This 2017–2019 Emerging Science Brief* highlights major trends reported in the ILSI North America 2017–2019 Science Trend Report: Insights and Implications (available here). To provide readers with quick access to further in-depth discussion, each highlight in this brief includes links to the respective sections in the full report.

The 2017–2019 Science Trend Report builds on previous two reports: the 2015 Science Trend Report: Insights & Implications for the Future and the 2016 Signals Watch. These reports provide emerging trends and signals developing in research, technology innovation, regulatory science, and/or consumer and market areas and include details on the methodology for how these reports are compiled and limitations therein.

This brief aims to provide readers an abbreviated guide for some of the more prominent trends in 2017–2019 that will provide useful background for decisions on research and development and strategic plans.

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*Limitations: The intent of this brief and report is for use as a directional guide only for identifying emerging areas. It is not meant to be either the primary source of reference or the definitive conclusion. It should serve as a stimulus for further discussion and confirmation. The data are derived from multiple publicly available sources that include, but are not limited to, the Internet, publications, journals, books, government brochures, customized searches on grants, and conversations and discussions with private-sector scientists and experts from government, academia, trade associations, and nonprofit organizations. In view of data sourcing limitations and applied filtering criteria, only megatrends are reported.
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Overview

2017 signifies the rapid ascent of the application of a convergence science approach to advance breakthroughs in the life sciences, particularly in biomedical research, intelligent sensors in manufacturing, and bioinspired technology innovations. Incredible advances are seen in many areas, including brain anatomical mapping, the use of aging plasticity to delay disease onset, microbiome and brain health, precision immunotherapies in cancer research, influence of the gene clock/circadian rhythm on metabolic functions, smart and digitalized sensors and wearable devices, Big Data and Internet of Things (IoT) applications, and personalization concepts in research and consumer decision making.

—Chor San Khoo

A. Global Aging—A Certain Trend

[One] trend is certain: the ageing of populations is rapidly accelerating worldwide. For the first time in history, most people can expect to live into their 60s and beyond. The consequences for health, health systems, their workforce and budgets are profound...

—Dr. Margaret Chan, Director-General, World Health Organization (2015)†

1. The Population Aged 60 and Older Is Growing

The global population aged >60 years reached 912 million in 2014, representing 12.6% of the global population. This segment is forecasted to increase to 1.5 billion or 18% in 2030. This accounts for a growth forecast of 39% between 2014 and 2030. The Asia Pacific (China, Japan, India, and Taiwan) region has the highest rate of population aging.1 China also has the highest number of individuals aged >60 years forecasted to increase by >46% between 2014 and 2030.2,3 Growth of the global older population presents several challenges, as countries see the number of nonworkers increase while the number of workers supporting them decreases. This is particularly apparent in China and India and is more gradual in the United States and European countries.

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2. Seniors Are Slow Adaptors of Technology

Seniors are slow adopters of technology and late users of digital technologies such as smart and mobile devices for potential eHealth monitoring.1,2 Reasons contributing to this include physical conditions or health problems, visual impairment, poor coordination and memory issues, affordability, and wariness of Internet access. These limitations mean seniors will need technical assistance to get them comfortable with and proficient in using these devices.1

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3. Poor Vision Is Linked to Increased Falls

A national survey of adults aged ≥65 with and without self-reported severe vision impairment reported an increased prevalence of falls among older adults with severe vision impairment as well as a variation in that prevalence among states.1 The US Centers for Disease Control and Prevention (CDC) reported that in the 2.8 million persons aged ≥65 years with severe vision impairment in 2014,2 an estimated 1.3 million likely experienced a fall in the previous year. Many eye diseases are asymptomatic; thus, early

Implications

These findings underscore the importance of promoting initiatives to improve vision health and reduce falls, especially among elderly individuals with severe vision impairment.
 detection and timely treatment are important. The National Eye Institute (NEI) has issued guidance to maintain healthy vision, which includes the following:

- Reduce smoking.
- Maintain a healthy weight.
- Reduce the risk of diabetes, hypertension, and multiple sclerosis.
- Maintain a diet rich in fruits, leafy greens, and fish high in omega-3 fatty acids.

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### B. Redefining Healthy Aging

Rapid and progressive growth of the 65 and older population globally necessitates the need to reevaluate current definitions of and measures for healthy aging. Although the WHO has defined healthy aging as complete physical, mental, and social well-being and not just the absence of diseases or infirmity, this concept has not been widely practiced in the health communities. Instead, the current dominant model of health has been a disease-centered medical model (MM).1

New findings from both consumer and medical modeling studies suggest that determinants for healthy aging extend beyond absence of diseases and inclusion of broader social, cultural, and behavioral measures.

#### 1. Global Consumer Survey

Euromonitor conducted a survey of older adults (aged ≥65 years) titled the “Determinants of Happiness: A 2015 Global Survey.”2 The survey focused on factors that consumers deemed important in aging successfully. The researchers found several determinants that older adults cited as critical for their happiness, including health, financial security, children and family support and relationships, satisfying work, strong social networks, and long-term goals. Spiritual beliefs ranked the lowest. Consumers regarded healthy aging more holistically than just absence of illnesses. Psychophysical, social, cultural, and economic determinants are equally important for successful aging.

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#### 2. Empirical Model Study

A 2016 study by McClintock et al.3 approached this issue using a comprehensive model (CM) of health consistent with the WHO definition, giving statistical weights to multiple health domains, including medical, physical, psychological, functional, and sensory measures. The authors applied a “data-driven latent class analysis (LCA)” to model 54 specific health variables from the National Social Life, Health, and Aging Project (NSHAP), a nationally representative sample of US community-dwelling older adults.3 McClintock et al. found that specific medical diagnoses (cancer and hypertension) and health behaviors (smoking) are less critical than mental health (loneliness), sensory function (hearing), mobility, and bone fractures in defining vulnerable health classes.3 Furthermore, although the MM places two-thirds of the US population into “robust health” classes, the CM reveals that one-half belong to less healthy classes, independently associated with higher mortality. The CM showed six distinctive health classes that predict mortality/incapacity; the healthiest aging group tended to be the group that was “robust” and had a higher weight. The two classes, with twice the

**Implications**

The 60 and older population is forecasted to reach 1.5 billion by 2030, and a better understanding of what healthy aging entails will benefit the development of sustainable and practical intervention initiatives and tactics.

This growing market presents several challenges and opportunities to target subsets of the population for health and nutrition interventions. Absence of disease may be too restrictive in defining healthy aging and may need to take into account other factors such as social, cultural, economic, and family support.

Those who are developing products or dietary programs for these populations may need to consider learnings from both research and consumer studies. Use of mobile and digital technologies to collect information for eHealth (e.g., food intake, physical activity, medication usage, etc.) in elderly individuals may prove challenging due to their slower adoption of these advances. The EuroMonitor “Happiness” survey may provide good insights into more positive ways to target the elderly population and help improve longer-term interventions and approaches.
mortality/incapacity, were people with healed broken bones or poor mental health. This approach provides an empirical method for inclusion of broader determinant measures for health. Inclusion of these broader measures will be beneficial for health policy planning in the future.\(^1\)

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**C. State of Global Malnutrition**

The United Nations General Assembly pronounced the period 2016–2025 as the Decade of Action on Nutrition against a backdrop of multiple challenges.\(^1,2\) The following issues were identified:

- Malnutrition remains a global issue, with 800 million people chronically undernourished.
- 159 million children under 5 years of age are stunted.
- Micronutrient deficiencies affect about 2 billion people globally.
- The incidence of overweight and obesity is increasing in all regions. About 1.9 billion adults are overweight, of which 600 million are obese. Childhood obesity is a growing concern.
- Poor dietary habits and unhealthy diets underlie the current nutrition issue.
- Recent confirmation that the global climate is changing has added burden to food security, sustainability, and nutrition security.

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**D. Maternal-Child Malnutrition—An Urgent Need and a New Opportunity**

Global maternal-child malnutrition is on the rise and now exists in over 30 countries.\(^2\) Global maternal undernutrition accounts for 800,000 neonatal deaths yearly from multiple causes, including small for gestational age births, stunting, wasting, and nutrient deficiencies. Worldwide, over 165 million children are stunted as a result of malnutrition.\(^2\)

Intervention is most effective from pregnancy to 2 years of age. After age 2 years, undernutrition will have caused irreversible damage for future development. About 80% of undernourished children live in 20 countries across regions in Africa and Asia.

Proven successful interventions to reduce childhood stunting and micronutrient deficiencies have included breastfeeding counseling, vitamin A, and zinc supplementation. For optimal maternal health, adequate dietary intake in pregnancy and supplementation with iron, folic acid, and calcium are approaches of value.\(^3\)

To date, there is no known single approach or technology that is effective in eradicating multinutrient associated with global malnutrition. Social, economic, and political changes are critically important to improving maternal-child malnutrition. This issue presents an opportunity for developing and testing new dietary intervention approaches.

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**Implications**

National nutrition intervention programs to successfully eradicate undernutrition in maternal-child health will require government support to ensure scale-up nutrition interventions, systems to monitor and evaluate those plans, and laws and policies to enhance the rights and status of women and children. There is concern that the international nutrition system may need better global leadership, more resources, and harmonious systems in order to be successful.
E. Fortification Technology

Advances in fortification technology have opened new opportunities for improved nutrient delivery and stability for use in deficiency intervention. Micronutrient deficiencies are estimated to underlie nearly 3.1 million child deaths annually. To date, no single intervention strategy has been successful in eradicating undernutrition. A 2013 meta-analysis by Bhutta et al. showed that the use of a multinutrient fortification intervention presents potential success in reducing risks of multiple nutrient deficiencies (e.g., iron, zinc, and vitamins A and D). In assessing the benefits of fortification on different outcomes with various nutrient fortificants, Bhutta et al. proposed a framework that shows the complexity in the interconnection between risk factors, interventions, and mortality in the LIST Trial (Lives Saved Tools). In a scale-up model, the investigators also demonstrated the beneficial effect of fortification interventions in reducing the number of deaths in studies that compared before and after outcomes.

Future research needs to focus on long-term effectiveness and efficacy of fortification intervention on maternal zinc supplementation, omega-3 fatty acid supplementation in pregnancy, antenatal psychosocial assessment, and cognitive behavioral therapy for depression.

Biofortification is a viable approach to enhance iron, provitamin A, zinc, and folate content in staple foods; however, progress is slow, as widespread acceptance by the target population is low, making this a rate-limiting step. More research is needed to determine how to get these foods to be accepted for widespread usage.

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F. Healthy and Low Environmental Impact Diets Share Common Features

The Food and Agriculture Organization of the United Nations (FAO) believes that healthy dietary patterns also have low impact on the environment and vice versa. Both areas share several common features, including the following:

- Minimally processed, focusing on field grown, less prone to spoilage, less reliance on energy-intensive transport modes
- A wide variety of diverse foods
- Balance of energy needs and intakes
- Rich in whole grains, fruits, vegetables, legumes, and tubers
- Moderate quantity of meat; consume all animal parts, reducing waste
- Moderation in dairy products or alternatives (e.g., fortified milk substitutes and other calcium-rich foods and micronutrients)
- More fish and aquatic products
- Limited consumption of foods high in fat, sugar, or salt and low in micronutrients
- Tap water in preference to soft drinks.

An FAO-supported global survey of national dietary guidelines worldwide found that:

- Most dietary guidelines provide clear, context-appropriate dietary guidance to maintain good nutritional health, and rationales for policies to shift consumption patterns in healthier directions.
- Not all countries have national food-based dietary guidelines (FBDGs) that include sustainability-oriented information.
- 83 of the 215 nations surveyed had FBDGs. The absence of FBDGs is more apparent in low-income nations. In countries where FBDGs exist, the content link to policy is not clear or widely communicated and the target audience is unclear.

Implications

In the United States and Canada, fortification is an approach that has improved nutritional intakes and status in needed subpopulations. Future fortification approaches can incorporate advances made in genomics, systems biology, and nanotechnology to provide customized or personalized fortification of multinutrients (or bioactives) as part of precision nutrition/medicine intervention.

Unintended consequences of changes in dietary patterns to meet sustainability goals need to be assessed, not just economically but also from nutritional and social/cultural perspectives in any countries adopting the integration. In addition, changes to food, agricultural, and manufacturing systems need to be considered.
The study identified that further research is needed to better validate the following:

- Long-term benefits of integrating healthy dietary patterns and food sustainability practices to gain low environment impact
- Environmental impact of consuming more sustainable aquaculture and plant sources of omega 3s
- Determining a sustainable level of meat and dairy product consumption consistent with environmental costs and benefits
- Better understanding of the environmental impacts of high-sugar, high-fat, and high-salt processed foods
- Implications of sustainability and diets on social and economic impacts in developing countries

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**G. WHO Calls for Restricting Free Sugars From Foods**

The WHO has issued new guidelines aimed to reduce intakes of free sugars from foods to reduce deaths related to noncommunicable diseases (NCDs). NCDs are the leading causes of death, accounting for 68% (38 million) of the world’s 56 million deaths in 2012. The WHO report indicated that a high level of intake of free sugars was linked to poor dietary quality, obesity, and an increased risk of NCDs. Another concern was a link between dental caries and intakes of free sugars.

- WHO recommends a reduced intake of free sugars throughout the life course (strong recommendation).
- In both adults and children, WHO recommends reducing the intake of free sugars to less than 10% of total energy intake (strong recommendation).
- WHO suggests a further reduction of the intake of free sugars to below 5% of total energy intake (conditional recommendation).

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A. Slowing Aging to Delay Disease Onset

It is clear that directly targeting aging is theoretically superior to treating individual chronic diseases, but until recently, translation approaches to achieve this goal is just that—purely theoretical.

—Kaeberlein et al. (2015)

Traditionally, biomedical research has focused on pathogenesis and treatment of specific diseases, particularly those affecting morbidity and mortality. This disease-specific approach has led to many medical breakthroughs in treatments, improving quality of life and longevity. In spite of these advancements, delaying, ameliorating, or preventing disease onset has not yielded much progress. In 2015, Kaeberlein et al. proposed that aging may play a critical role in disease pathogenesis and progression. Because the biological aging process is pliable and thus modifiable, tangible approaches can be developed to slow the rate of aging, which would delay disease onset and progression as shown in predictive models. This strategy is significant when developing intervention treatments for chronic diseases, cancer immunotherapies. Delaying the rate of aging would increase longevity by controlling for multidisease onsets, which would delay later declines in function (“longevity dividend”). Several intervention types have been proposed, including dietary restriction and exercise.


Implications

Delaying aging is a recent strategy receiving considerable interest as a way to delay disease onset and progression by modifying aging plasticity. Several intervention approaches have been studied that could delay aging progression, including caloric restriction, exercise, metformin, mammalian target of rapamycin (mTOR) inhibitors, modifiers of senescence and telomer delay, mitochondrial targeted therapies, hormonal and circulating factors, and sirtuin activators. The effect of dietary factors and compounds, potentially customized to disease types and outcomes desired, might be opportunities to apply modifiers of aging plasticity.
B. Dietary Reference Intakes for Chronic Disease Endpoints

Dietary reference intake (DRI) values are used in Canada and the United States in dietary assessment of healthy populations and they provide nutrient-based intakes to prevent nutrient deficiency. DRI values have not been established for intakes that affect chronic disease outcomes, despite growing evidence that supports a link. The increasingly aging population and growing prevalence of chronic diseases, overweight, and obesity, which predispose to chronic disease, underscore the importance of providing DRI guidance for chronic disease prevention and control.\(^1\)\(^-\)\(^3\)

Since 2015, the National Academy has formed two committees to provide guiding principles for inclusion of chronic disease endpoints to be used by committees setting future DRIs.

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C. Is There a Linear or U-Shaped Relationship Between Sodium and CVD Mortality?

Studies have shown that sodium (salt) intake is linearly associated with blood pressure in hypertensives, although such an effect is less obvious in prehypertensives and normotensives.\(^1\)\(^-\)\(^2\) Whether salt reduction also translates into a beneficial effect for reducing cardiovascular disease (CVD) and all-cause mortality remains to be confirmed.\(^1\)\(^-\)\(^3\) Data on the lower ranges of sodium intakes are limited, and many of these studies reported confounding error and inaccurate sodium intake measurement.

To address these questions, Cook et al. conducted a meta-analysis, published in the *Journal of the American College of Cardiology*, investigating the relationship between sodium intake to CVD risk and mortality.\(^4\) The researchers examined the relationship between urinary sodium excretion and long-term mortality using the TOHP (Trials of Hypertension Prevention) phase I trial from 1987 to 1988, over 18 months, and phase II from 1990 to 1995, over 36 months. The authors concluded that the study provided support for a linear relationship and no evidence of a J-shaped or U-shaped curve between sodium intake and mortality risk and total mortality. There was an increased risk of mortality for high sodium intake and a direct relationship with total mortality, even at levels below 2300 mg. The

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**Implications**

(1) Establishment of DRI values for chronic disease endpoints will provide target-level guidance, which is critical for developing future personalized food and dietary interventions targeted for different chronic disease end points. It will also provide more definitive guidelines and incentives for future research, exploration, and innovation of novel ingredients and food products. The establishment of agreed-upon biomarkers for different disease end points will simplify the process not only for furnishing evidence in support of health claims for food products/diet programs for the industry but also for developing new health claims for regulation. (2) Having DRIs for chronic disease endpoints will pave the way for advancing research on nutrigenomics and precision foods and dietary interventions, learning from and keeping pace with the NIH National Precision Medicine Initiative. On the other hand, if the DRI Committee decides at the end of deliberation that current evidence is not sufficiently robust to establish DRI values for chronic disease endpoints, one possible outcome is that the committee will either delay or recommend against using chronic disease endpoints for setting DRIs.

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**Implications**

This study supports previous findings of a linear relationship between blood pressure and sodium intakes across a wide range of sodium intakes (<2300 to >4800 mg). Such linearity was also confirmed using the Na/K ratio measure. This study, unlike others, used urinary sodium excretion to measure sodium intakes, instead of food records as used in other studies. The 24-hour urine test is widely accepted but still has limitations for estimating sodium intake. Limitations of this study include its lack of power at the lower and higher sodium dosages. More research is needed to confirm this finding. Reducing sodium in foods as part of a dietary strategy to reduce blood pressure, CVD risk, or mortality may have added benefits from increasing potassium levels as well.
authors indicated that the results supported a benefit of reduced sodium and sodium/potassium intake on total mortality over a 20-year period.

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D. Reducing Blood Pressure Will Lower Vascular Risk and Comorbidities Independent of Starting Baseline Level

Lowering blood pressure is widely used to prevent development and progression of CVD and premature death. However, less is known about the extent of the impact of blood pressure lowering as influenced by various factors, including individual variations in baseline blood pressure, presence of comorbidities, age, gender, or drug class. To address some of these questions, Ettehad et al. conducted a systematic review and meta-analysis of large-scale randomized controlled trials (RCTs) of blood pressure–lowering treatments performed between 1966 and 2015. The study, supported in part by the National Institutes of Health (NIH), included all RCTs of blood pressure–lowering treatment with a minimum of 1000 patient-years of follow-up in each study group. Outcomes of major CVD events, coronary heart disease (CHD), stroke, heart failure, renal failure, and all-cause mortality were collected, and an inverse variance weighted fixed-effects meta-analysis was used to pool the estimates. The authors identified 123 studies with 613,815 participants for the tabular meta-analysis. Findings of the study were published in the Lancet in 2016.

The authors concluded that blood pressure lowering significantly reduces vascular risk across various starting baseline blood pressure levels and comorbidities, supporting a strong case for reducing systolic blood pressures below 130 mmHg and for providing blood pressure–lowering treatment to individuals with a history of CVD, CHD, stroke, diabetes, heart failure, and chronic kidney disease.

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E. Nutrition Research Roadmap

The release of the first National Nutrition Research Roadmap for 2016–2021 by the Interagency Committee on Human Nutrition Research (ICHNR) has significant opportunities for the nutrition and food communities to consider. The ICHNR identified eating pattern research as one of the major focal research topics directed at three key questions, with the objective to change current population eating patterns to a healthier pattern: (1) How can we better understand and define eating patterns to improve and sustain health? (2) What can be done to help people choose healthy eating patterns? (3) How can we develop and engage innovative methods and systems to accelerate discoveries in human nutrition?

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F. NIH Charts 10-Year Nutrition Plan

In 2016, the NIH announced the formation of the Nutrition Research Task Force (NRTF) initiative, which will develop a 10-year nutrition strategy for the NIH.

“We hope that the strategic planning will encourage scientists to conduct innovative and really ground-changing studies in nutrition as they relate to health,” stated Griffin P. Rodgers, MD, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) director and NRTF co-chair. Dr. Rodgers identified several areas of potential interest for the NRTF:

- Dietary and physical activity assessments and advances in technologies including wearables
- Development of a strategic planning effort that cuts across a wide range of diseases
- Studies on food intake on human growth and development
- Genetic influence on human nutrition and metabolism
- The effect of the gut microbiome and its likely role in nutrition
- Food intake as it relates to the timing of the meal and circadian rhythm (e.g., digestion and metabolic functions and issues related to circadian rhythms and eating pattern when they are out of sync)
- Physical activity effect on weight regulation and cardiovascular health
- Insulin resistance and its role in obesity and diabetes
- Intergenerational transmission of type 2 diabetes risk, where environmental influence may begin in utero (maternal metabolic status and nutritional exposure imprint on infant and later life development of diabetes and obesity)


G. Circadian Rhythm on Eating Patterns, Sleep, and Health

Understanding the mechanisms by which food, light, and ambient temperature affect the daily sleep-wake cycle and metabolism has increasing importance for humans who are living under diverse work schedules, lifestyles, and food preferences.

—Satchidananda Panda (2016)

Researchers are investigating circadian rhythm and how it impacts eating patterns, food and cellular metabolism, sleep, and disease pathogenesis and progression. Most species undergo rhythm changes in their behavior and physiology regulated by the daily dark/light cycle governed by a biological clock located in the two brain suprachiasmatic nuclei. The circadian cycles have periodicity of approximately 24 hours and they can be synchronized to environmental time signals but can also function in the absence of such signals. The internal “clock” consists of an “array of genes and the protein products they encode.” These chemicals regulate cellular metabolic and physiological functions throughout the body. Disruptions of the circadian rhythm (CR) can interfere with normal function and impacts an organism’s health. Recent interest focused on the effect of CR on nutrition and energy metabolism, as well as factors that disrupt the biological clocks and subsequent consequences on health. To date, many factors have been identified, including alcohol, sleep, diet, fasting duration, physical activity, medications, body weight, and so forth.

Panda and his team at the Salk Institute studied the link between CR and eating patterns, time-restricted feeding (TRF), and sleep-wake cycles on health using mobile devices that provided a 24-hour data feed on eating...
sleep, and food pattern behavior in animal and human models. The scientists believe that disruptions to these cycles, either by genetic alterations or light/dark cycles (as in humans) via eating patterns, contribute to obesity and metabolic dysfunction.

The time restriction to food (TRF) can affect metabolic cycles and reduces blood lipid, glucose, and body weight. More research is needed to understand the relationship between feeding pattern and metabolism, which could yield novel therapies for the obesity pandemic. The effect of TRF on the gut microbiome may involve a cascade of events involved in regulating feeding rhythms: for example, dynamic fluctuation of the gut microbiome could induce changes in the levels of gut short-chain fatty acids (SCFAs) and GPR43 activation, which downregulates insulin signaling in adipocytes, promoting the utilization of lipids in other ways and hence maintaining metabolic homeostasis. Dynamic fluctuations in the gut microbiome can also trigger cyclical fluctuation of primary and secondary bile acids (BAs), modulate FXR and TGR5 activation, and downstream signaling, affecting energy expenditure and influencing cholesterol, lipid, and glucose homeostasis.

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**H. Gut Microbes and the Brain: Paradigm Shift in Neuroscience**

Research has shown the complexity, diversity, and active role that the gut microbiome may play in multiple organ functions beyond the gut (skin, immune system, reproductive system, brain, etc.).

Recent interest has turned to whether the gut microbiome has a mediating role in brain function. Mayer et al. reported that a “growing body of pre-clinical literature demonstrated bidirectional signaling between the brain and the gut microbiome, involving multiple neurocrine and endocrine signaling pathways. While psychological and physical stressors can affect the composition and metabolic activity of the gut microbiota, experimental changes to the gut microbiome can affect emotional behavior and related brain systems.”

These findings have led to some postulations that manipulating changes (e.g., antibiotics, stressors, dietary, probiotics) to the gut microbiome may present opportunities to alter the pathophysiology of some human brain diseases, including autism spectrum disorder, anxiety, depression, and chronic pain. Ongoing large-scale population-based studies of the gut microbiome and brain imaging studies looking at the effect of gut microbiome modulation on brain responses to emotion-related stimuli are seeking to validate these speculations.

Mayer et al. concluded that:

Not only is the concept of gut-microbiome-brain interactions in health and disease paradigm breaking, the emerging data-driven, analytical methodologies that are required to pursue the integration of massive amounts of data are equally revolutionary. It is difficult to predict the trajectory of [this] exciting period of discovery: Will the gut microbiome add paradigm-transforming insights to our existing understanding of human brain function in health and disease, resulting in novel therapies, or will it represent an incremental step in understanding the inner workings of our brains? The next few years of research hold the potential of uncovering intriguing connections between gut bacteria and neurological conditions that may possibly impact human health.

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Emerging Technology Innovations and Discoveries

A. Technologies Are Reshaping Life Science Research and Approaches to Human Health

In 2016, the World Economic Forum (WEF) identified the following top 10 technologies impacting future biomedical, health, and energy research.1

1. Nanosensors and the Internet of Nanothings (tiny sensors that can connect to the web)
2. Next-generation batteries with large-scale power storage
3. Blockchain A revolutionary decentralized trust system
4. Two-dimensional materials (these “wonder materials” are becoming increasingly affordable)
5. Autonomous vehicles (self-driving cars coming sooner than expected)
6. Organs-on-chips (using chips instead of organs for medical testing purposes)
7. Perovskite solar cells (making progress toward ubiquitous solar power generation)
8. Open artificial intelligence (AI) ecosystems (from artificial to contextual intelligence)
9. Optogenetics (using light to control genetically modified neurons)
10. Systems metabolic engineering of chemicals from sources’ microorganisms


B. Convergence Science

In 2016, we interviewed Dr. Andrew Maynard, a member of the WEF Global Futures Council on the Future of Technology, Values, and Policy and currently Director of the Risk Innovation Lab and Professor in the School for the Future of Innovation in Society at Arizona State University, on his insights into the future of technology trends in the life sciences. Dr. Maynard highlighted the emerging importance of “convergence” between multiple technology platforms as the new approach for breakthroughs in manufacturing, processing, and biomedical research. The integration of Big Data, AI, computational sciences, sensor advancement, systems biology, cellular genomics, and nano- and material technologies has opened new doors for combination technologies targeted to customized applications.

The Wyss Institute at Harvard University reported that “Convergence science is now the new norm approach to solve multicomplex problems.” The convergence science approach is gaining popularity as an efficient and effective way to solve complex multidisciplinary problems. At Wyss Institute, convergence science has been applied in many programs including bioinspired research programs, and researchers are applying engineering and physical principles to solve biomedical problems. Often, the convergence science approach in research produces unexpected and synergistic transformations. Examples of such breakthroughs include nanotechnology, genomics, cell engineering, photonic tools, and data science/mathematical modeling. Recent advances in material sciences combined with physical and chemical sciences have enabled research at the atomic, molecular, and system biology levels exemplified in stem cells, bioengineered synthetic organs, microdevices, and computational modeling to study cell function, tissue regeneration, and complex organ physiology.

Source: (1) Wyss Institute at Harvard (2016).
C. Merging Living and Nonliving Systems

*Through the applications of biological principles to develop new engineering solutions for medicine, and other nonmedical fields never before touched by the biology revolution. In the near future, it is conceivable that the boundary between living and nonliving systems is slowly becoming an integrated entity.*

—Wyss Institute at Harvard University (2016)

1. Next-Generation Optogenetics: Exploring Aging Plasticity and Alzheimer’s Pathogenesis

*With optogenetics, for the first time in history neuroscientists can tune the activity of specific brain circuits to determine their contribution to functions such as perception, attention, memory and decision-making.*

—Bill Newsome, Director of the Stanford Neurosciences Institute and Professor of Neurology (2014)

It recent years, optogenetics has captured the NIH’s interest to advance this technology for research on brain plasticity and neural activities. Recent developments and advances in optogenetic technologies have enabled the ability to control the level of neural activities at a single neuron level in living model organisms through the control of light at appropriate wavelengths. New-generation optogenetic systems allow for multicolor and sophisticated spatial and temporal control of neural activity, thus enabling a broad array of applications of optogenetic tools to study neural systems at multiple levels, either *in vitro* or *in vivo*. Although optogenetic technologies have been utilized to address many fundamental questions in a variety of neuroscience disciplines, their application to aging and/or AD research remains limited.1,2

As a result, the National Institute on Aging (NIA) has provided funding support since 2013 to “encourage broad applications of optogenetic-based technologies to study basic and/or translational questions in aging neural systems (including sensory, motor, cognitive, emotional, sleep/circadian, epileptogenic, neurovascular and autonomic) and AD.”3

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2. DNA Nanostructures for Target Compound (Drug) Delivery

Customizable nanostructures can be built using DNA. Investigators at the Wyss Institute at Harvard University have developed a method that can build arbitrarily shaped nanostructures using DNA, with a focus on translating the technology toward nanofabrication and drug and compound delivery applications.1,2

“DNA-brick self-assembly” is currently a proprietary technology that uses short, synthetic strands of DNA that work like interlocking jig jaw pieces. It utilizes the ability to program DNA to form into preset shapes based on DNA base pairs, such that binding A (adenosine) only binds to T (thymine) and C (cytosine) only binds to G (guanine).

Another DNA nanofabrication method, DNA origami, uses rules of programmable self-assembly in which strands of DNA are directed to form custom, specific shapes of tightly cross-linked double helices using a single strand of DNA as a “scaffold.” The scaffold is formed using base pairing from numerous short, chemically synthesized DNA strands that are specially designed using computer software. In this manner, DNA origami is now being used to create 3D structures, with the goal of building nanoscale tools and drug delivery devices.

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3. Genetically Engineered Biofilms: Potential Probiotics?

Biofilms, produced by communities of bacteria, are slimy, tough matrices consisting of extracellular materials of mucopolysaccharides, proteins, and others. During biofilm formation, individual bacteria release proteins that self-assemble outside the cell. This process can be controlled by using genetic engineering to harness it to target for specific therapeutics and biologics applications (e.g., potentially a new generation of probiotics targeted for specific health applications).1–3

A novel protein engineering system, BIND (Biofilm-Integrated Nanofiber Display), developed by scientists at the Wyss Institute, could be used for future probiotic therapies and foundry templates for synthesizing biomaterials. These biofilms of microbes could be customized as probiotic pills. Ingestion of this probiotic would colonize microbiota in the gastrointestinal tract in patients with chronic inflammatory diseases. There, the bacteria would produce and secrete anti-inflammatory factors. These biofilms could be designed for use in treating inflammatory bowel diseases, cleaning up polluted rivers, manufacturing pharmaceutical products, fabricating new textiles, and more.

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4. Mannose Binding Protein: A New Way to Capture Pathogens

Pathogenic contaminants are found in foods, in the environment, and in manufacturing processes, requiring early detection, confirmation, identification, characterization, and removal options (i.e., therapeutics, decontaminants, etc).

Genetically engineered mannose-binding lectin (MBL) protein, called FcMBL, is used to capture viruses, fungi, parasites, toxins, and dead pathogen fragments released after antibiotic killing. A broad base of FcMBL platforms can be developed to trap various pathogen combinations.1

Native MBL binds to multiple microbial classes (Gram-positive/negative bacteria, fungi, viruses, and parasites). Scientists at Wyss Institute1 genetically engineered MBL by deleting complicating complement activation and coagulation-promoting domains and fusing it to an antibody Fc fragment (FcMBL), which stabilizes the molecule and enables rapid purification. FcMBL retains the ability of native MBL to bind to the same broad spectrum of pathogens, and it is easily coupled to surfaces for pathogen capture or biologically active therapeutics or diagnostic markers; it also can be produced with a thousand-fold lower cost and exhibits higher stability.

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Source: (1) Wyss Institute (2016).

5. Beyond 3D Printing
a. 4D Printing for Shapeshifting Devices

Investigators are examining 3D-printed hydrogel composite architectures that provide the ability to change shape over time for use in smart textiles, soft electronics, medical devices, and tissue engineering.

Organisms have dynamic morphologies that can change shape in response to environmental changes such as humidity, temperature, and light. Wyss Institute researchers have mimicked a variety of such dynamic shape changes in innovative 4D-printed hydrogel composites.1

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Source: (1) Wyss Institute (2016).
b. Printing Thick Tissues/Organs

This research will help to establish the fundamental scientific understanding required for bioprinting of vascularized living tissues.

—Zhijian Pei, National Science Foundation Program (2016)

The typical bioprinting technique creates thick 3D tissues composed of human stem cells and embedded vasculature. With potential applications in drug testing and regenerative medicine, bioprinting sets the stage for future tissue and organ replacement.

This is a new method for 3D bioprinting thick vascularized tissue constructs, made from human stem cells, extracellular matrix, and circulatory channels lined with endothelial blood vessel cells. The resulting network of vasculature contained within these deep tissues enables fluids, nutrients, and cell growth factors to be controllably perfused uniformly throughout the tissue. The advance was reported in *Proceedings of the National Academy of Sciences* in 2016. A technique developed by Alan Feinberg at Carnegie Mellon University extends the use of 3D printing technology to print heart and other thick tissues or organ structures.

The 3D-printed object of the material of choice allows the master scaffold framework for cells to grow into the desired organs. Bioprinting when coupled with imaging provides a powerful tool for surgeons to study the 3D layout of structures of organs and vessels prior to surgery.

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6. Organs-on-Chips for Toxicological and Disease Screening

The use of this new technology is generating much interest in terms of how it might better reflect the physiological response to an external perturbation/intervention. The NIH is funding several research initiatives that involve using one or multiple organs-on-chips for drugs and chemical screening, and investigators are exploring the use of this technology in future disease modeling.

The NIH National Center for Advancing Translational Sciences (NCATS) has led research in the Tissue Chips (Chip) Initiatives program in collaboration with other NIH institutes and centers, the Defense Advanced Research Projects Agency (DARPA), and the Food and Drug Administration (FDA). The Tissue Chip Project is now being applied for rapid drug screening, focusing on developing human tissue chips that “accurately model the structure and function of human organs—such as the lung, liver, and heart—to help predict chemical and drug safety in humans more rapidly, effectively, and efficiently. Currently, this program is focused on toxicity testing with plans underway to renew focus on disease modeling and efficacy testing.”

The Tissue Chips (or Organs-on-Chips) Platform centered on building 3D platforms designed to simulate functions of the human body and support living human tissues and cells. These devices are designed to be accurate models of the “in situ” structure and function of human organs, such as the lung, liver, and heart. Among the chips developed to date and tested with compounds already known to be safe or toxic in humans, the majority of these chips have been validated.

a. From Organs-on-Chips to a Human Chip Network

NIH has invested in technology and research to develop a whole human network of chips that mimic organs of interest. Some chips are further along in development than others. The current chips are designed to be modular, allowing investigators to connect one chip with another to test the effects of potential drugs or other compounds on several organ systems at a time. A “human body on a chip” is the ultimate goal of the program, enabling researchers to test the potential effects of a substance across the entire body before involving human clinical participants.

NCATS envisions that the tissue chips will help scientists generate data on drug safety and effectiveness to predict more accurately how specific drugs will respond in people. The new technology ultimately could help accelerate...
the drug or product development and approval process and, most important, enable health professionals to make new treatments available sooner to patients.

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Source: (1) NCATS (2016).

7. CRISPR

a. Global Recognition of CRISPR Technology Importance

CRISPR technology was recognized as a “Technology of 2015” and has potential for application in food safety and nutrigenomic research.1 Investigators are developing next-generation CRISPR technology that enables more “precise” editing using specific base pairs. Researchers involved in developing and applying the technology received Canada's prestigious Gairdner Award in 2016.2

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b. Next-Generation CRISPR-Cas9 Based on Base Pairing

A study by Komor et al.,1 published in Nature, reported an enhancement to the CRISPR gene editing technology. The current method requires breaking double-stranded (ds) DNA at a target locus as the first step to gene correction, which is inefficient, potentially introducing an abundance of random insertions and deletions (indels) at the target locus resulting from the cellular response to dsDNA breaks.1 The researchers developed a new approach using “base editing” to genome editing that enables “direct, irreversible conversion of one target DNA base into another in a programmable manner, without requiring dsDNA backbone cleavage or a donor template. By combining CRISPR/Cas9 and a cytidine deaminase enzyme that retain[s] the ability to be programmed with a guide RNA, this reduces dsDNA breaks, and mediate[s] the direct conversion of cytidine to uridine, thereby effecting a C→T (or G→A) substitution. The resulting ‘base editors’ convert cytidines within a window of approximately five nucleotides, and can efficiently correct a variety of point mutations relevant to human disease.”1

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8. Advances in Packaging Material

Researchers have developed a new soft packaging material using nature’s skins, such as chitosan and even shrimp shells. For example, shrimp shells and protein (“Shrilk”) were used to create a bioplastic that is flexible and environmentallyfriendly.

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Source: (1) Wyss Institute (2016).
A. The Increasingly Digital World

Advances such as the “data mesh,” artificial intelligence (AI), smart sensors, Big Data analytics, and data visualization are increasing in importance and are advancing avenues for precision medicine, manufacturing, and consumer daily digital experiences.

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B. The Future Workforce

The Institute for the Future has identified 10 skills that it deems critical for the workforce of 2020.

1. Sensemaking
2. Novel and adaptive thinking
3. Social intelligence
4. Transdisciplinarity
5. New media literacy
6. Computational thinking
7. Cognitive load management
8. Design mindset
9. Cross-cultural competency
10. Visual collaboration

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5

Emerging Food Safety Trends

A. Whole-Genome Sequencing

Whole-genome sequencing technology will change how federal agencies detect, characterize, report, and regulate food contamination and how the food industry needs to respond to product and ingredient contaminants.

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B. National Strategy for Combating Antibiotic-Resistant Bacteria

Multiple programs related to this work are in place at the NIH, USDA Food Safety and Inspection Service, and US CDC. The National Science Foundation and NIH are funding research for novel antibacteriosides, including exploration of soil and dirt (blue clay) for such use.

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C. Adulterated Foods

The adulteration of foods with fraudulent and even unsafe additives by some exporting countries is now a heightened area of concern.

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D. Unintended Consumer Uses

Unintended consumer uses of foods will continue to increase with growing consumer interest in raw or undercooked, natural (preservative-free) foods that can be prepared quickly or are not cooked sufficiently.

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Regulatory Science, Science Policy, and Movements

A. Changing Consumer Food Expectations and Food Environments
Regulatory science in Canada and the United States will face changing consumer food expectations and purchasing environments.
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B. Deliverology
The use of deliverology in Canada will change how programs funded through tax dollars will change program reporting and accountability, including relevance and benefits.
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C. DRIs for Disease End Points
Release of recommendations for dietary reference intakes (DRIs) for disease end points will be one of the most significant events influencing food and nutrition research guidance and policy in the future. Final recommendations are not expected likely until 2018 but could signal potential inroads into nutrigenomic and precision diets for disease interventions.
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D. Food GRAS Rule and Health Claims
The US Food and Drug Administration (FDA) issued a GRAS final rule in 2016, as well as guidance on use of the claim “healthy” on food labels. In 2016, the European Union also approved health claims on calcium and bone health.
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E. Healthy People 2020 Targets
Dietary improvements are made through small gradual changes by including more fruits and vegetables; however, a recent analysis indicated that the 2020 Healthy People targets on increasing vegetable intake have not been met (current intake is 0.77 cups compared with the target of 1.13 cups).
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F. Healthy People 2030
The Healthy People 2030 committee was formed in 2016 and members are developing targets in progress under the direction of the US Department of Health and Human Services.
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A. Natural, Green, and “-Free”
Consumers are gravitating to food products that are natural, “greener,” and chemical free. They desire better clarity regarding food labels, including added sugars, country of origin, and front-of-pack information. Consumers are avoiding foods that have high sugars, high fructose corn syrup, salt, and preservatives.

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B. Sustainable Foods
Four out of 10 consumers believe that conserving nature and reducing use of preservatives in food is an important approach to producing sustainable foods.

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C. Food Waste
Consumers are concerned about climate change and desire to reduce “food waste.” Six out of 10 consumers take food home from restaurants and many feel that the top contributor to food waste is buying too much fresh produce, forgetting about perishables.

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D. Convergence in Food and Health
Food and health are converging, and interest in antiaging foods and time-saving convenience options continues to grow.

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E. Taste
Taste remains at the forefront of consumer decisions when food shopping, surpassing price, healthfulness, convenience, and sustainability.

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F. Trusted Sources of Nutrition Information
Consumers view dieticians, health professionals, and government institutions as the most trusted sources of nutrition information.

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G. Confidence in the Food Supply
US consumers have confidence in the safety of the US food supply (66%); however, they are more likely to trust food that is grown locally or served in local restaurants.

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H. Healthy Eating
Healthy eating practices include eating in moderation, portion control, and variety, with inclusion of healthy foods as building blocks.

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