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FASEB Symposium Papers Overview

R.M. Krauss

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FASEB Symposium Papers Overview

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This work was supported in part by the U.S. Department of Energy under Contract No. DE-AC03-76SF00098, by the National Institutes of Health Program Project Grant HL 18574 from the National Heart, Lung, and Blood Institute, and by a grant from the National Dairy Promotion and Research Board, administered in cooperation with the National Dairy Council.

FASEB Symposium Papers

Overview

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FASEB Symposium Papers

Overview

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7 The topics addressed in this symposium relate to a fundamental issue of
8 emerging importance in nutrition namely, the role of one's genetic milieu in
9 influencing dietary response to nutrients, and hence in determining optimal
10 dietary intakes of these nutrients. In the case of dietary fat and cholesterol, we
11 are dealing with key components that influence metabolic pathways involved in
12 the development of atherosclerosis and cardiovascular disease. These in turn are
13 now coming to be understood in terms of the genes involved in their regulation.
14 At this time there are dozens of well-characterized genes that have been found to
15 determine the structure and metabolic processing of plasma lipoproteins, and
16 yet, as the papers in this section illustrate, we are only getting a hint of the much
17 larger number of genes that are likely to be found to have a role in regulating
18 plasma lipoprotein levels. In view of the intimate connection between diet and
19 plasma lipoprotein metabolism, it is clear that many of the involved genes will be
20 responsive to change in fat and cholesterol intake, and others will influence the
21 nature and extent of the lipoprotein response to these nutrients. Indeed, it is
22 reasonable to suggest that some genes affecting plasma lipoproteins evolved
23 differently in different population and ethnic groups in conjunction with
24 differing nutritional environments and metabolic needs.

25 The information presented in the papers from this symposium are based
26 on studies in animal models, and in subgroups of human populations defined by
27 genetic and metabolic parameters that have been found to influence the
28 lipoprotein response to dietary fat and cholesterol.

1 Animal models are of considerable importance in this area since they
2 afford us the opportunity to study regulatory mechanisms at the molecular and
3 cellular level and to relate dietary response to atherosclerosis directly. Using
4 molecular and biochemical tools, Dr. Lawrence Rudel and his group have
5 investigated the basis for hypo- and hyperresponsiveness to dietary fat and
6 cholesterol in nonhuman primates. Dr. Beverly Paigen has pioneered the mouse
7 as a model for genetic effects on atherosclerosis susceptibility and dietary
8 responsiveness. The mouse has proved to be particularly useful for investigating
9 genes modulating the protective effects of HDL on diet-induced atherosclerosis,
10 and Dr. Paigen reviews her work in this area, as well as recent studies identifying
11 genes responsible for formation of gallstones on high-fat diets.

12 The remaining papers focus on genetically-influenced factors affecting
13 dietary fat and cholesterol response in humans. Dr. Margo Denke reviews
14 evidence for interindividual variability in lipid and lipoprotein response to
15 dietary fat and cholesterol, and describes recent studies linking dietary fat
16 responsiveness to carefully defined metabolic markers that distinguish
17 pathophysiologic mechanisms underlying lipoprotein disorders. Dr. Darlene
18 Dreon and I present recent work from our laboratory in which the definition and
19 measurement of individual subclasses of human plasma LDL has proven useful
20 for characterizing genetic influences on lipoprotein response to dietary fat.
21 Finally, Dr. Barbara Howard reviews emerging data dealing with the importance
22 of gender, race, and other intrinsic modulators of dietary responsiveness in
23 human populations.

24 The work presented here is but an early indication of the wealth of
25 information that is likely to arise from the application of new genetic and
26 molecular tools to the understanding of factors influencing responsiveness to
27 dietary fat and cholesterol. In advancing our understanding of these phenomena,

1 we are also recognizing that optimal dietary practices will differ among
2 individuals. This has important implications not just for defining specific
3 metabolic mechanisms and gene-diet interactions that may be of importance in
4 the pathogenesis of coronary artery disease (as well as a number of other
5 conditions affected by dietary fat intake), but also for helping the medical,
6 nutritional, and general community to appreciate the biological basis for the
7 wide interindividual differences in dietary responsiveness that they encounter in
8 attempting to promote and follow standard dietary recommendations for heart
9 disease prevention. Ultimately, we might anticipate a sufficient fund of
10 knowledge regarding gene-diet interactions in cardiovascular disease so as to be
11 able to tailor optimal dietary recommendations to individuals or groups with
12 differing needs.

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