The article, “Plasma Lipidomic Profile Signature of Hypertension in Mexican-American Families: Specific Role of Diacylglycerols,” appears in the current issue of *Hypertension*. This original work further illuminates the exciting potential of a new millennial science, first appearing in the literature in 2003. Building on prior studies of lipidomics in hypertension, Kulkarni et al. found that diacylglycerols, generally, and diacylglycerols 16:0/22:5 and 16:0/22:6, specifically, together accounted for ≈2.5% to 3.0% of variance in systolic, diastolic, and mean blood pressure and risk for incident hypertension in Mexican American families. The fact that the diacylglycerols noted were related to incident hypertension suggests an important risk factor or risk marker role in disease progression. The article raises several intriguing points, 3 of which will be addressed in this commentary.

First, the variance in blood pressure and incident hypertension explained by the 2 diglycerides noted above and others listed in Table 1 seem quite modest. However, when considering these relationships are based on blood pressure measured at 1 time point, the variability of blood pressure, and the multiplicity of factors regulating blood pressure, the estimates for variance explained are likely conservative. In other words, assessing the relationship of various lipid fractions to blood pressure by correlating the 2 values in a group of individuals is complicated by the fact that interindividual variation of basal systolic blood pressure is ≥100 mm Hg.

The relationships among specific lipid fractions, blood pressure, and incident hypertension and other health conditions, including diabetes mellitus and nonalcoholic fatty liver disease, could be causal or coincidental. These questions can be and are being addressed in studies of genetically engineered cells and small animals. Insight from these studies is informing the development of traditional and novel therapeutics to alter the abundance or activity of enzymes/proteins underlying variations in the lipidomic profile and related phenotypic expression, including blood pressure, glucose metabolism, insulin dynamics and action, and organ-specific lipid storage. The available information raises exciting potential for additional clinical therapeutic tools beyond current medications, including metformin, thiazolidinediones, and statins that impact fat metabolism and storage.

Second, the author’s finding that the various lipid species were largely genetically determined and reflected only a minor environmental component seems at variance with previous reports. In their insightful review, Chavez and Summers posited that excess dietary calories and lipids (environmental) were a major factor in the generation of lipid species (eg, ceramide, diglycerides, and other lipid species that are plausibly linked to diabetes mellitus, hypertension, and nonalcoholic fatty liver disease). They quoted the 17th century English writer Robert Burton, “Gluttony is the source of all our infirmities, and the fountain of all our diseases. As a lamp is choked by a superabundance of oil, a fire extinguished by excess of fuel, so is the natural health of a body destroyed by intemperate diet.”

Burton’s conclusions are consistent with ancient writings. More than 2000 years earlier, King Solomon wrote, “When you sit to dine with a ruler, note well what is before you, and put a knife to your throat if you are given to gluttony. Do not crave his delicacies, for that (royal) food is deceptive (Proverbs 23:1–3).” More than 300 years later, Daniel and his 3 friends, exiled from Israel to Babylon, refused to eat the royal food. They offered a 10-day challenge, “give us nothing but vegetables to eat and water to drink. Then compare our appearance with that of the young men who continue to eat royal food.” At the end of 10 days, they looked healthier and better nourished than any of the young men who ate the royal food (Daniel 1:11–12, 15).

One potential explanation for reconciling these different viewpoints could be that the nutritional environment of Mexican Americans living in San Antonio is relatively homogeneous. Ecological observations suggest that, where there is no access to excess calories and calorie-dense foods with added sugars and fat (and salt) and where there is a dearth of labor-saving devices and passive entertainment, obesity and the metabolic syndrome, hypertension, and diabetes mellitus are virtually nonexistent. When these populations have access to excess, the health risk profile deteriorates. Thus, some minimal level of access to excess (environmental) is critical in expressing genetic risk. In environments where many, if not most, individuals have access to excess, variation of genetic expression to that excess may dominate the restricted range of environmental variation.

Third, estimated glomerular filtration rate and blood pressure on the third study visit were not correlated. The authors concluded that the association between diglyceride species and blood pressure was unlikely to be explained by an
association with kidney function. However, if kidney function is viewed more broadly than estimated glomerular filtration rate, several lipid species impact ion transport and pressure natriuresis linked to blood pressure regulation. Thus, future studies on lipidomics and blood pressure regulation could be strengthened by more comprehensive assessment of renal function.

In summary, the report on lipidomics and blood pressure offers exciting potential for better understanding gene–gene and gene–environment interactions that impact blood pressure regulation, glucose metabolism, and lipid metabolism and deposition. This research may help explain the variable expression of the metabolic syndrome features between individuals and groups with access to excess. If causal relationships are defined, this third millennial science may inform and accelerate novel therapeutic approaches to efficiently prevent and manage the metabolic syndrome.

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