

Commentary

The Chinese Human Genome Diversity Project

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The Chinese population comprises one-fifth of the human species. The Chinese government officially recognizes 56 ethnic groups, one of which is the Han majority (1 billion and 100 million people), and the other 55 are ethnic minorities (totaling about 100 million). The latter are spread over most of China, but especially in the south. Close to half of the minorities are found in one of the 28 provinces of China, Yunnan. The distinction is primarily linguistic but corresponds closely to other cultural differences. The paper by Chu *et al.*, published in this issue of the *Proceedings* (1), explores the genetic stratification of about half of the official ethnic subdivisions by means of microsatellites, a class of genetic markers recently discovered that has proved very useful for several purposes. The paper represents the collective effort of several institutes participating in the Chinese Human Genome Diversity Project (CHGDP). The broader Human Genome Diversity Project (HGDP) was generated in 1991 by the international Human Genome Organization (HUGO) and is regionally organized (see <http://www.stanford.edu/group/morriinst/HGDP/html>). The CHGDP has started collecting cell lines from the official ethnic groups and testing their DNAs. The 56 official ethnic groups do not exhaust current Chinese diversity, as there are more than 100 languages spoken in China, but they include the most important ones.

Microsatellites are repeats of short DNA segments, practically less than five nucleotides long. They have a high mutation rate and therefore a large number of alleles, which makes them perhaps three times more informative on average than the most common type of genetic polymorphisms, single nucleotide substitutions, which are mostly biallelic. They are used very widely in genetic linkage studies and have begun to be used in evolutionary analyses (e.g., refs. 2–4). Thirty microsatellites were tested by Chu *et al.* (1) for reconstructing a tree of 14 East Asian populations, which were studied along with 11 populations of a standard set representing the rest of the world. A subset of 15 of the same microsatellites were used to construct a second tree from 32 East Asian populations. These include the first 14 and are compared with the same 11 populations from the rest of the world.

Bootstrap (5, 6) values (measures of reproducibility of the tree branchings, varying from 0 to 100) are high in both trees for the fewer populations outside East Asia, which are rather remote both geographically and genetically from each other. These comparisons present the greatest genetic divergence, and their analysis by tree is therefore more reproducible. Results agree closely with a previous comparable analysis (2). The comparisons among East Asian populations involve much smaller genetic differences and, as expected, bootstrap values are much smaller. Because of their closer geographic proximity they are also likely to have had a much greater reciprocal gene flow than the more distant populations from the rest of the world. Studying populations much closer geographically and genetically puts analysis by tree to a more severe test. Even so, all East Asian populations cluster together in both trees. Their nearest genetic neighbors from the rest of the world are, not

surprisingly, Native Americans. A little less close genetically is the small cluster formed by Australian aborigines and New Guineans, in agreement with the fact that Australia was settled before the Americas and had more time to differentiate (7, 8).

The first outlier within the East Asian cluster of the first tree is the Cambodian branch, and the second a small cluster made of two Altaic language-speaking populations (Buryat and Yakut). These populations live not too far from China, south and north of it, respectively. The other 11 East Asians form two fairly sharp clusters. One includes four Taiwan aborigines and two Chinese ethnic minorities from the western part of the Yunnan province. The other cluster includes Korean, Manchu, Japanese, and two groups of Han (one from Yunnan and the other from the United States). Usually, most Chinese immigrants to the U.S. (and to other countries, like Singapore, Malaysia, the Philippines, Taiwan, etc.) come from southern China, and this is certainly true of the cell lines from California residents from China born in the mainland, collected by Louise Chen and Alice Lin at Stanford and used in our surveys (2, 7, 8). Han living in the south of China mostly came originally from the north, but they did so at very different times, and thus had different times for gene flow from the earlier settlers, that is the minorities. In general, there is a correlation between the average genotype for protein polymorphisms of Hans from the different provinces and of local minorities, but there are exceptions (R. Du, H. Chungtze, E. Minch, and L.L.C.-S., unpublished work).

The second tree is based on more populations but fewer microsatellites, and the bootstraps are inevitably worse in the East Asian part of the tree. Conclusions therefore must be taken with greater caution. The southern group of populations falls into three clusters. S1 contains all four Taiwan aborigines and five Yunnan ethnic minorities. S2 contains Cambodians and six ethnic minorities from various southern provinces other than Yunnan, and also Han from the province of Henan, a north-central province on the north-south boundary. S3 is the tightest cluster and is made up of only two minorities, both from western Yunnan.

The northern group of populations falls into two clusters, N1 and N2. N1 is a classical northern cluster, with Japanese, Manchu, Korean, and Siberian. The Chinese are Han from the North—the northern Chinese by definition—and Han from the Yunnan, probably late immigrants who had no time to receive gene flow from the local people. There are also the Uyghur from the Xinjiang province at the extreme west of China, who received a ca. 25% genetic contribution from ancestors of European origin, showing in their genes and, albeit qualitatively, in their phenotype and dresses (9). Their mummies, the oldest of which are from 3,800 years ago, show unquestionable evidence of European origins in their physical and cultural traits. They are probably descendants of people speaking Tocharian, an extinct Indo-European language. The residual 75% of their genotype must be from admixture with neighbors: 1% gene flow per generation (a very modest quantity) would be enough to cause the level of admixture observed (8).

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Nucleotide Pyrophosphatases/Phosphodiesterases Rik Gijsbers,2003-09 Ecto nucleotidases Extracellular nucleotides and their metabolism Nucleotide Pyrophosphatase Phosphodiesterase NPPs Mammalian NPP isoforms NPPs are modular proteins Enzyme activities of NPPs Functional diversity of NPPs Aims and strategies Materials and methods Results and discussions A family of NPP proteins Characterization of the catalytic domain of NPPs Characterization of the non catalytic ectodomains of NPPs NPP1 and the pathogenesis of insulin resistance Conclusions and Perspectives NuSAP, a Novel Microtubule-Associated Protein (MAP) involved in Mitotic Spindle Organization Tim Raemaekers,2003-09 Vitamin D and bone Linking the fields of vitamin D and bone with those of the nucleus and mitotic spindle Nucleus structure and dynamics Organization of the nucleus Microtubules and associated proteins Mitosis and spindle assembly Control and mechanism of spindle formation and dynamics Materials and methods NuSAP and novel MAP involved in spindle organization NuSAP expression in cultured osteoblasts regulation during development and by 1,25 dihydroxyvitamin D₃ Analysis of NuSAP gene expression at the tissue level and chromosomal localization of human and mouse NuSAP Developmentally regulated expression of NuSAP in the rat testis and mouse embryo Chromosomal localization of human and mouse Nusap General discussion and perspectives **Study of the Mechanisms Involved in the Pathogenesis of Foreign-Body Infections Caused by Coagulase-Negative Staphylococci** Stefaan J. Vandecasteele,2003-11 General introduction Quantification of the expression of Staphylococcus epidermidis housekeeping genes with Taqman quantitative PCR during in vitro growth and under different conditions Use of gDNA as internal standard for gene expression in Staphylococci in vitro and in vivo The effect of systemic administration of antibiotics on quantitative culture of explanted catheters Housekeeping gene expression in Staphylococcus epidermidis during in vitro and in vivo foreign body infections Expression of biofilm associated genes in Staphylococcus Epidermidis during in vitro and in vivo foreign body infections Reliability of the ica aap and atfE genes in the discrimination between invasive colonizing and contaminant Staphylococcus epidermidis isolates in the diagnosis of catheter related infections Discussions Physiological Study of Presenilins and Bace2, Two Proteases Involved in the Pathogenesis of Alzheimer's Disease Jos Tournay,2006 Pathogenesis of Hemodynamic Changes During Raised Intracranial Pressure Johannes Jacobus Louisa van Loon,2003-09 Cerebral cardiovascular control anatomical and physiological aspects Catecholamine response to a gradual increase of ICP Course of ICP changes in two models of progressive intracranial hypertension Pathogenetic aspects of the hemodynamic changes during raised intracranial pressure Summary and Conclusions **Rearrangement of EWSR1 and TAF15 with the Transcription Factor CIZ/NMP4 in two Novel Recurrent Translocations t(12;17)(p13;q11) and t(12;22)(p13;q12) in Acute Leukemia** Alessandra Martini,2004-09 Experimental Evaluation of the Host Immune Response to Xenogenic Bio-derived Collagen Grafts in Rodent Models Fang Zheng,2006-09 *Genetic Analysis of Herpesvirus Entry Receptors and Host Susceptibility to Herpes Simplex Virus Infection* Frank Struyf,2004-09 *Long-Term Clinical Pharmacokinetic Study of Tacrolimus and Mycophenolic Acid and*

Metabolites in de Novo Renal Allograft Recipients Dirk Kuypers,2003-11

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Tine Van De Sande,2004 This is a Ph D dissertation The present thesis forms an integral part of the efforts to understand the molecular mechanisms and the biological and clinical significance of increased lipogenesis in tumor cells In part I it is explored whether the PI3 kinase Akt pathway a signal transduction cascade which is frequently dysregulated and constitutively activated in cancer cells may contribute to increased lipogenesis In part II the authors have tried to gain more insight into the functional significance of tumor associated lipogenesis by unraveling the nature and fate of newly synthesized lipids in cancer cells To put these studies in a proper perspective the authors will provide a more detailed overview of the present understanding of the mechanisms the role and the clinical significance of increased lipogenesis in human cancer

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protein NIPP1 Nuclear Inhibitor of Protein Phosphate 1 which was initially described by the host laboratory in 1992 and still is the major focus of its research efforts The first part of the introduction describes our current insights into the structure and function of NIPP1 with the exception of aspects that directly deal with this doctoral project For reasons of clarity the data are presented in a logical manner which implies that they are not necessarily presented according to their order of discovery In the final sections of the introduction a brief overview will be given of the state of the art of the structure and function of ribonucleases and transcriptional repression mechanisms two topics that directly related to this research project Contents include Introduction The Structure and Function of NIPP1 The Structure and Function of Ribonucleases Transcriptional Repression in Eukaryotes Aims and Strategies Materials and Methods Results and Discussions Mapping of the RNA binding and Endoribonuclease Domain of NIPP1 Screening for Proteins that Interact with the C Terminal domain of NIPP1

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Table of Contents Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity

1. Understanding the eBook Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity
 - The Rise of Digital Reading Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity
 - Advantages of eBooks Over Traditional Books
2. Identifying Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity
 - Exploring Different Genres
 - Considering Fiction vs. Non-Fiction
 - Determining Your Reading Goals
3. Choosing the Right eBook Platform
 - Popular eBook Platforms
 - Features to Look for in an Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity
 - User-Friendly Interface
4. Exploring eBook Recommendations from Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity

- Personalized Recommendations
 - Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity User Reviews and Ratings
 - Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity and Bestseller Lists
5. Accessing Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity Free and Paid eBooks
- Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity Public Domain eBooks
 - Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity eBook Subscription Services
 - Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity Budget-Friendly Options
6. Navigating Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity eBook Formats
- ePub, PDF, MOBI, and More
 - Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity Compatibility with Devices
 - Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity Enhanced eBook Features
7. Enhancing Your Reading Experience
- Adjustable Fonts and Text Sizes of Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity
 - Highlighting and Note-Taking Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity
 - Interactive Elements Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity
8. Staying Engaged with Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity
- Joining Online Reading Communities

- Participating in Virtual Book Clubs
- Following Authors and Publishers Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity
- 9. Balancing eBooks and Physical Books Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity
 - Benefits of a Digital Library
 - Creating a Diverse Reading Collection Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity
- 10. Overcoming Reading Challenges
 - Dealing with Digital Eye Strain
 - Minimizing Distractions
 - Managing Screen Time
- 11. Cultivating a Reading Routine Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity
 - Setting Reading Goals Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity
 - Carving Out Dedicated Reading Time
- 12. Sourcing Reliable Information of Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity
 - Fact-Checking eBook Content of Reconstruction Of The Evolution Of Chinese Populations By The Study Of Human Genome Diversity
 - Distinguishing Credible Sources
- 13. Promoting Lifelong Learning
 - Utilizing eBooks for Skill Development
 - Exploring Educational eBooks
- 14. Embracing eBook Trends
 - Integration of Multimedia Elements
 - Interactive and Gamified eBooks

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