

The *JLR* opens up its heart (and liver, fat, muscle) to patient-oriented research

This issue of the *Journal of Lipid Research (JLR)* is devoted significantly to reviews of patient-oriented research that should be of interest to our readers. As described in an editorial by Drs. Dennis and Witztum in the June issue, the *JLR* has a new category, "Patient-Oriented Research," and so it is fitting to celebrate this initiative with a series of articles, from leaders in their fields of work, that review major areas of lipid and lipoprotein, nutrition, and atherosclerosis research. The *JLR* has a long tradition of publishing research involving humans; the first such paper was published in the second issue in January 1960 (Bragdon, J. H., and A. Karmen. 1960. The fatty acid composition of chylomicrons of chyle and serum following the ingestion of different oils. *J. Lipid Res.* 1: 167–170). In recent years, however, fewer patient research articles have been submitted and, I believe, there was a growing feeling among patient-oriented investigators that the *JLR* was not as receptive to such work as it once had been. The editors and editorial board members felt, therefore, that it was important to dispel such feelings and open our journal, in a formal way, to patient-oriented research. I am extremely pleased to have been able to participate in this effort and to organize this "special" issue.

As someone whose research has relied on studies in cultured cells, mice, and humans, I believe I understand the role that patient-oriented research deserves within the spectrum of science that belongs in the *JLR*. We must all realize that there is no approach to gaining knowledge that is intrinsically better, or worse, than any other approach.

Test-tubes, cells, mice, people—they each have strengths and weaknesses as model systems. If you work with test-tubes and cells, you can plan your schedule with little chance of upset, you can control the conditions of the experiment optimally, and you can repeat experiments almost infinitely (or until they work); but the optimal conditions may not always be physiologic, the cells are typically transformed or otherwise tampered with, and someone will want you to extend the work to a living organism. If you work with mice, you can usually plan your schedule (unless the animal facility becomes contaminated or they lose your animals), you can reasonably control the conditions, and you can repeat experiments in genetically identical animals; but the diets we feed our mice are often extreme, marked overexpression or complete deletion of a gene can have consequences that we cannot control,

and, most importantly, mice are simply not people, particularly in terms of lipid metabolism and atherosclerosis. Work with people and you can never plan your schedule, you have modest (at best) control of the conditions, genetic heterogeneity is often a major confounder, the studies take so very long to complete, and you rarely get to repeat the experiment; but what you find can be, if our overreaching goal is to learn how to prevent and/or treat disease, most relevant to the human condition.

So patient-oriented research is very hard to conduct successfully, and because it is, it must be planned and executed with extreme care. That does not, however, mean that it can be conducted with less rigorous requirements; we cannot lower the bar simply because it is difficult to jump over. In this vein (a patient-oriented pun), the authors of each review were asked to not only provide an overview of the published work in their respective areas, but to offer insights regarding the difficulties inherent in each area of investigation. Methodologic issues are no less important in human investigations than in other types of research. In fact, we owe it to our participants to be certain that the data we collect are based on the most sophisticated and validated methods available and that we collect enough data to have the statistical power to reach a conclusion.

The areas chosen for review should not surprise our readers, considering the name of the journal. Metabolism of lipids and lipoproteins has a long and honorable history of research reported in the *JLR*. Hugh Barrett introduces us to the theory and practice of lipoprotein kinetics, a field that made its appearance in the *JLR* in January of 1961 (Dole, V. P., and M. A. Rizack. 1961. On the turnover of long-chain fatty acids in plasma. *J. Lipid Res.* 2: 90–91)—a study, by the way, in which 12 medical students ingested cream labeled with [¹⁴C]palmitate (this was prior to Institutional Review Boards). Over the years, the approaches to modeling of lipids and apolipoproteins have evolved, and seminal findings related to the regulation of plasma lipid and lipoprotein levels were published in the *JLR*. In reviews by Klaus Parhofer and Gary Lewis and their colleagues, we hear about recent studies of VLDL, LDL, and HDL metabolism. Although the Dole and Rizack paper was published 45 years ago, Michael Jensen and his group have added significantly to those original findings, conducting arduous and sophisticated studies of fatty acid metabolism. Elizabeth Parks and Marc Hellerstein take us inside the human liver to provide insights regarding the sources of VLDL and hepatic triglycerides, combining multiple tracers and mathematics to move science forward.

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Moving to another favored area, we have included a review of the effects of dietary nutrients on lipid metabolism by Alice Lichtenstein and a review of dietary nutrient effects on insulin resistance by Jim Mann. Both of these areas have more publications than anyone can digest (sorry again), and Alice and Jim have tried to point out why more is not always better in the field of nutritional science. Finally, we asked John Crouse to provide an update on non- or minimally invasive imaging of atherosclerosis. He and his colleagues have provided an extensive and detailed review that will bring all of us up to date in this important and rapidly moving area of clinical investigation.

I believe that this collection of reviews, which the *JLR* plans to publish in a separate format, is a treasure chest of

information. The authors have given us most of the relevant data in each area but, more importantly, have surrounded their literature reviews with honest and understandable presentations of the strengths and weaknesses of what they and their colleagues do as they search for patient-relevant knowledge. This is a good start for what should be a rewarding (re)new(ed) initiative for the *JLR*. We hope that these outstanding reviews will signify to the research community the *JLR*'s commitment to the publication of outstanding papers on lipid metabolism involving human subjects.

Henry N. Ginsberg,
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