Book Reviews

Am. J. Hum. Genet. 69:667–668, 2001

Genome Diversity: Applications in Human Population Genetics. Edited by Surinder S. Papiha, Ranjan Deka, and Ranajit Chakraborty. New York: Kluwer Academic/Plenum Publishers, 1999. Pp 246. $135

The rush to get publishable units of raw data to consumers in human population genetics often translates into symposium papers that fail the test of time. However, this volume contains some gems within the field of anthropological genetics that connect historical accounts of human diversity that are based on serum protein electrophoresis with a deeper understanding of hybrid populations that emerges from the application of new technologies, including single-nucleotide polymorphisms (SNPs) and simple tandem repeats (STRs), to augment RFLPs, VNTRs, mtDNA, and Y haplotypes. What follows is a comprehensive and complementary set of essays that focus on genome systems in humans dispersed by geography and language. However, anyone expecting unanimity in interpretation of the signals that these different genetic systems yield for a given population may be surprised by a continued difficulty in assembling the final synthesis. If we compare two groups and discount the Y haplotypes, which conflict with the mtDNA, microsatellite data, and the SNPs, what are we left with? A final appeal to linguistics and archaeology for help documenting sexual selection or differential migration rates? The problem of discordant signals quickly surfaces in a comparative genetic study of five Brazilian tribal populations summarized by Hutz et al. Most geneticists, I suspect, prefer well-defended arguments based on extensive and appropriate sampling, relevant mathematical models, and deep understanding of molecular biology. Using this logic, we can discover whether the source of disparity unmasked with different molecular markers is truly a feature rooted in the history of the population examined or simply a peculiar and predictable genetic feature of the system targeted.

For this reason, some of the most useful chapters (one on trinucleotide repeats, by Deka and Chakraborty; one on Y haplotypes, by Tyler-Smith; one on ancient DNA work, by Kolman; one on interspersed repeats, by Deininger et al.; and one on microsatellite statistics, by Chakraborty) do not focus on particular populations but reflect knowledge and judgment about particular systems with their advantages and shortcomings. I would wish for a cohort of beginning graduate students to routinely read these chapters before preparing theses proposals, so that expectations of advisor and student about the level of resolution possible with a given system more closely matches the experience of these experts in their respective fields. These particular chapters are also a valuable reminder to senior researchers about the need for healthy skepticism when it comes to evaluating fantastic media reports of new breakthroughs in human evolutionary biology. There are many unanswered questions in these chapters suggesting how chromatin architecture, recombination rates in haplotypes spanning similar lengths of sequence but drawn from different genomic regions, and responses to drift in uniparental systems possibly contribute to the disparity documented for American Indians of Brazil and other populations highlighted later in the volume.

One case study illustrating the tough choices investigators must make when interpreting discordant data is seen in the very first chapter, by Papiha and Mastana. They explored the origins of the Sinhalese of Sri Lanka. Previous classical studies with protein markers suggested this population might be closely related to Bengalis from northeastern India, following oral traditions. However, this account was later disputed by additional protein studies showing that their closest relationship was actually with the Tamils of Southern India. Noteworthy in this dispute was the fact that the second study drew on Sinhalese and Tamil populations sampled from Singapore, not from Sri Lanka. VNTRs now support the original assertion of a migration from northeastern India, but six STRs from the three southern Indian tribal groups also examined indicate that populations in the south are strongly differentiated from each other. Equivalent STRs for Sinhalese or Tamils are not presented. Is this an instance of sex-biased dispersal coupled with simple genetic drift? Or does suspected disparity in sampling a gene pool from two nonequivalent sources now allow us to dismiss the dispute? The authors don't state that they will be testing Y and mtDNA markers for a complete picture but imply that their four VNTR loci are a better predictor of dispersal than 15 classical protein markers. This will be an interesting case to follow.

Hope that resolution will ultimately come stems from an exhaustive study of six STRs located on the Y chromosome in Turkish subjects (Rolf et al.). This report confirms that both Y and mtDNA haplotypes reveal the same percentage and source of admixture from East Asia, stemming from medieval times. Linguistic and historical records predicted such a result, but it was difficult to show with classical genetic markers and contributed to a general muddling of the picture concerning farmers and their origins in the Middle East, recalling the old dispute about Neolithic demic diffusion versus localized Paleolithic gene pools (which is more fully the subject of the highly informative but difficult-to-follow chapter on mtDNAs of the trans-Caucasus, by Metspalu et al.)

Microsatellite analysis is the subject of an additional chapter examining the relationships between indigenous populations of Columbia and admixture with blacks and whites in the region. How many loci are necessary to dissect admixture and identify its sources? Guarino et al. show that nine are too few—or did they simply show that ABI's Profiler Plus PCR Multiplex System loci were the wrong nine to test? Understanding the location of these loci and the mutational forces to which they respond may be important for quantification of allelic truncation rates.

Uniparental genome scenarios involving Y haplotypes included in this volume range from a localized focus (Pakistani

men) to a more global view (using primarily haplogroups 3 [or M9-G] and 7 [or 92R-7 C]). Zerjal et al.'s male-focused worldview, combined with microsatellite analysis, helps flesh out the recent expansion of certain male lineages in haplogroup 3. However, the chapter by Mehdi et al. discussing present-day Pakistani populations contains a figure that may potentially cause dismay. It portrays genetic relationships as distances for 35 microsatellite loci and depicts African Pygmies in a trifurcation with other all human groups and chimpanzees. I am all for recognizing an African origin of modern humans, but this is an insensitive way to portray that hypothesis.

The uniparental focus also extends to chapters on mtDNA. An attempt by Francalacci et al. to standardize the mtDNA world database is presented for haplogroups, but control-region sequences are restricted to HV1. This is useful for African, European, and some Asian populations but is of limited relevance for tribal populations of southeast Asia and Oceania, as well as for some American Indians. Europeans and central Asians are the primary subject of the contribution of Metspalau et al. on maternal markers. Finally, the chapter by Merriwether et al. on the mtDNAs of the southwest Pacific is a model of clarity and shows just how much information can still be extracted from a single, well-characterized genetic locus.

To complete this set of chapters, Antunez-de Mayolo et al. explore the use of a unique *Alu* insertion in intron G of the progesterone-receptor gene to mark migrations in recent times. Sub-Saharan Africans and most East Asians lack this insertion, which is more common in Europeans and tribal populations from northern and western Asia. When the Americas are assayed, the Maya Campeche of Central America show frequencies comparable to those in modern Germans (.063 vs. .069), which the authors consider evidence of some Caucasian component to American Indian founder populations. This suggestion corroborates the finding of lineage X mtDNA haplotypes in both groups and our inability to map Siberian gene genealogies directly with American Indian ones.

How does this volume stand up to others? It does not give a single worldview on the biogenetic basis of human diversity, as does the recent translation *Genes, People, and Languages* by L. L. Cavalli-Sforza (North Point Press, 2000). However, it is more detailed in many respects and is clearly meant for a different audience. With the recent explosion of haplotypes from the Y chromosome, we have more powerful means of examining who moves where and why. For the next 2 years, however, *Genomic Diversity* will be an excellent place to begin, with signposts to the past for those who seek to learn from the mistakes of others.

REBECCA L. CANN
Department of Genetics and Molecular Biology
University of Hawaii at Manoa
Honolulu

0002-9297/2001/6903-0023$02.00

Am. J. Hum. Genet. 69:668, 2001

Advances in Twin and Sib-Pair Analysis. Edited by Tim D. Spector, Harold Snieder, and Alex J. MacGregor. London: Greenwich Medical Media. Pp. 266. $39.95 (hardcover)

This book is a useful reference for both the researcher new to the field of twin and sib-pair studies and the seasoned researcher seeking a convenient single source of information about many issues related to this type of research. The book begins with a thorough review of the history of twin and sib-pair studies. The historical review is followed by a chapter that outlines various study designs and the advantages and disadvantages associated with them. Next, the experiences obtained from conducting one of the largest twin studies, the Finnish Twin Cohort, are discussed. There is also a chapter on conducting twin studies in developing countries, which discusses the advantages and pitfalls involved in undertaking such research. Additionally, the chapter discussing the generalizability of twin studies and the assumptions underlying them concisely summarizes the major criticisms of twin studies and the evidence refuting them. These chapters provide a solid introduction to twin and sib-pair studies, one that would benefit anyone thinking about embarking on such research for the first time.

For the researcher already conducting a twin and/or sib-pair study, the methodology chapters offer both basic information regarding methods of analysis—introducing such concepts as concordance rates and the estimation of genetic variance—and more advanced concepts, such as dealing with gene-by-environment and gene-by-gene interactions. Modeling the effects of age and survival analysis methods as they apply to twin and sib studies are additional advanced concepts that are nicely dealt with.

However, perhaps the most appealing chapters to the researcher involved in twin and/or sibling studies are those dealing with the use of such studies for mapping the genetic loci underlying complex traits. Current methods of association and linkage analysis are summarized, and advances, such as the power of multivariate analysis, are presented. There is also a chapter on how to extend the twin and sibling models of genetic variance, which are introduced earlier in the book and are implemented in the program Mx, to performing such analyses of molecular data. Finally, the utility of twins in the field of pharmacogenetics is discussed.

STACEY S. CHERNY
Wellcome Trust Centre for Human Genetics
University of Oxford
Oxford
United Kingdom

0002-9297/2001/6903-0024$02.00