CHORI-bar, a nutrient-rich, fruit-based, high fiber, low calorie, good tasting supplement bar to tackle diseases associated with obesity and aging

**Background.** The increasing prevalence of obesity is taking a huge toll on public health, adding significantly to global health care costs. Since poor diets are well known to be a major cause of obesity, an obvious approach is to improve dietary habits. Conventional approaches that encourage weight loss by reducing caloric intake and modifying lifestyle can be successful, but wholesale changes in diet and behavior are difficult for many to initiate and sustain.

Over the past 10 years, a team of Childrens’ Hospital of Oakland Research Institute (“CHORI”) nutrition scientists and clinicians assisted by local United States Department of Agriculture collaborators developed a nutrient-rich, fruit-based supplement bar (referred to herein informally as the “CHORI-bar”) as a non-traditional means to positively impact the obesity epidemic by improving the metabolic dysregulation that frequently accompanies obesity and is the primary cause of increased risk of many diseases such as diabetes and cardiovascular disease.

The motivating idea behind development of CHORI-bar was that dietary-induced metabolic dysregulation is due as much to what poor diets are lacking (e.g., vitamins, minerals, and fiber) as to what they contain (e.g., trans fats, sugar). Thus, ingredient selection for CHORI-bar emphasized food components whose deficiencies were linked to increased disease risk and which were known to be deficient or missing in typical Western diets. There is considerable evidence in the literature as well as from Dr. Bruce Ames’ work on micronutrients that support this idea\(^1\)-\(^4\). Development of the CHORI-bar was also guided by Dr. Mark Shigenaga’s ideas on the importance for disease prevention of maintaining a healthy gut, known to be impaired in the obese.

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**CHORI-bar Fills Gaps in Poor Diets**

From a disease risk perspective, the problem with poor diets is as much due to what they do *not* contain, as to what they do contain

Supported by research of Drs. Ames, Shigenaga, and a large body of evidence in the published literature

**Health improvements occur in both the lean and overweight/obese without requiring a change in diet or other lifestyle habits.**

HDL-c ↑, small LDL ↓, Triglycerides ↓, Blood pressure ↓, Heart rate ↓, Insulin resistance ↓, Weight ↓, Waist circumference ↓

**The CHORI-bar Development Team**

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A high fiber, low-calorie (110-130 kcal), good tasting bar formulation has been developed and produced in pilot scale quantities. Throughout development of CHORI-bar, formulation modifications to improve palatability and efficacy were guided by a series of over 15 small clinical trials\textsuperscript{5,6}. A straightforward experimental design was used for these trials. Participants acted as their own controls, and were not required to modify their existing diets during the course of the trial, consistent with our hypothesis that adding back deficient dietary components would be sufficient to result in positive change.

**Clinical Trials**

**Metabolic Dysregulation.** Early clinical trials guiding development of CHORI-bar were of short duration (2-weeks). They included predominantly lean or only slightly overweight adults.

Our published report\textsuperscript{5} showed that twice-daily consumption of CHORI-bar for 2-weeks resulted in a striking increase in HDL-c, particularly the large HDL particle, HDL-L (aka HDL-2b), associated with lower cardiovascular risk (see top figure).

Subsequent trials of longer duration (2-months) focused on overweight/obese (OW/OB) adults. The metabolism of many OW/OB is abnormal in ways that put them at high risk of short lifespan and a wide range of diseases. As shown in the figure, in the OW/OB compared to the lean, HDL is lower, LDL is higher, triglycerides are higher, and the OW/OB are insulin resistant, which impairs the ability of the body to carry out many essential tasks. Importantly, although the OW/OB do not have a fever, most have a low-level of internal inflammation called “chronic inflammation” that has broad-spectrum adverse effects, and may actually be a major cause of much of their other metabolic dysregulation.

The major goal of the 2-month trials was to test whether CHORI-bar consumption without requiring other lifestyle modifications could shift metabolic dysregulation in the OW/OB toward a “leaner” profile.
Results were striking, as shown in the 2 figures.

Statistically significant improvements were observed in indicators of cardiovascular health [HDL-c (primarily the less atherogenic particle HDL 2b), the LDL particle profile, triglycerides, heart rate, diastolic blood pressure], glucose metabolism (insulin resistance, insulin, glucose), inflammation (high sensitivity C-reactive protein: hsCRP) and obesity (weight, waist circumference). Improvements occurred primarily in the OW/OB with less chronic inflammation, as measured by high sensitivity C-reactive protein (hsCRP<1.5).

As shown in the top figure, there do not appear to be any effects of CHORI-bar consumption on LDL-cholesterol (LDL-c). But, LDL-c is actually comprised of a collection of particles of different sizes. In general, people who have mostly smaller, denser particles are at greater risk for cardiovascular disease. CHORI-bar consumption actually shifted the LDL particle profile toward one with less cardiovascular risk. The “higher risk” particles all decreased, and the “lower risk” particles increased. Thus, while there was not a significant overall decrease in the total LDL cholesterol, there was a striking shift toward a lower risk LDL profile. The 2 HDL particles shown on the left side of the figure are a large “low risk” particle (HDL2b) and smaller “higher risk” particles (HDL3_2a). Almost all of the increase in HDL cholesterol is due to increase in the lower risk particle HDL2b.

We think the broadscale improvements in virtually all aspects of the dysregulation of obesity by CHORI-bar consumption may be due to the restoration of impaired critical underlying functions, such as poor energy production by mitochondria and an unhealthy gut wall. Restoration of these critical functions by supply of dietary components deficient in Western diets with CHORI-bar would be expected to have multiple favorable consequences similar to those observed.
Obesity-Associated Conditions. Obesity per se does not increase disease risk; the culprit is the metabolic dysregulation that accompanies obesity in about 70% of the obese and in about 30% of the lean. A primary motivating factor guiding our research is the conviction that the key to reducing disease risk in all people is restoring healthy metabolism. Thus, we believe that the primary focus of the medical community on weight loss as the solution for the obesity problem is misdirected, and we think that it is plausible that a healthy metabolism will make it easier to achieve and maintain a healthy weight. We have begun to use the CHORI-bar, which we know improves metabolism, as a tool to explore the viability of this hypothesis. We have obtained preliminary evidence that 8-weeks consumption of 2 CHORI-bars a day improves lung function in obese teenagers with asthma.

Two family-based 8-week pilot clinical trials were conducted in obese adolescent asthmatics in the summers of 2012 and 2013 in collaboration with our Children’s Hospital pulmonary department. Most asthma is allergy-based, but obese asthma is not. It is poorly understood and difficult to treat. The characteristic of obese asthma that led us to test whether the CHORI-bar might be of help is that it occurs in people who have the kind of metabolic dysregulation that the CHORI-bar improves. In two separate clinical trials, both conducted over 8-weeks, groups of obese teen-age asthmatics and their parent/guardian attended weekly classes and the teens ate 2 CHORI-bars daily. A comparable group of obese asthmatics attended parallel classes but were not given CHORI-bar to eat. At each class, participants received the same nutrition and exercise instruction. At the end of 8 weeks, effects of CHORI-bar consumption on lung function and metabolism were compared.

In both trials, lung function improved only in the group that ate CHORI-bar. Results from the trials were combined, and are shown in the adjacent figure. Forced Expiratory Volume, the amount of air that can be forcefully breathed out of the lungs in 1 second (“FEV1”), Forced Vital Capacity, the total amount of air that can be forcefully breathed out (“FVC”), and Forced Expiratory Flow, the speed that air is breathed out during the middle half of FVC (“FEF 25-75%”) were measured to determine how well the patient’s air passages are working.

After eating 2 CHORI-bars each day for 2 months, some participants continued in the trial for 4 more months, eating 1 CHORI-bar each day. Statistically significant improvements in lung function were still evident compared to controls, even though the number of people was quite small. In addition, there was significant weight and waist circumference loss. These preliminary results are very encouraging. The metabolic analyses are still in process.

Optimization for Maximal Benefit. Because the composition of CHORI-bar is controlled and defined, it can be used in a cost-effective way to understand how diet and dietary components interact with metabolic pathways in disease and health. As a research tool, CHORI-bar presents significant opportunities to better understand mechanisms whereby nutrients delivered at physiological doses in a food-based matrix positively
impact metabolism linked to future disease risk. This is virtually impossible to do, and enormously expensive, with an entire diet that must be individually controlled and managed in every participant. Because of CHORI-bar’s potency, it is effective without requiring participants to modify their existing diets. Thus, clinical trials of “deconstructed” CHORI-bar offer a new approach for understanding relationships between diet and disease, which will provide the information needed to optimize diets that prevent disease.

A series of clinical trials are ongoing to determine which CHORI-bar ingredients are required to improve HDL-c. Preliminary results suggest that raising HDL-c is a synergistic or additive effect and requires fruit, fiber and at least one other as yet unidentified component in the complete CHORI-bar formulation. Additional “deconstruction” trials can help to design the optimum diet for raising HDL-c. This general approach can also be applied to understand which complex of components in dietary interventions is most effective in improving other aspects of metabolism linked to disease risk.

**Conclusion.** The power of nutrient-rich, properly formulated food-based supplements to restore healthy metabolism and thereby prevent or ameliorate disease has not yet been adequately appreciated by the medical and scientific communities. This is in part because the field of nutritional supplements and natural products is tainted by uncritical and biased science. It is also because complex food-based supplements are not usually suitable for traditional placebo-controlled, double-blind clinical trials, considered the “gold standard” for testing drug efficacy.

These problems should not deter serious investigators because the promise of appropriately formulated nutritional supplements to prevent and ameliorate disease is enormous and could be paradigm-shifting. Why use an expensive drug with undesirable or unknown side effects to improve cholesterol when the same effect may be possible with a natural food-based supplement that has no negative side effects? The full potential of food-based supplements to do the work of some drugs without their negative side effects is just beginning to be seriously investigated, but it will require critical un-biased scientific investigation and creative experimental designs. These questions motivate the CHORI-bar research team.

**The Opportunity.** After more than 10 years of research, we now have available a precisely formulated, nutrient-rich, fruit-based supplement bar that significantly improves key features of the metabolic dysregulation of obesity and its related co-morbidities. CHORI-bar’s dietary approach, naturally efficacious without undesirable side effects, has the potential to provide a healthy alternative to drugs for treatment of obesity-related conditions. The Ames Nutrition and Metabolism Group at CHORI is now seeking a strategic partner with the nutrition science expertise and capabilities to complete development, scale up production and commercialize the CHORI-bar under the licensee’s brand name.

A U.S. patent application claiming CHORI-bar formulations, composition-of-matter and uses has been filed. Information regarding bar components and formulation, production, clinical trials, and more can be provided under appropriate confidential non-disclosure terms.
1 Ames, B. N. (2006) Low micronutrient intake may accelerate the degenerative diseases of aging through allocation of scarce micronutrients by triage. PNAS 103, 17589-17594.


7 CHRCO/CHORI (2009). Pending United States patent application no. 13/877,103, owned by Children’s Hospital & Research Center Oakland, California.