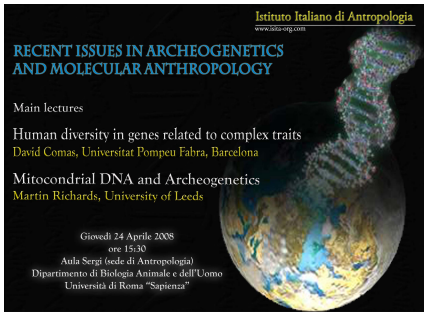
Recent Issues in Archeogenetics and Molecular Anthropology



Giovedi' 24 Aprile 2008 - 15:30 – 18.30

Aula Sergi, Dipartimento di Biologia Animale e dell'Uomo - Universita' di Roma "Sapienza"

Chairman: Davide Pettener (Università di Bologna)

HUMAN DIVERSITY IN GENES RELATED TO COMPLEX TRAITS

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Complex traits are characterized by being determined by several genetic and environmental factors. With regard to the genetic component, a lot of effort has been invested in determining the variants that confer susceptibility/protection to several complex diseases. For instance, several polymorphisms have been widely implicated in psychiatric and behavioural disorders, with numerous reports of associations and almost equally as numerous reports of the failure to replicate a previous finding of association. The failure to replicate findings of association may be explained by population based differences in allele frequencies and linkage disequilibrium within the set of genes analysed.
In order to investigate the effect of population genetic differences in association studies of complex traits, we have analysed two set of genes involved in the human nervous system: the NRG1 gene region, and a set of dopamine and serotonin neurotransmitter pathway genes. These genes were analysed in a set of 39 worldwide populations representing global genetic diversity.
Our analyses resulted in apparently divergent conclusions: extreme population differences have been found in the NRG1 gene, whereas a surprising homogeneity of the allele frequencies across worldwide populations was found in dopamine/serotonin genes. These findings suggest that ethnic differences are not major generators of artefacts in genetic association studies of psychiatric disorders with dopamine/serotonin and factors other than ethnic differences in genetic variation may explain the discrepancies reported among genetic association studies with this set of genes to date. On the contrary, extreme differences have been found for the NRG1 gene, suggesting that some of the failures to replicate association study findings may be due to population differences in the studies performed.
Our results reinforce the idea that population genetic differences should be taken into account for every gene region analysed in future association studies, with these studies providing just such information for future studies involving genes from this set.

MITOCHONDRIAL DNA AND ARCHAEOGENETICS

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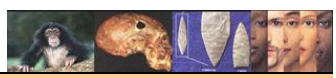
Despite the development of other marker systems and genomic approaches, mitochondrial DNA (mtDNA) remains one of the most powerful genetic tools for deciphering signals of human dispersal history. Nevertheless, the possibilities of using information from the mtDNA control region alone have become all but exhausted, and complete mtDNA genome sequencing is becoming more and more widely used. This allows for a far more accurate reconstruction of the phylogeny, and much more precise age estimates, and has already led to considerable refinement of models of prehistoric human dispersals. One example we will discuss is the prehistory of island Southeast Asia, where the dominant archaeo-linguistic settlement model for many years has been of a Neolithic expansion out of Taiwan. However, the study of mtDNA haplogroup E at the level of



complete sequences has suggested that at least some dispersals were centred on island Southeast Asia itself, and were most likely triggered by rising sea levels due to global warming after the Last Glacial Maximum. These and other analyses, both of humans and domesticated animals such as cattle, have benefited greatly from the greater precision afforded by complete mtDNA sequence data. Recently, however, the calibration of the mtDNA molecular clock has been brought into question, with the discovery that weakly deleterious mutations in the coding region render the rate non-linear. We will therefore also describe our efforts, based on the entire available complete mtDNA sequence database, to remedy this problem.

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mtDNA DIVERGENCE OF AYMARA FROM QUECHUA AND UROS POPULATIONS OF THE TITICACA LAKE REGION (PERU)

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Over the centuries, the Titicaca Lake has been a cradle for the major civilizations of the South American pre-history. At present time, it is possible to find the presence of three native cultures: Uros, Aymara and Quechua. These three major cultures imprinted their influence in shaping the present-day structure of highland communities, reflecting different population histories.
The partial lack of archaeological data requires complements from other fields, i.e. Linguistics and Molecular Anthropology, in order to further investigating these pre-Columbian civilizations. In the absence of significant genetic data from previous work, this study aims to contribute to the reconstruction of the archaeo-genetic history of the Titicaca region drawing a novel genetic-molecular landscape.
The sample investigated derives from a field survey conducted in May 2007 on a total of 83 individuals, from which it has been obtained the first mtDNA HVSI sequences from native people of the Titicaca region, and the first representative data for the Aymara population. A complete database of Amerindian populations has been assembled to further analyze both the collocation of our sample and the genetic structure of this region.
Our preliminary results reveal an interesting pattern for the Aymara population. Their differentiation within the Andean context suggests the persistence of an original genetic component carried up across the centuries, surviving the Inca and the European conquests.
This investigation also gives the opportunity to discuss some hot points about the genetic variability in South America and in the whole American continent. Recent studies had shed light on the first steps of human entry in North America adding new chronological and demographic data. For South America, on the other hand, a clear scenario has not been described yet. Hence, the debate on the first colonization is still open.

SAMPLING ITALIANS FOR THE GENOGRAPHIC PROJECT: A STRATEGY BASED ON SURNAMES AND POPULATION MOBILITY

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The peopling of Italy can be compared to a mosaic in which multiplehistoric layers in different geographic areas are differently superimposed. As a consequence, any study aiming to reconstruct the genetic history of Italian populations requires a carefully designed sampling strategy. In this study, sampling criteria are defined on the basis of a biodemographic approach. Nearly 80,000 surnames, representing around 13,000,000 of individuals, are used to depict five centuries of internal migrations in Italy. Results provide lists of founder surnames in every Italian province, information on the probability of collecting founders by random sampling per province, the definition of genetically homogeneous areas. Finally, we show how these data are applied in the current Genographic Italy sampling campaign.