



Nutraceuticals and the Genomic Revolution

Addressing the nutraceutical
industry's shift to a
science-paradigm



Nutra Biosystems

A DIVISION OF INVIVO BIOSYSTEMS

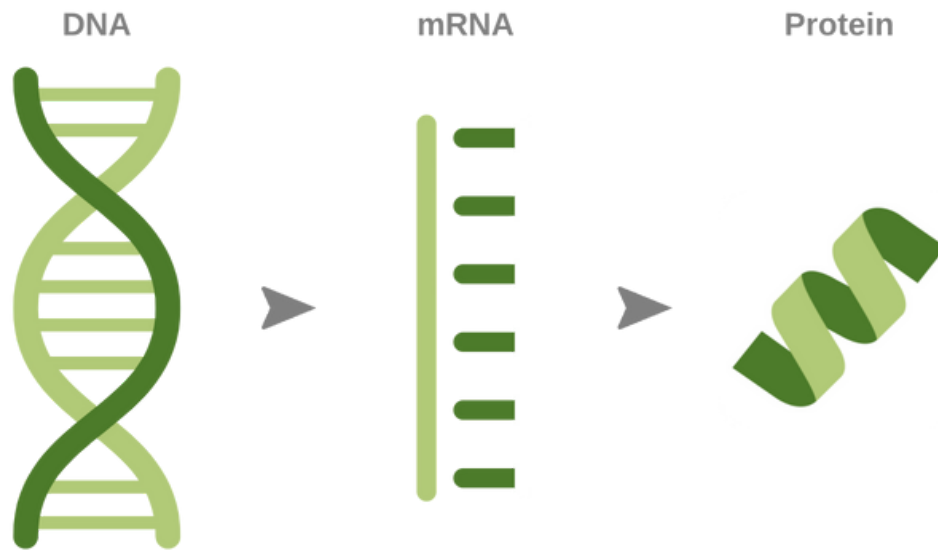


Figure 1. The Central Dogma of Biology. In the Central Dogma, The DNA is first transcribed into a messenger RNA (mRNA). Next, the mRNA is translated into protein which then participates in the cellular signaling pathways of the cell.

When the human genome was sequenced in the early 2000s, it promised to change the field of biomedical research by providing better insight into the human body and how drugs and other substances affect us. Perhaps surprisingly, the genomic revolution has also greatly impacted the nutraceutical industry – scientific data began entering public consciousness and consequently, consumer interest in nutraceutical products have skyrocketed, but these customers have also begun demanding more research to back-up product claims.

So, in this rapidly growing, competitive market, how can you leverage scientific studies to increase your customer confidence, attract new investments, develop new products, and protect your intellectual property (IP)?

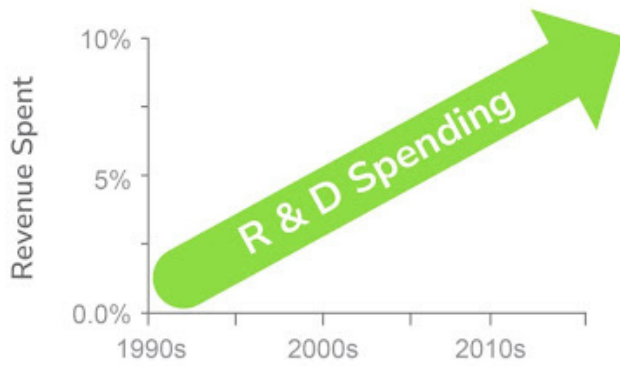


Figure 2. Nutraceutical companies are spending more on R&D. In the past, only 0.5% of the total revenue was invested in R&D, now up to 10% is invested in research and development.

82%
of people don't trust
nutraceutical companies

71%
of people don't trust
pharmaceutical companies

Source: Internal Survey, Mikra Cellular Sciences, Inc.
n=9,904

The Changing Landscape of Nutraceuticals

There is growing demand, from both customers and regulators, for nutraceuticals to provide proper substantiation of their safety and effectiveness. Consequently, the nutraceutical industry is experiencing a rapid shift - adopting a science paradigm in the belief that research will ultimately strengthen marketing efforts and provide businesses a competitive advantage [1].

To this end, a growing list of brands are insisting on launching products based on true innovation, proprietary science and finished product-specific data [2]. Beyond safeguarding from problems in post-market claims, and lending nutraceutical products legitimacy, the scientific evidence obtained from the R&D effort can also be used to generate new IP and secure market exclusivity.

One of the genomic advances that is fueling innovation in the nutraceutical industry is next-generation sequencing technologies. Applying these sequencing technologies can enable a better understanding of the mechanism of action (MoA) of a product, and effectively identify genetic signatures associated with health concerns such as longevity, healthy aging, immunity, inflammation, brain health, and gut health.

Finding the needle in the haystack

Next-generation sequencing works by conducting massive parallel processing, and is able to detect the changes in gene expression when exposed to a compound or formulation [Figure 3.]. This incredibly powerful new technology is a high-throughput, scalable, fast method of identifying common and rare genetic variation, however, its main advantage - its ability to simultaneously analyze the entire genome - is also its main disadvantage as it can be difficult to interpret this amount of data and find the valuable information pertaining to your product, formulation or compound.



Figure 3. Genetic analysis for MoA. When exposed to a compound the differences in gene expression for 10 genes are shown (small differences, big differences, no differences and inverted differences).

First, gene expression profiles can be made by ranking the changes in gene expression [Figure 4]. By clearly seeing the pattern in gene expression, a study can focus in on a set of genes or gene modules that affect a certain cellular signaling pathway - pair down the data to look at the particular molecular mechanisms involved.

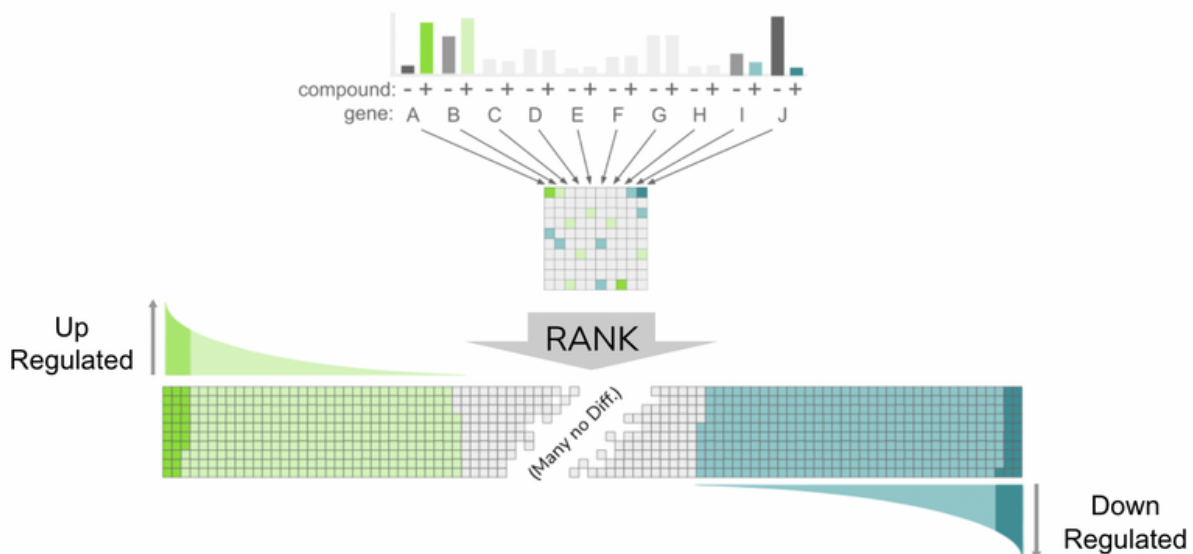


Figure 4. Genetic analysis expanded to the entire genome (20,000 genes), resulting in a mountain of data. Ranking the genes into upregulated, down regulated, and no difference of expression makes the data more interpretable.

Once the genes of interest are identified, a preclinical study can be conducted. While in the past mammalian animal models were most commonly used in preclinical studies, there has been a rise in alternative model organisms such as the zebrafish, *Drosophila melanogaster* (fruit fly), and *C. elegans* (nematode) as they offer fast, cost-effective ways of modeling. Most importantly, while these organisms are different from humans in many ways, the genes involved in human diseases are strikingly conserved. We at Nutra Biosystems utilize the zebrafish and *C. elegans* models, which have a version of the human related disease gene, a homolog, for 84% and 98% of disease-related genes respectively [Figure 5].

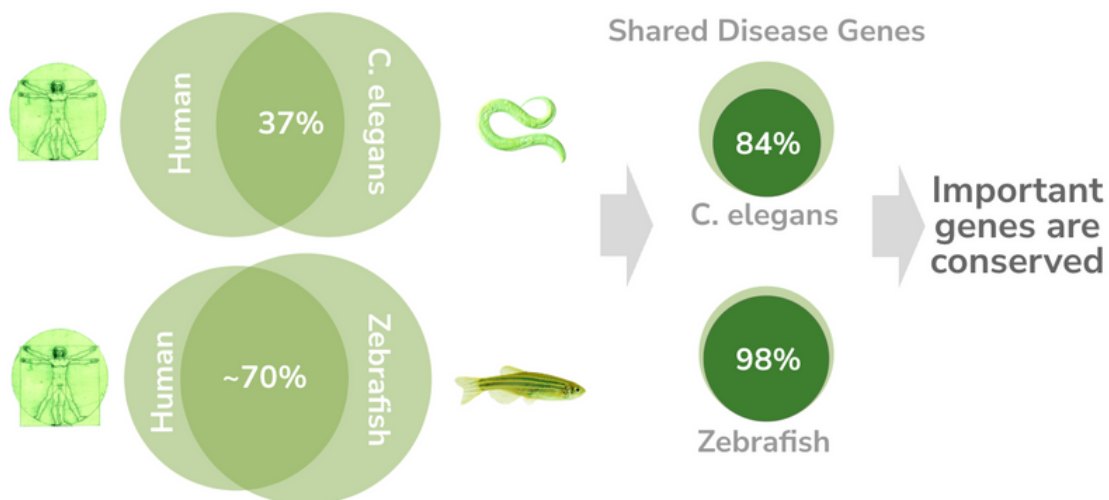


Figure 5. Overall, humans' genes differ from *C. elegans* and zebrafish genes. However, genes important in human disease are highly conserved in *C. elegans* and zebrafish .

Finally, these models can undergo an assay or *in vivo* study [Figure 6] which can inform a nutraceutical company of how the model system responds to activation of a cell signaling pathway. In turn, formulators can fine-tune their products and be more informed about what claims their products can make. For example, a compound could be found to affect the healthy aging pathway that is conserved in both humans and model system, leading to a claim of 'supports or promotes longevity'.

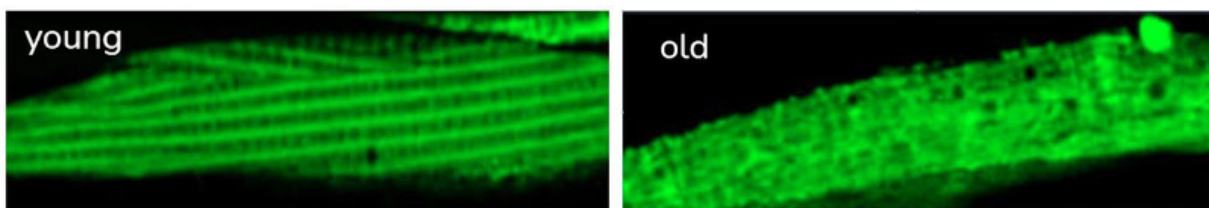


Figure 6. Highly ordered mitochondria in young *C. elegans* muscle tissue (left) versus disorganized mitochondria in old *C. elegans* muscle tissue (right) (PMID: 34211399).

Case Studies: How companies are currently utilizing “Omics” data

The ability to look at all the gene expression changes in an animal can also be referred to as “transcriptomics”. This and other “omics” technologies (e.g., proteomics and metabolomics) in which all the genes, proteins, or metabolic products in an animal are examined at the same time - have been born out of the genomic revolution and have only been possible for a few decades. Yet, they are already making a significant impact on nutraceutical compound studies. Currently, these tools are being used to create patent-protectable formulations, attract investors, and build better branded ingredients.



Using gene expression analysis to determine healthy-aging effects

One company engaging with us to use omics data is Mikra, a biosciences and consumer wellness company. Recently, Mikra issued a press release, announcing that it is launching a novel cellular therapeutic compound targeting systemic fatigue, “CELLF.” This product works by aiding in the creation of mitochondria, increasing their efficiency, which combats systemic fatigue, inflammation, and brain fog. It also promotes the upregulation and downregulation of certain cellular detoxification pathways.

Prior to bringing this product to market Mikra wanted to file for patent protection and reached out to our team at Nutra Biosystems to conduct a preclinical study, supplying the scientific data needed to back up their products’ claims.

Next-generation sequencing can be used to identify potential health concerns. For instance, we may find the Mikra product is stimulating healthy aging and inhibiting inflammation [Figure 7].

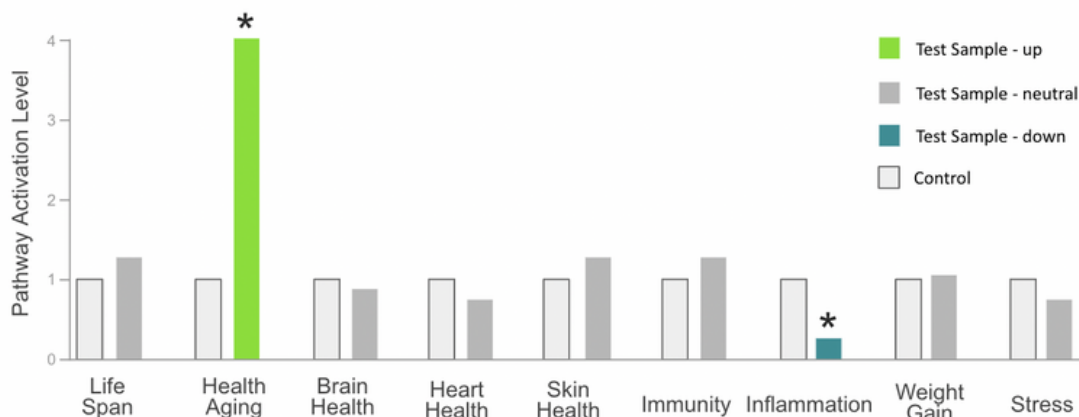


Figure 7. Genetic analysis for MoA and Functional Test for Mikra - cluster of upregulated gene modules in mitochondrial health, healthy aging pathways.

If effects in healthy aging are observed, we can next test the effect of CELLF on healthy aging. We look at the mitochondria in *C. elegans* as they age and compare the worms that are treated with CELLF and those that are not. As you age your muscles atrophy, *C. elegans* experience a similar breakdown of their orderly mitochondria structure overtime [Figure 8]. When treated with effective aging products, however, the worms retain their mitochondrial organization. With data from a preclinical mitochondrial-integrity study, Mikra will enhance their product launch, add more patent protection to their branded formulation, and become more confident in their marketing claims.

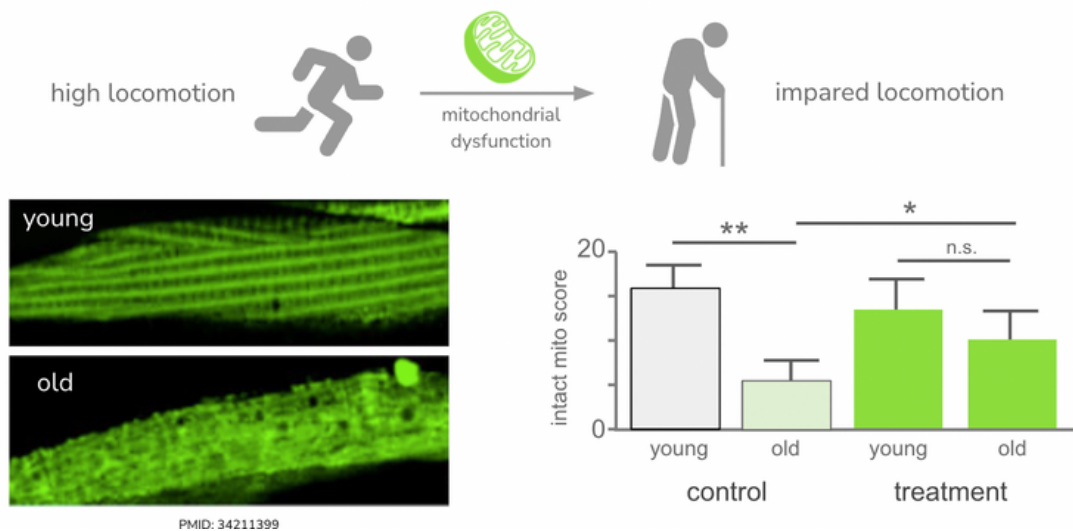


Figure 8. Treatment of Mikra’s CELLF product results in a less fragmented mitochondria.

Mikra’s founder and CEO, Faraaz Jamal, explained why he thinks investing in scientific data is essential for his company, saying that “health and nutrition technology has come so far, yet the [general] population is suffering and it’s only exacerbated by mistrust, confusion. The term snake oil is often attached to nutraceutical companies, and so it’s never been more important to be data-driven and transparent.”



Exploring/determining potential anti-aging effects in a novel compound using RNA Seq analysis

Thaena has developed a novel postbiotic, Thaenabiotic, which is the first fecal-derived, full-spectrum, sterilized product of its kind. While Thaena has been using their product in clinics for several years to support a balanced microbiome, they wanted to explore other potential applications for this product. To support any additional health claims, and attract another round of investment, Thaena needs the science-based evidence that a preclinical study can provide.

C. elegans are widely recognized as an excellent longevity model, in part because their short lifespan (3-4 weeks) means that a study can collect data over their entire lifetime. Using a longevity assay, we explored whether a particular compound or formula is having an impact on a whole population of animals - a question which has been historically difficult to answer as this type of study isn't feasible on humans. Like the numerous longevity studies we have completed for many clients, we will be testing Thaenabiotic for its anti-aging effects in *C. elegans* by monitoring their daily movement for their entire life. In this lifetime analysis, we will be able to determine whether those treated with Thaena's formulation stayed healthy and active longer.

Additionally, these types of studies are particularly helpful in product development. For instance, we can examine whether individual compounds can act synergistically when combined, producing an effect which neither compound can achieve when taken alone [Figure 9].

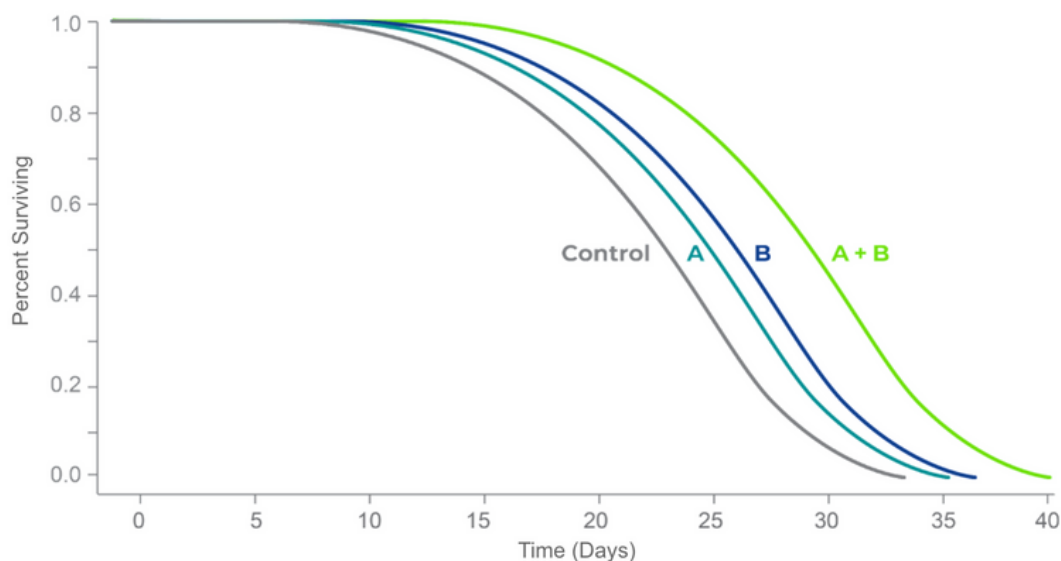


Figure 9. Testing anti-aging effects for a formulation. Ingredients A and B of Test Sample have synergistic effects on healthy aging. Together they provide the scientific evidence that the combination is better than A or B alone in allowing a model organism to be more active later on in its life.

The Nutra Biosystems Approach



Figure 10. Example of how Nutra Biosystems can work with nutraceutical companies (in this case Thaena) to provide the needed data.

The future of assessing natural products

The advancement in sequencing technology and genetic analysis has opened the door for future innovation in nutraceuticals. The studies discussed in this paper provide nutraceutical companies with the scientific evidence needed to patent their product, attract new investment, and create new, synergistic, formulations. Moreover, these studies enable nutraceutical companies to determine which of their compounds or formulations are most promising - and thus, whether it is worth pursuing a clinical study.

The widespread adoption of these robust preclinical studies in the nutraceutical industry will benefit both companies and consumers, ultimately producing more competitive, efficacious products while gaining consumer confidence and trust.

References:

- [1] Sept. 01, 2005 by Rebecca Wright, Nutraceuticals World
- [2] August 31, 2018 by James Gormley in NIE 2018, NIE 2018 09, Nutrition Industry Executive

About Nutra Biosystems

We are dedicated to serving the nutraceutical industry by generating unique and comprehensive science-based evidence of efficacy in supplements, formulations, ingredients and medicinal foods using next gen sequencing technology.

An expert in genetics, we specialize in genetic analysis using model systems to detect the mechanism of action for a compound at the molecular or cellular level. We deliver scientific proof for naturally derived ingredients or formulations and help ingredient innovators and suppliers substantiate their claims, file IP patents, or find new applications using the best science-backed measures of outcome.

Why work with us?

Get data that helps you:

- De-risk leads for better outcomes in clinical trials.
- Identify novel properties of ingredients and formulations.
- Create molecular data for precise structure function claims
- Exhibit science-based evidence of efficacy for nutraceuticals, dietary supplements and medicinal foods.

Contact us to start a conversation about how our services can support you.



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