

Using CRISPR Technology to Improve Health by Increasing the Consumption of Fresh Fruits and Vegetables**

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Summary: Dietary factors are the number one disease risk globally. In the U.S., on average, Americans consume approximately 50% of the daily recommended intake for fruit and 65% for vegetables. While there are myriad factors that influence diet and food choices, both individual experiences and consumer data demonstrate that many fruits and vegetables are not always available, are unpalatable, and/or have limited shelf-life—all factors that contribute to low consumption of fruits and vegetables and high food waste. While the underlying genetics for addressing many of these problems already exist in wild and domesticated species of fruits and vegetables, it could take decades or even centuries to use traditional plant breeding to achieve the needed improvements. Although molecular breeding and genetic modification are viable tools in addressing this major health challenge, the use of these technologies has focused primarily on increasing yields in a few large acreage row crops. Whereas the emerging CRISPR technology can increase productivity for crops such as corn and soy, broader technology uses can more quickly improve public health by increasing the quality, convenience, and availability of fruits and vegetables at lower costs.

Current realities: Globally, while humans cultivate and consume about 200 different plant species, only three crops (i.e., corn, wheat, rice) provide over 50% of the world's calories. In the U.S., about 88% of cropland is planted with corn, soy, and wheat. Thus, attention given to addressing the global food challenges via plants is disproportionately focused on row crop agriculture with two major outcomes: (i) the economics of row crops are almost exclusively focused on maximizing and protecting yield and (ii) crop improvements using molecular breeding and other technologies are narrowly focused on just a few plant species.

Globally and nationally, diet is the number one cause of poor health. A 2012 Lancet study identified the most significant global health risks, and, with the exception of tobacco use, diet was the main contributing factor to several major health challenges, including high blood pressure, obesity, childhood malnutrition, high fasting plasma glucose, iron deficiency, high cholesterol, etc. Although a subset of these problems can be partially addressed by transforming row crops, many of these disease factors can only be addressed by increasing fruit and vegetable consumption. In the U.S., only about 20% of people's diets meet the USDA recommendation for fruit and vegetables and the average person eats only about 50% of fruit and about 65% of vegetables. Unfortunately, this problem is not a new challenge. Total produce consumption has only improved by about 10% in vegetables and 5% in fruit since 1970 (Figure 1). Despite education campaigns, improvements in school lunches, and better nutritional information, relatively little significant progress has been made.

Scientifically credible approaches and challenges: Outside of cost, enticing consumers to eat more fruits and vegetables needs to focus on three factors: (i) consistent flavor and quality, (ii) year-round availability, and (iii) convenience. Although there is no one solution for all produce, modern plant breeding tools (e.g., CRISPR) in individual crops could improve the consumer experience and increase produce consumption. Since many produce crops are genetically underdeveloped, and in some cases barely domesticated, CRISPR could significantly improve produce relative to more advanced row crops.

Research has shown that consumers make their first purchase of berries based on appearance, but repeat purchases are based on flavor. Thus, a negative consumer experience can delay a second purchase for months. Delivering consistent flavor is a complex challenge because flavor derives from a combination of environmental and genetic factors in addition to seasonality and ripeness components. In many cases, the underlying genetics are generally understood; therefore, an opportunity exists for CRISPR to increase the yield, shelf-life, and ripeness of the more flavorful varieties to meet consumer priorities.

Year-round availability is another important factor for increasing consumption. More than 40 years of conventional breeding enabled blueberry production in warmer climates, and this enabled southern U.S. production and imports, which led to year-round availability in 2008. As a result, consumption of blueberries increased four times in the last 10 years (Figure 2). Similar increases in consumption are likely if other fruits (e.g., cherries, peaches, plums) were available year-round. CRISPR technology can be used to rapidly adapt the growing regions for many plants, thereby making popular fruits more available.

The impact of convenience on escalating consumption reflects the general trend of consumer eating habits for increased snacking (10% of 1970s U.S. consumers snacked once a day, versus the current 94% snacking at least once a day and 50% snacking more than twice daily). While nut consumption has increased, fruit and vegetable consumption has not, with notable exceptions such as ready-to-eat salads and baby carrots. One recent example demonstrates that consumption can increase with convenience: easy-to-peel, seedless mandarin oranges became widely available this decade, and in the last five years consumption of them doubled, increasing the overall consumption of the fresh orange category by 30%. While traditional breeding efforts cannot keep up with consumer demands for ready-to-eat food, breeding innovation such as CRISPR technology could be used to make the same popular fruits and vegetables more consistently flavorful, available, and snackable. In turn, this could lead to healthier snacks improving societal diet and health.

One challenge with traditional plant breeding in produce is that consumer palates have evolved with a specific taste profile for specific produce. The predominant sweet cherry variety, Bing, was introduced in 1875 and still has significant market share even though its yields are 3 times lower than more recent, slightly different cherries varieties. Thus, plant breeders are always challenged with reproducing exact flavor profiles that consumers expect, while also trying to add agronomic benefits to increase yields for farmers. Since both goals cannot always be achieved with traditional breeding, growers are cultivating the same avocado, peach, and potato varieties used for generations to maintain taste without taking advantage of the opportunities offered by biotechnology (e.g., CRISPR) for more sustainable production.

Although there are numerous technical and marketplace challenges for the use of CRISPRs in plants, in many cases the largest barrier is technical and involves introducing the CRISPR enzymes into the plants. This transformation process has largely been developed in private industry. Collectively, it is estimated that billions of dollars have been invested in developing efficient transformation systems for row crops. There are a few vegetables for which transformation systems have been developed, but in most cases, commercial ready systems are not available. While both university labs and companies can build off the existing row crop transformation lessons for fruit and vegetables, each distinct plant species and sometimes each distinct variety needs its own unique transformation protocol. This takes time and a considerable investment of private capital to achieve the performance required for specialty crop-breeding innovation using CRISPR.

The availability and patience of private capital largely depend on the perception of public acceptance and the belief in a reasonable and predictable regulatory system. Despite the business opportunities and broad potential public benefit of improved produce, specialty crops would be too expensive to develop if a regulatory environment similar to that of genetically modified organisms (GMOs) were implemented. If gene-edited products were regulated as GMOs, many companies otherwise interested in developing improved produce through CRISPR would focus their priorities on row crops instead, thus limiting the impact of CRISPR technology for public health benefits. Public acceptance is paramount, but for too long, the dialogue has focused on the technology itself. What is needed is a public dialogue about how better fruits and vegetables can create benefits for everybody.

Evidence-based options and real-world opportunities: The supermarket of the 20th century has focused mainly on the availability of produce, often at the sacrifice of product flavor and quality. With CRISPR technology, the supermarket of the 21st century can have great tasting produce year-round by progressively taking a more informed and sophisticated approach to genetic variation. These improvements are derived from the inherent potential of a plant's biology to create better tasting, healthier, better yielding, and safer food. Most applications of gene editing are a more precise method of doing what breeders have already been doing for a very long time in plants and, therefore, do not need to be regarded as a GMO. The following options are scientifically justified and would be highly supportive of our shared goals of increasing consumption of fresh fruits and vegetables.

- Update governmental regulations based on the following principles: (i) it is the product and not the process that should be considered when reviewing safety concerns (i.e., "like products must be regulated in like ways") and (ii) gene-editing that does not introduce foreign DNA is a more precise method of traditional breeding and should not be treated like a GMO.
- Create a strong record, defining and supporting the "Gold Standard" for science-based updates to regulatory policies for gene-editing.
- Promote healthy food choices through informative nutritional labeling and recommended daily allowances.
- Ensure consumer trust in the integrity of safe fruits and vegetables by emphasizing the significant post-market oversight authorities, responsibilities, and actions taken by federal and state regulatory agencies and departments to ensure the safety of the American food supply.
- Emphasize to the public the significant oversight responsibilities fulfilled and actions taken by governmental (federal and state) regulatory agencies and departments to ensure the safety of the American food supply.

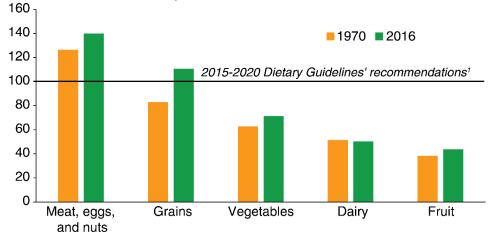
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Figure 1.



Estimated average U.S. consumption compared to recommendations, 1970 and 2016

Percent of 2015-2020 Dietary Guidelines' recommendations

¹Based on a 2,000-calorie-per-day diet.

Loss-adjusted food availability data are proxies for consumption. Rice availability data were discontinued and thus are not included in the grains group. Source: USDA, Economic Research Service, Loss-Adjusted Food Availability Data and *2015-2020 Dietary Guidelines*.

https://www.ers.usda.gov/data-products/chart-gallery/gallery/chart-detail/?chartId=58334

Figure 2. Year around blueberry supply increases consumption

