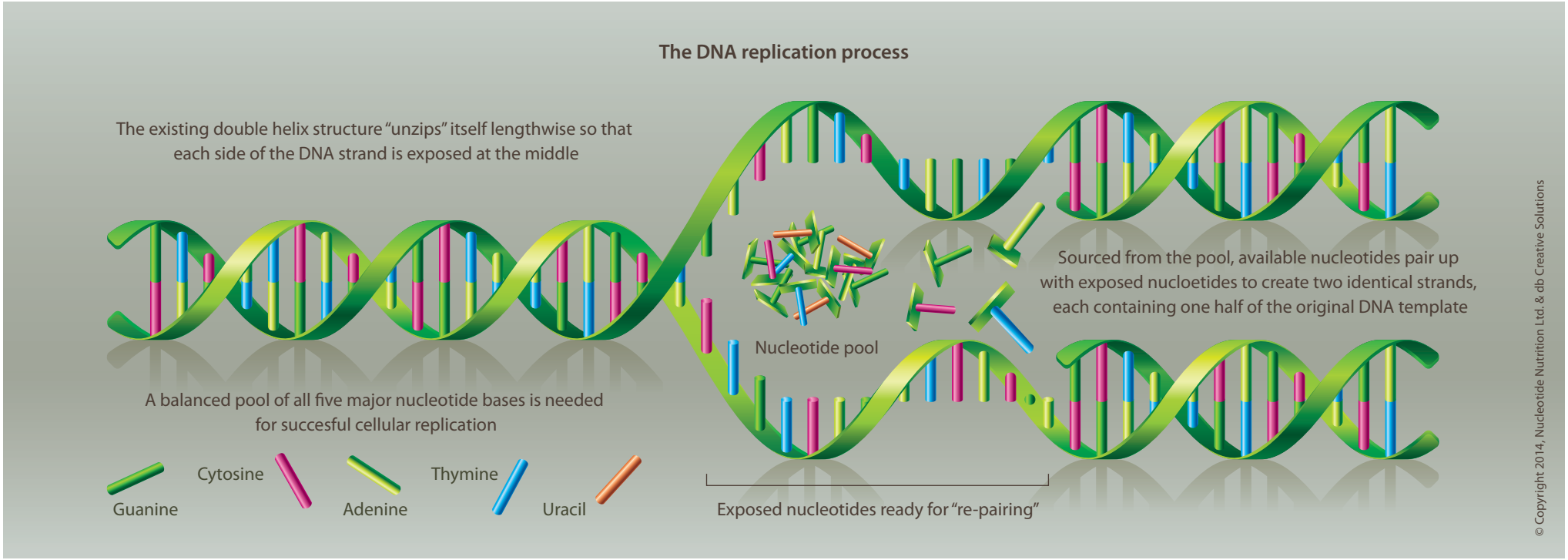
nucleotide
nutrition

Nucleotides – the building blocks of DNA and RNA

- Nucleotides have a major role in cellular development within the body, and an extremely important effect on the reactivity of the immune system.
- Nucleotides are most familiar as the building blocks of DNA/RNA.
- Nucleotide supplementation in a highly available form and added to the diet in a balanced way can have a significant effect on health.



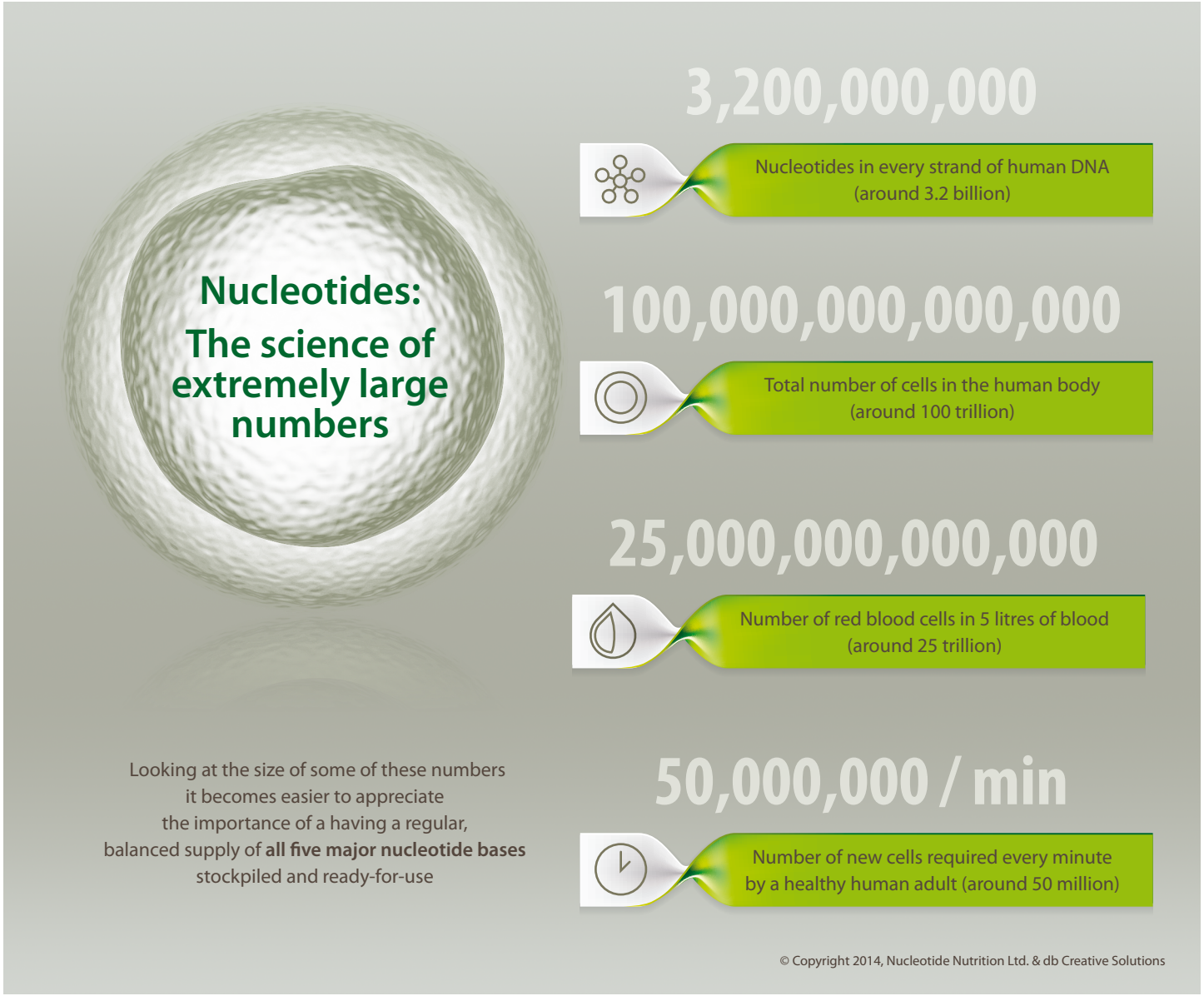
The science of nucleotides. *The DNA molecule consists of nucleotides in which the sugar component is deoxyribose and the RNA molecule consists of nucleotides in which the sugar is a ribose. The most common nucleotides are divided into two groups, called "purines" and "pyrimidines", based on the construction of their nitrogenous bases. In DNA, the purine bases include adenine (A) and guanine (G) while the pyrimidine bases are thymine (T) and cytosine (C). RNA includes adenine, guanine, cytosine, and uracil (U) instead of thymine (thymine is produced by adding a methyl to uracil).*



Nucleotides – new cell production

- The human body has a relentless demand for new cell production.
- The cells of our body are in a constant flow of formation and degradation.
- Nucleotides are further involved in all activities of our cells and metabolic processes.

The DNA replication process.
The existing double helix structure "unzips" itself lengthwise so that each side of the DNA strand is exposed. While unzipped, the two complimentary halves of the nucleotide pattern are exposed so that any freely available nucleotides can be matched up, in their relevant pairs, to create two identical versions, each containing one half of the original genetic template.



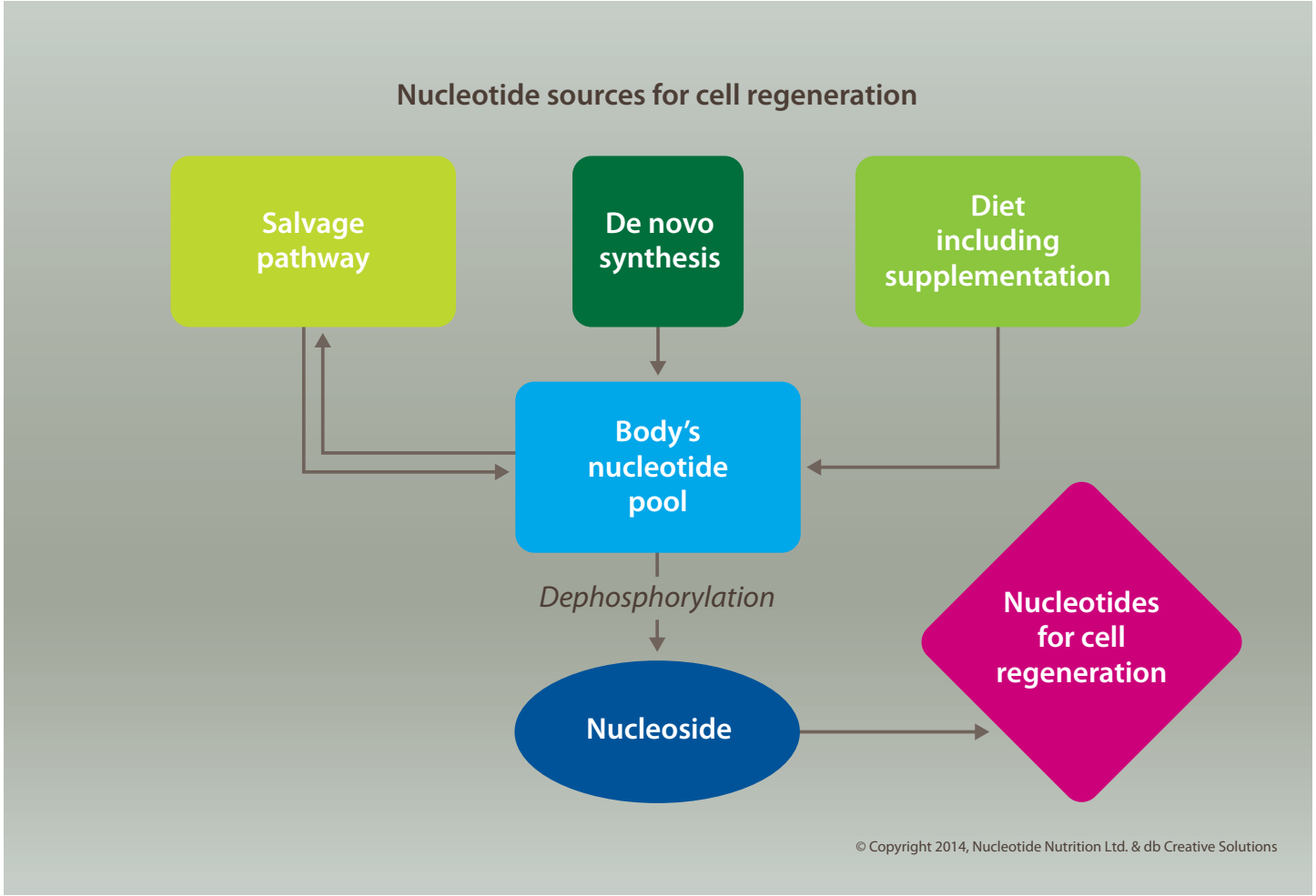
Extremely large numbers.
Some of the mind-boggling large numbers associated with human cellular and microbiology.

Nucleotides – a science of extremely large numbers

There are approximately 10^{14} (100 trillion) cells in the average adult human body.

With the exceptions of a few different cell types, such as red blood cells, each cell has its own copy, or often copies, of DNA.

So, consider: 100,000,000,000,000 cells x 3,200,000,000 nucleotides per cell, that's a truly staggering amount of nucleotides in the average adult human body. Many of these cells (approx. 100,000,000 per minute) are constantly requiring replacement, repair or regeneration; it makes it a little easier to appreciate the importance for the body to have a very good supply of all five nucleotides stockpiled and ready-for-use.



Sources of nucleotides for cell regeneration

There are four ways in which the human body can obtain the nucleotides that are essential for cell regeneration:

- synthesised in the body from amino acids or glucose
- salvaged from DNA and RNA degradation
- obtained through the diet
- taken in the form of a nutritional supplement

Why dietary nucleotides? *There are certain types of cells (cells that form the lining of the digestive system, 'good' bacteria in the intestinal tract, white blood cells of the immune system, and red blood cells) that must complete their requirement for nucleotides from dietary sources.*

Absorption of 'food' nucleotides in the gut

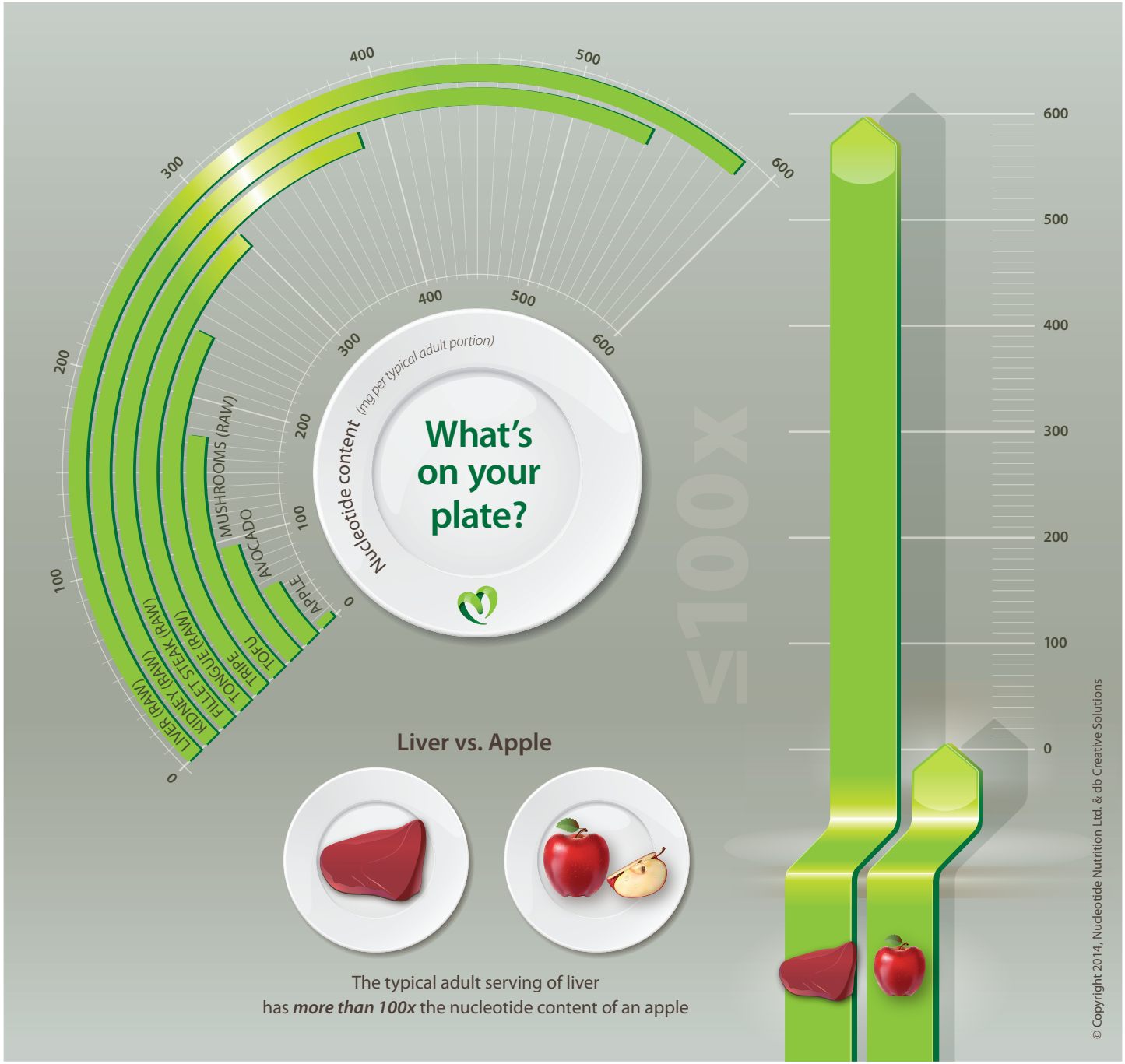
The uptake of nucleotides from food is restricted because nucleic acids in the cells are well protected.

There is only 5–15% uptake.

Absorption of pure nucleotides in the gut

Supplemented nucleotides that are freely available (unprotected) have a much superior absorption in the gut.

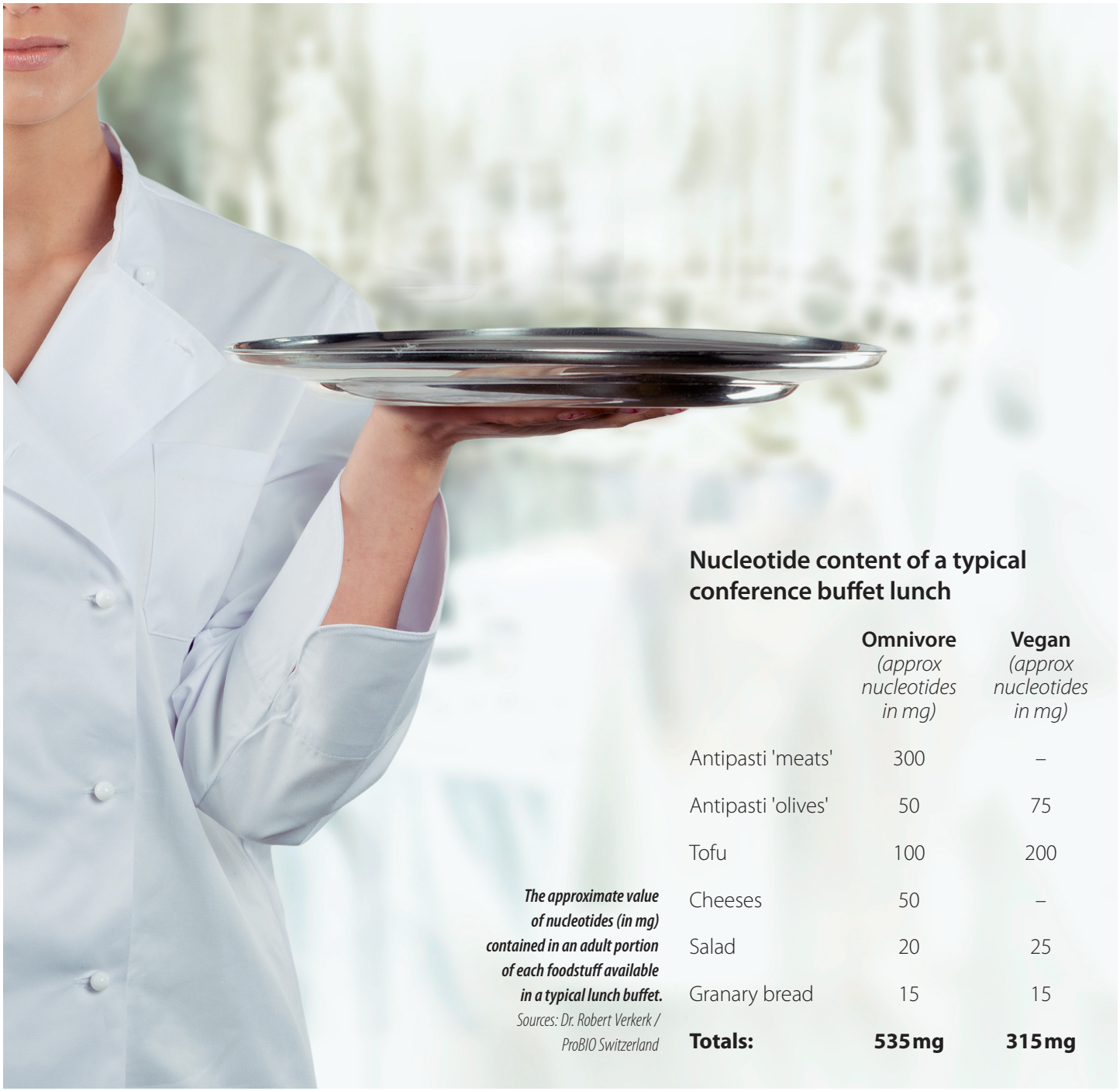
Uptake is 80–90%.



The low nucleotide content of our modern diet

- Nucleotides are found in low levels with a low bio-availability in today's modern diet e.g. vegetables, fruits, meat, fish and milk products
- Nucleotides are found in their highest concentration in offal type-foods: intestines, kidney, liver – all staple foods from our evolutionary past that were present in post-war diets
- Over 80% of nucleotides sourced from food are of the purine form. This means that dietary deficiencies of nucleotides are generally of the pyrimidine form.

What's on your plate?
The results reveal some dramatic differences in the likely nucleotide intake again pointing to the highest contents in offal-type (or organ) meats that are far less likely to be found on dinner plates today.
Source: Chemoforma/Pro Bio.



Nucleotide content of a typical conference buffet lunch

	Omnivore *(approx nucleotides in mg)*	**Vegan** *(approx nucleotides in mg)*
Antipasti 'meats'	300	–
Antipasti 'olives'	50	75
Tofu	100	200
Cheeses	50	–
Salad	20	25
Granary bread	15	15
Totals:	**535 mg**	**315 mg**

The approximate value of nucleotides (in mg) contained in an adult portion of each foodstuff available in a typical lunch buffet.
Sources: Dr. Robert Verkerk / ProBIO Switzerland

Nucleotides – what a typical buffet lunch plate delivers

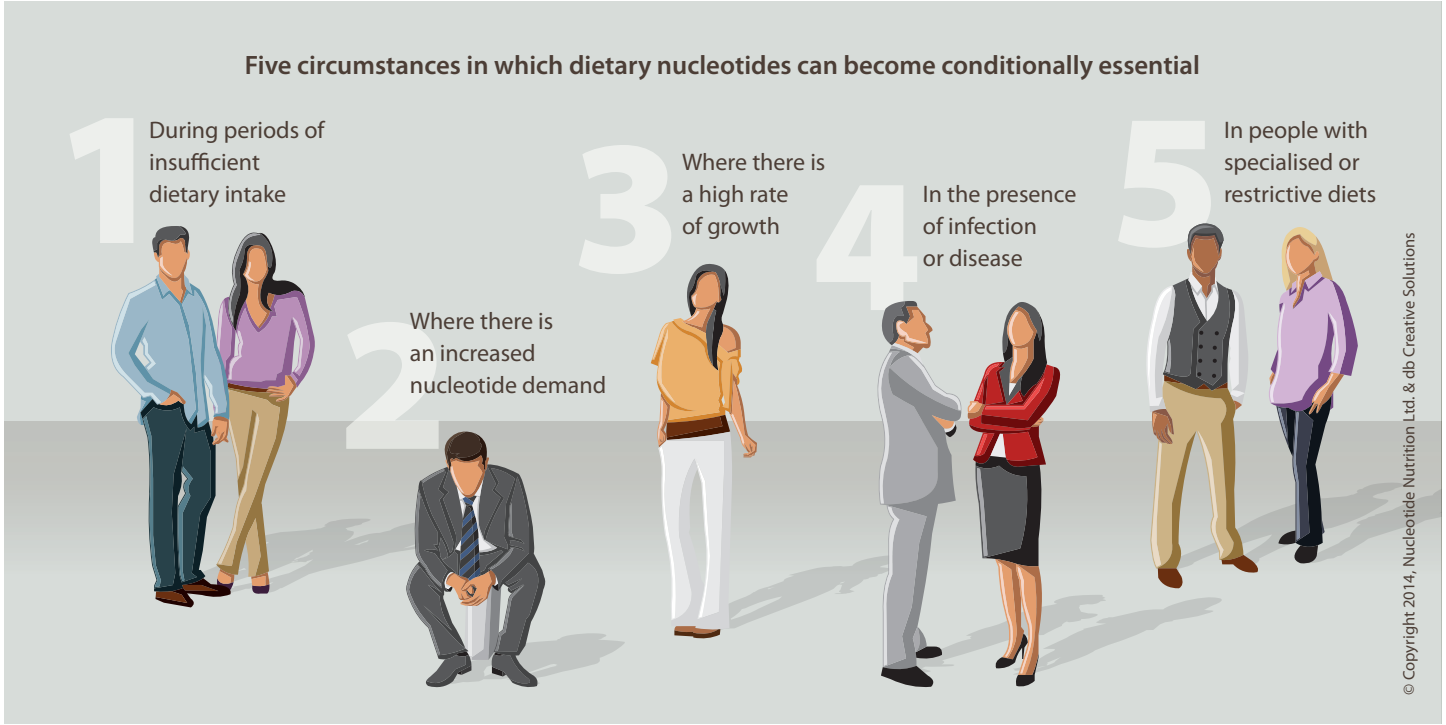
- Dietary nucleotides are essential for the short-lived gut lining, gut flora, and bone marrow cells
- dietary nucleotide requirement for healthy living is a minimum of 1500 mg "balanced" nucleotides per day
- any shortfall results in the body expending energy in order to recycle or produce "de novo" its nucleotide requirement. Resulting in fatigue and ill health due to a slow response of the immune system and a poorly maintained gut lining
- 80% of the nucleotides from food sources are of the purine type
- supplementary nucleotide absorption (approx 85%) is more efficient than 'food' sourced nucleotides (around 15%)
- Providing dietary nucleotides in a purified form, especially the pyrimidine types, leads to a swift response

The effects of dietary simplification

There is now widespread recognition among scientists that dietary simplification, along with associated factors including the industrialisation of the food supply chain, is contributing to an increased incidence of preventable chronic, inflammatory diseases, which now places the greatest burden on healthcare systems the world over.

Poor food choices and other contributing factors of today's modern, hectic lifestyle, including increased physical inactivity and consistently high levels of chemical, physiological and immunological stress only serve to exacerbate the problem.

Due to these dietary, lifestyle and stress related demands on the body's nucleotide pool, that simply cannot be met by internal synthesis or salvage alone, the optimum daily requirement for dietary nucleotides is estimated to be well over one thousand mg/day for adults.



Supplementary intake, for many, remains one of the few reliable methods of ensuring a good balance of relevant nucleotides. This is especially the case if intake is to be achieved consistently; as the body needs on a daily basis, week in, week out, year after year.

Above all else a healthy, varied diet and regular exercise are always the best solution but there are certain circumstances, encountered in everyday life, in which dietary nucleotides can become thought of as "conditionally essential".

The 5 main circumstances in which dietary nucleotides become conditionally essential *during periods of insufficient intake, where there is a high demand, where there is a high rate of growth, in the presence of infection or disease, and in people with specialised or restrictive diets.*

Other important roles of nucleotides

Transfer of energy
ATP is the universal energy source together with GTP/UTP

Hormone signals
c-GMP in signal transduction and translation.

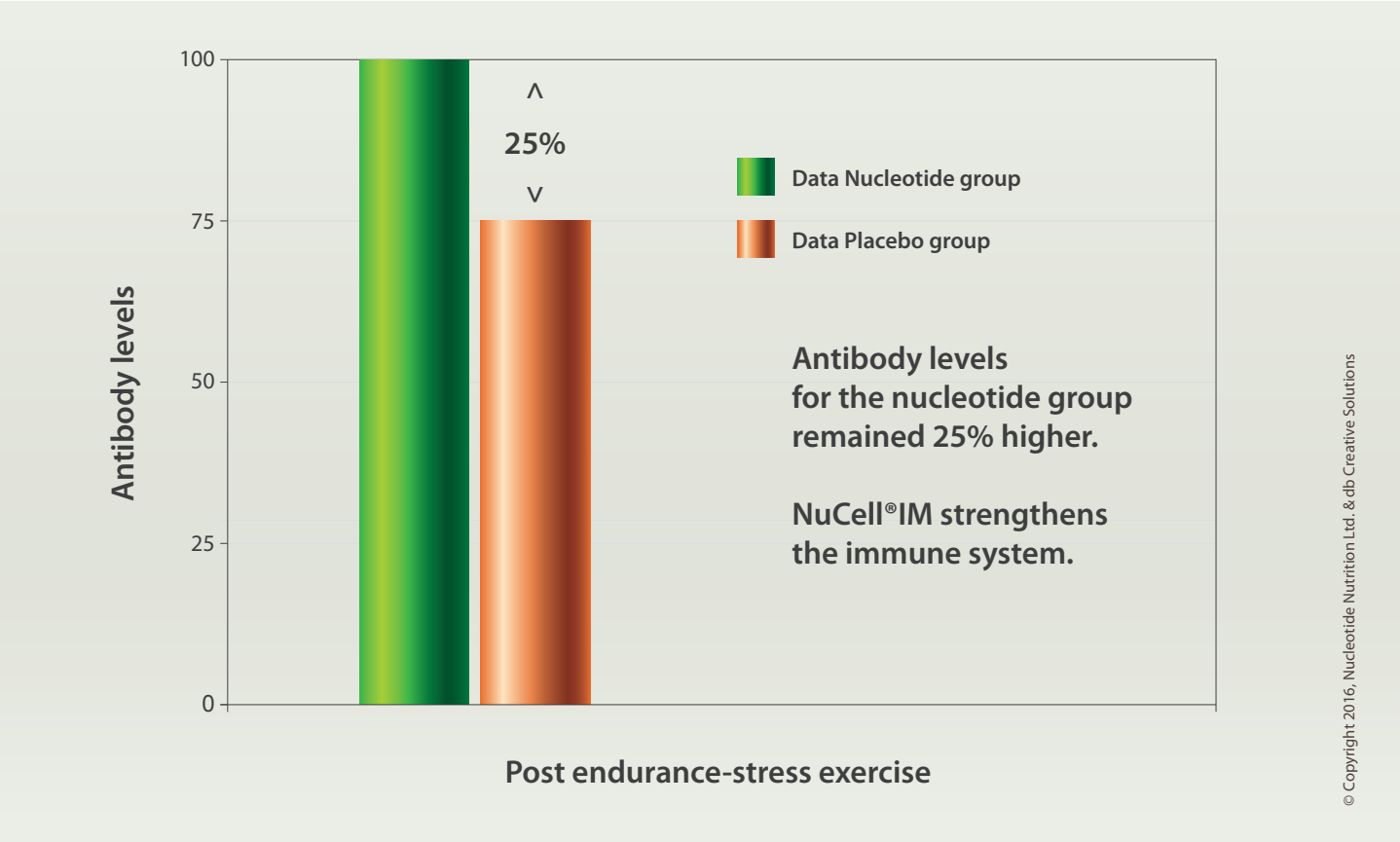
Protein synthesis
The first step is often the limiting step in the protein synthesis because of a lack of nucleotides. UTP and CTP are vital intermediates in the synthesis of pyrimidine sugars and lipids involved in protein glycosylation and membrane biosynthesis.

Tissue repair (wound healing)
The first step in wound healing is the cleaning of the wound through macrophages. Considerable amounts of ATP are turned over daily in wound healing.

Intestinal flora
Nucleotides are growth factors for various species of bifidobacteria or act to promote the release of other growth factors into the intestinal lumen.

Gut integrity
Effects of nucleotide supplementation on gut cells (within 3 weeks):

- 25% higher villi
- Increases in mucosal surface area of the gut
- Enhanced vaccination efficacy

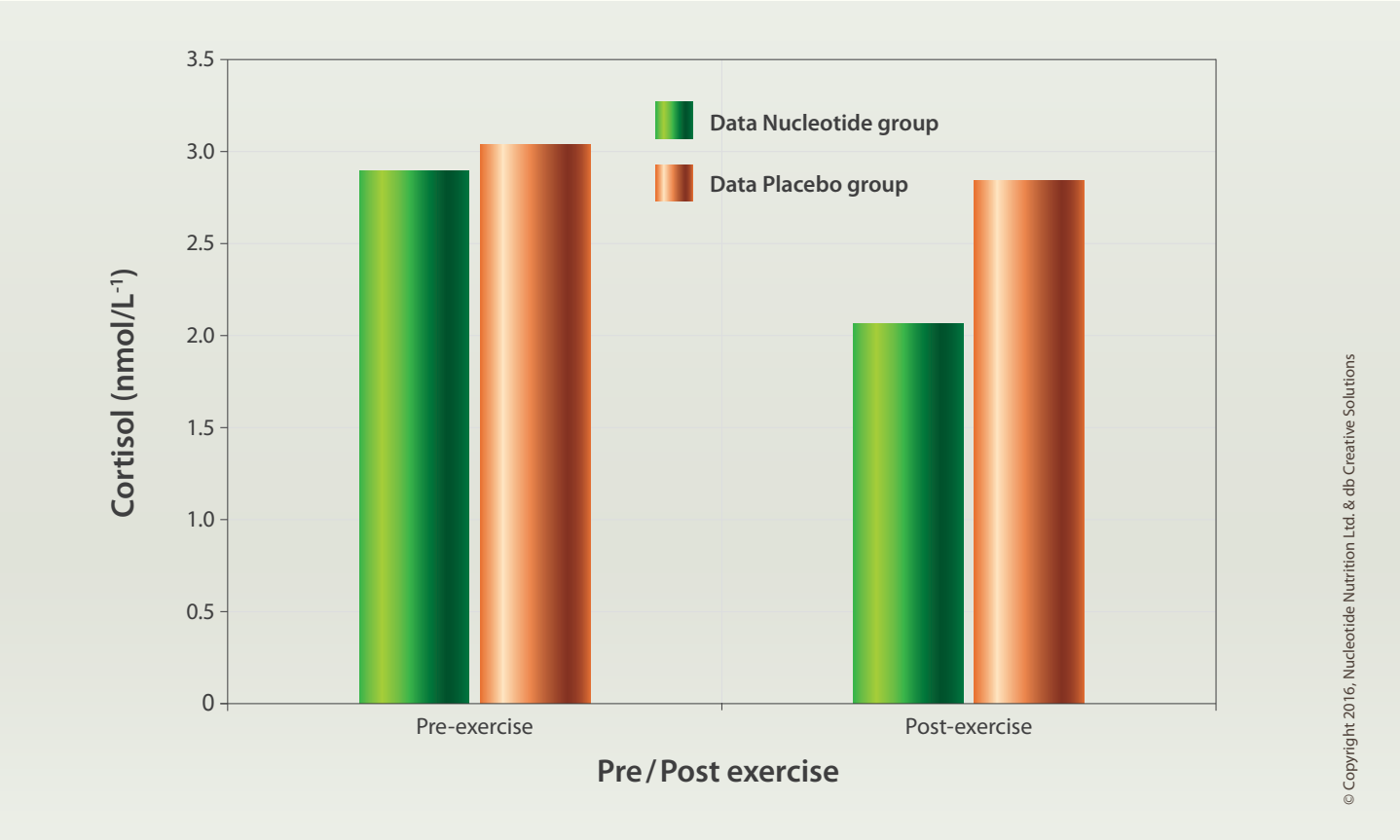


A double-blind randomised placebo -controlled trial.
McNaughton et al.

Nucleotide nutrition – important immunological effects

The effects on the immune and metabolic response to short-term, high-intensity exercise

- Reduced immune suppression following intensive exercise
- Seen by SIgA levels for the nucleotide supplemented athletes remaining 25% higher than the placebo group after exercise



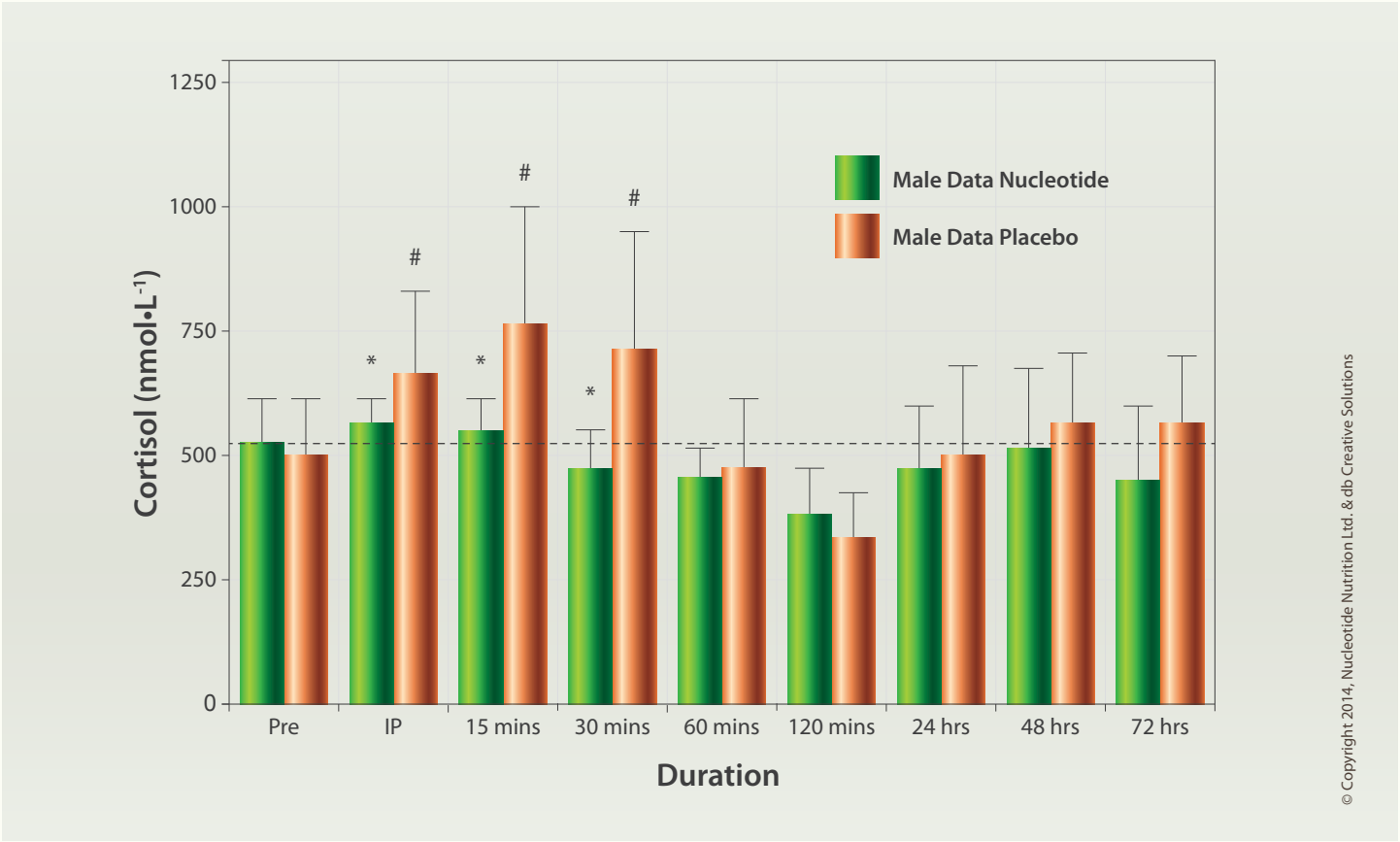
A double-blind randomised placebo -controlled trial.
McNaughton et al.

Nucleotide nutrition – important effects on cortisol

(high-intensity exercise)

The effects on the immune and metabolic response to short-term, high-intensity exercise

- Significantly reduced salivary cortisol following periods of intensive exercise in the supplemented group
- Cortisol levels for the nucleotide supplemented athletes remaining 28% lower than the placebo group after exercise



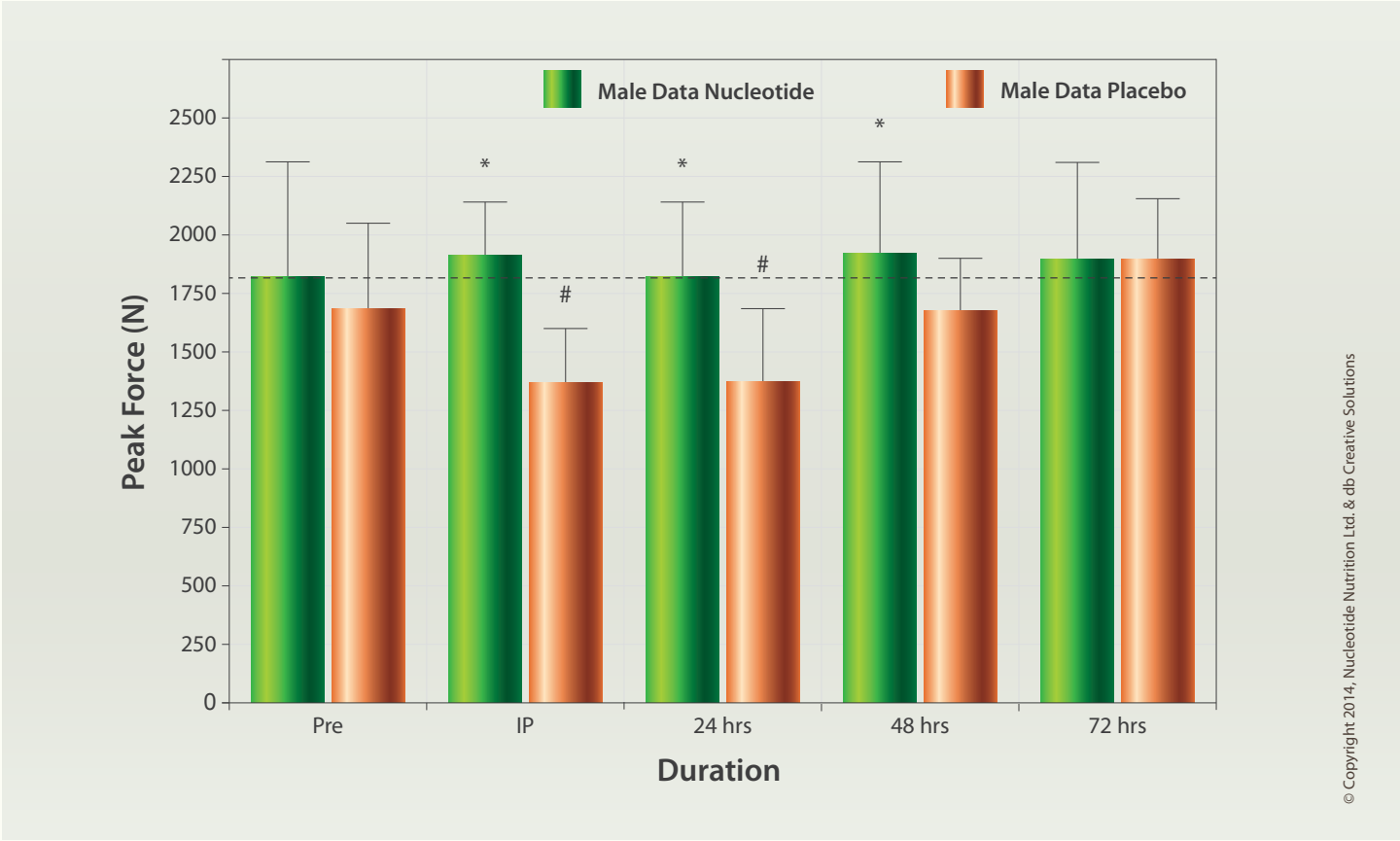
A double-blind randomised placebo -controlled trial.
Sterczala et al.

Nucleotide nutrition – important effects on cortisol

(resistance exercise)

Effects of nucleotide supplementation on resistance exercise stress (males)

- The cortisol levels of the supplemented group at 15 & 30 mins after exercise were significantly lower than the placebo group.
- The cortisol levels of nucleotide supplemented athletes remained on roughly the same level, a significant increase can be observed in the placebo group up until 60 mins after exercise.



A double-blind randomised placebo -controlled trial.
Sterczala et al.

Nucleotide nutrition – important effects on performance and recovery

Effects of nucleotide supplementation on resistance exercise stress (males)

- Results in supplemented athletes did not change after acute heavy resistance exercise, whereas the peak force of non-supplemented athletes was significantly reduced and they required 72 hours for full recovery.
- It can be postulated that the supplementation of nucleotides reduces exercise-induced muscle damage.

Nucleotides – the forgotten nutrients

In summary

- Nucleotides, both pyrimidine and purine forms, are essential for all activities of our cells and metabolic processes.
- There are five different Nucleotides used as the building blocks for cellular DNA and RNA.
- The human body has a relentless demand for new cell production.
- There are four mains ways that body obtains its nucleotide requirement: *De novo, salvage pathway, the diet, and supplementation*.
- Dietary nucleotides are essential for cells of the gut lining, 'good' gut flora, and bone marrow cells (white and red blood cells).
- For healthy living there is a daily requirement of over 1500mg of dietary nucleotides.
- The modern Western diet rarely includes food sources high in nucleotides, esp. offal meats. Vegan/vegetarian meals rarely reach 400mg nucleotides.
- Nucleotides from food sources are low in Pyrimidine nucleotides (less than 20% content) and are not efficiently absorbed (around 15% uptake).
- This creates a deficiency, that leads to fatigue, a sluggish immune response and breakdown of the gut lining.
- This impact on health can be resolved by supplementation with purified nucleotides, which are absorbed efficiently in the gut.
- Five circumstance in which dietary nucleotides become conditional essential, and supplementation advisable: *Periods of insufficient intake, high demand, high growth rate, presence of infection or disease and restrictive diets.*
- The efficacy for nucleotide supplementation includes published clinical studies covering stress, immune response, gut health and recovery/performance.

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For more details of the papers and articles listed here plus an ever growing number of additional published works relevant to the subject of nucleotides visit our web site or contact Rachel Hoyle, CEO, directly using the details above.

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