The International Symposium on the Role of Soy in the Prevention and Treatment of Chronic Disease was held in San Diego, California, on November 4–7, 2001. It was the fourth in a series of symposia on this topic that began in Mesa, Arizona, in 1994. Although the number of attendees was influenced by security concerns in place at that time, scientists representing 21 countries and 5 continents attended the symposium, reflecting the very wide interest in soy research. A total of 36 scientists gave oral presentations, including four overviews of soy research (metabolism of soy isoflavones, breast and prostate cancer, hormonal effects in women, and the benefits and risks of soy infant formulas). The remainder of the talks represented new research data—these were selected by the symposium advisory committee from the submitted abstracts. Two poster sessions were held in which other research data were presented and discussed. These included the effects of soy on coronary heart disease and atherosclerosis (31 posters), cancer (15 posters), bone (14 posters), kidney (5 posters), blood pressure (3 posters), and cognition (1 poster). There were 17 posters on the metabolism and analysis of isoflavones and another 21 posters on a variety of miscellaneous categories.

The symposium received substantial but unconditional support from several companies from the soy and food industry and from the United Soybean Board. These and other companies with products and services based on soy contributed to an exhibit area for the benefit of attendees. The staff of the American Oil Chemist's Association provided the managerial organization for the symposium during the year leading up to and during the meeting. A satellite session was held on the morning of the opening day of the symposium. A summary of the main part of the symposium is presented in the following article (1). The goal of the satellite session was to introduce to the soy research community the areas of genomics, bioinformatics and proteomics. These topics came to the fore after publication in 2000 of the first complete draft of the human genome. The new technologies will require changes in the usual research paradigm. Traditionally, investigators have carried out research posing hypotheses that involve one or at most a few variables. They have examined whether the feeding of a soy product, either as the naturally occurring mixed form in the soy matrix or a purified soy compound, causes specific changes to a measurable variable (e.g., total plasma cholesterol). This straightforward view of life is statistically robust but is also myopic. It may miss or ignore other factors that could explain an overall effect, which may be crucially important because experiments carried out in simplified systems are often used as the basis for more grandiose interpretations regarding human risk or benefit. For example, it was assumed before 1996 that all the estrogenic effects of the isoflavones were occurring at the level of a single estrogen receptor. However, it was hard to reconcile the estrogenic and antiestrogenic effects of isoflavones this way. The discovery of a second estrogen receptor (ERβ) (2) with selective high-affinity binding to the isoflavone genistein and with differential tissue and cellular expression (3) has allowed for rational explanations of much more complex effects of isoflavones in vivo. However, the story does not end here—the estrogen receptor binds to specific regions of DNA in the form of a complex with many other protein partners (4). The possibility exists that each estrogen or estrogen-like compound alters the transcription of a quite different set of genes after binding to ERα or ERβ.

Many of the institutes of the National Institutes of Health are encouraging the use of Gene Chip/DNA microarrays to investigate genome-wide changes in gene expression. John Milner, chief of the Nutritional Science Research Group in the Division of Cancer Prevention at the National Cancer Institute (NCI) noted that NCI already funds investigators studying the relationship between risk of cancer and consumption of soy and individual soy components. He described a research funding announcement (RFA-CA-01-004) to set up cooperative, specialized centers to study nutrient-gene inter-

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1 Presented as part of the Fourth International Symposium on the Role of Soy in Preventing and Treating Chronic Disease held in San Diego, CA, November 4–7, 2001. This conference was supported by Central Soya Company; Monsanto; Protein Technologies International; SoyLife Nederland BV/Schouten USA SoyLife; the United Soybean Board; Archer Daniels Midland Company; Cargill Soy Protein Products/Cargill Nutraceuticals; Illinois Soybean Association/Illinois Soybean Checkoff Board; Indiana Soybean Board; Cyvex Nutrition; Nichimo International, Inc.; Nutri Pharma Inc.; Revival Soy; Solbar Plant Extracts Ltd.; Soyatech Inc.; AOCSS Press; Dr. Soy Nutrition; Eurofins Scientific/Product Safety Labs; and Optimum Nutrition. This publication was supported by (in alphabetical order) the Indiana Soybean Board, the Kentucky Soybean Board, the South Dakota Soybean Research and Promotion Council, Soyfoods Council, Cargill, and the United Soybean Board. Guest editors for this symposium were Stephen Barnes and Mark Messina.

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3 Abbreviation used: NCI, National Cancer Institute.
actions and the prevention of cancer. In addition, he noted that research funding announcements will be forthcoming concerning the identification of new surrogate endpoint biomarkers for cancer. It is reasonable to expect that other institutes of the National Institutes of Health will follow the example of the NCI and provide funds for investigation of nutrient-gene interactions in other chronic diseases that already interest the soy research community. These may include cardiovascular disease and osteoporosis.

Michael Troutman (Affymetrix) provided an overview of how mRNA is isolated from cells and tissues and is converted to cDNA and how DNA sequences are selected for inclusion in the large sets (up to 60,000) of DNA that are chemically bound to chips. He stressed the importance of designing DNA sequences in which one or more nucleotide base can be changed so that nonspecific binding can be assessed. He provided an example of the normalization of gene expression by angiotensin converting enzyme inhibition by captopril after a heart attack.

In parallel to the work on the human genome, considerable advances have been made in determining and manipulating the genome of plants. John Davies (Exelexis) explained how plant scientists have introduced into plants new, but foreign, genes that confer specific and useful properties (e.g., the genes that result in the synthesis of isoflavones can be transferred into the mustard plant, Arabidopsis thaliana). Although this has caused some vigorous discussion because of the transgenic aspects of this approach for the introduction of pesticide resistance into soybeans, the same appreciation of the genetic makeup of a naturally occurring species is enabling genomics-assisted plant breeding to occur. Thus, soybean strains containing different levels of individual components could be prepared by the soybean seed companies for use by soy farmers and ultimately by soy researchers.

Although there is so much interest in genes and gene expression, in the end in the cell, the expressed genes are the blueprints for proteins. The set of proteins that is produced in cells is that cell’s proteome. The proteome is much larger than the set of genes that is expressed in a cell as a result of differential mRNA splicing and more importantly posttranslational modifications (e.g., phosphorylation, glycosylation and tyrosine nitration). John Yates (Scripps Research Institute) described how mass spectrometry has revolutionized the identification of proteins. Proteins, when digested with individual proteases, yield specific and reproducible peptide fragments. The molecular weights of the peptide fragments generated from the open reading frames of genes can be predicted by computers even if the protein product of the gene has never been isolated previously. Mass spectrometry accurately measures the peptide molecular weights of a given protein and thereby allows comparison with information in databases of whole genomes. The key issue is how to separate and display all the protein forms from a cell—two-dimensional isoelectric focusing/sodium dodecyl sulfate-polyacrylamide electrophoresis has been the method of choice. However, other multidimensional liquid chromatography techniques, including those pioneered in Yates’s laboratory (5), are superseding this method. Ultimately, protein chips, analogous to GeneChips, will be manufactured. These may overcome the big limitation of mass spectrometry—sensitivity.

In summary, the technologies that were the subject of this session will be ones in the years to come used by investigators in soy research. Indeed, already there was one presentation in the cognitive function session of the main symposium that described the influence of a soy diet on the proteome of the brains of mice (6).

LITERATURE CITED