ABSTRACTS

Introduction

Patricia Rodriguez-Tomé, InToResearch, Pula, Italy

In the past few months conferences and round-tables involving women scientists have been organized in Sardinia (Cagliari, November 2008) and Turkey (Istanbul, March 2009) as part of the "Set-Routes, Women in science" initiative, a project funded by the European Union under the Framework 6 Program. These events have begun promoting the idea of networking around Europe, and with a particular focus towards the Southern area around the Mediterranean Basin.
Mediterranean populations have a history of more than 3 millennia of commercial trade. Ceramics, wine and grain have been found far away from their points of origin. Population themselves have mixed. Population studies point to the similarities in the genetics background. Genetics show that disease have common origins and form around the Mediterranean, different from other European areas.
Sardinia is a perfect place for a multidisciplinary encounter on the genetic characteristics of the Mediterranean populations. This workshop, "Genetica nel Bacino Mediterraneo" is not yet another workshop on genetics. All speakers in this event are women scientists from different disciplines - biology, linguistics, history - whose working interest is in the Mediterranean area and its populations.All of them come with with a strong commitment to collaborations and exchange of ideas and discussions.
We hope that this workshop in Pula will be the first of a serie that we in Sardinia will be very glad to host. We are convinced that such encounters will strengthen the collaborations between research groups around the Mediterranean Sea.

Genetic of Type1 and atypical diabetes

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Our research are currently focused mainly of the monogenic form of diabetes - "strange" diabetes or not, by studying families or selected populations. The populations in our studies are mainly populations with a high level of consanguinity, founders effects or isolated like in Lebanon, Iran , Palestine, Tunisia and Algeria.
We wish to collaborate with other laboratories working on mediterranean populations, to extend this work to the study of other strong effects that influence the risk of diabetes (predisposition or protection): environmental factors, cultural and individual, which present a diversity and important wealth in the mediterranean populations.

Per una linguistica del Mediterraneo

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Il Mediterraneo è stato da sempre oggetto di particolare interesse per diversi studiosi appartenenti a più ambiti di ricerca. Tuttavia, tale area meriterebbe un maggior approfondimento anche da un punto di vista linguistico. Infatti, moltissimi sono i contatti che si sono avuti nella regione mediterranea sin dalla preistoria. Nello specifico, sarebbe utile appurare quanto tali contatti abbiano influito sull'assetto attuale delle lingue del Mediterraneo. Come vedremo, negli ultimi vent'anni alcuni passi in avanti sono stati fatti, ma ancora molta strada deve essere percorsa. È necessario infatti ridefinire metodi, strumenti e prospettive di ricerca, al fine di ridare maggiore consistenza all'ipotesi di una eventuale area linguistica panmediterranea.

Genetica della Sclerosi Multipla in Sardegna

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La sclerosi multipla (SM) è una malattia autoimmune demielinizzante del sistema nervoso centrale, causa comune di disabilità nel giovane adulto. La patologia presenta una distribuzione geografica caratteristica e segue la latitudine, infatti incidenza e prevalenza aumentano in entrambi gli emisferi man mano che ci si allontana dall'equatore.
Un'eccezione a questa regola è rappresentata dalla Sardegna, un'isola del mediterraneo caratterizzata, nonostante la sua posizione geografica, da una elevatissima prevalenza di malattia. Inoltre anche altri disordini autoimmuni come il diabete mellito di tipo 1 (T1D) sono molto frequenti nell'isola. Recentemente è stato osservato che i pazienti SM Sardi sono ad alto rischio per T1D e questo supporta l'ipotesi di un elevato carico genetico predisponente all'autoimmunità nell'isola. Inoltre negli ultimi 50 anni in Sardegna è stato osservato un incremento dell'incidenza associato ad una riduzione dell'età d'esordio.
La modesta ereditabilità della SM riflette l'effetto di una complessa interazione tra fattori genetici e fattori ambientali. In particolare nel modello animale di SM la malattia sembra essere regolata da molti geni (probabilmente più di 100) ognuno con un piccolo effetto. Studi sull'uomo hanno suggerito una situazione simile.
Nonostante importanti sforzi in questo ambito, l'unico fattore genetico legato alla malattia è rimasto per decenni l'HLA. Recentemente sono stati introdotti anche nella SM degli studi in cui, tramite metodiche innovative, si analizza in dettaglio l'intero genoma umano (con i cosiddetti "genome wide association studies") alla ricerca di geni associati alla malattia. Questi hanno permesso negli ultimi due anni di identificare nuovi geni di suscettibilità nella SM, in particolare sono stati inequivocabilmente dimostrati essere in associazione con la malattia (nonostante ognuno abbia un minimo effetto) i geni che codificano per le seguenti proteine: recettore alfa dell'interleukina 2 (IL2RA), recettore dell'interleukina 7 (IL7R), CLEC16A (KIAA0350) e CD58.
I progressi nelle tecnologie di genotipizzazione e una migliore comprensione della struttura funzionale del genoma umano, insieme al miglioramento della definizione del fenotipo di malattia, possono costituire attualmente gli strumenti adatti per identificare i geni coinvolti nella patogenesi della SM.
La Sardegna è un isolato genetico: la popolazione attuale mostra evidenza di effetto fondatore, è il risultato di una fissazione di alleli e aplotipi rari o assenti altrove e non mostra una eterogeneità genetica su larga scala. I Sardi sono quindi la popolazione ideale per studiare malattie autoimmuni complesse quali la SM. La genetica della SM in Sardegna è stata ampiamente studiata negli ultimi decenni e i risultati ottenuti verranno discussi.

Disease Gene Hunt in Turkey

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Within the scope of the Human Genome Project (HGP), the total human genetic information (genomic sequence) has been obtained. The most significant contribution of the generated data was to provide the basic genomic information that will facilitate the deciphering of the functions of our genes. So far, functions of only a fraction of our genes have been described, while the majority of the genes are classified unknown. The main purpose of "proteomics", the most important research area post HGP, is to decipher the functions of our genes. The most certain route to the identification of the function of a gene is via investigating the clinical manifestations in individuals (patients) with defects in that gene. The genes responsible for rather frequent monogenic diseases have been identified already, and at present human genetics research is focusing on rare disorders. To identify a rare disease gene, first the gene is localized and subsequently those genes at the locus that are assessed as good candidates are analyzed for mutations in affected individuals. Detection of a mutation in a candidate gene of a patient would ascertain that it is the gene responsible for the disease. This would reveal the molecular basis of the disease and the function (if unknown) of the gene. Future work would include the investigation of the genes that interact with the disease gene and of the molecular mechanisms the gene plays a role in. Other contributions of the research are the training of young scientists and contributing to scientific research that utilizes the genetic resources of our country. Once the gene is identified, genetic counseling service could be offered for pregnancies at risk. In addition, whether other diseases with similar clinical manifestations also result from defects in the same gene could be investigated. Also, patent application can be done for possible means of cure or treatment that could be developed only after the elucidation of the molecular basis of a disease

In Anatolian families, hundreds of rare diseases are observed. Some of those diseases are novel. The research area of our team is to define new gene functions by identifying new disease genes. Due to the high rate of consanguineous marriages, most of the diseases are inherited in an autosomal recessive fashion. We have already published our results on the identification of the genes responsible for pulmonary alveolar microlithiasis and a recessive split-hand/foot malformation. Other genes identified are for azoospermia, arthrogryposis multiplex and microhydranencephaly. We are still in search of genes responsible for another microhydranencephaly, spastic paraplegia and rare neurological diseases. Having good genetic material available is opposed by the labor-intensive and expensive methods and the dependency on good clinical evaluations.

Il mito della purezza delle origini ad Atene.

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Il mito degli Ateniesi purosangue fu al centro della ideologia democratica ateniese tra V e IV sec. a.C., quando esso operò in funzione della determinazione di Atene di limitare la cittadinanza e la sovranità politica ai soli discendenti di «sangue puro». Lo studio della documentazione rivela che tale mito non trovi invece alcun fondamento nella mentalità ateniese del secolo precedente, il sesto, quando l'azione politica dei grandi riformatori

democratici, Solone e Clistene, appare al contrario contrassegnata da un volontà di apertura e di integrazione nei confronti degli «impuri».

Molecular investigation of genetic disorders in Tunisia, current situation and perspectives

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Tunisian population, like other North African populations, is characterized by its heterogeneous ethnic background and a high rate of consanguinity. The rate of consanguineous mating is estimated to 33% in northern Tunisia. Depending on the studied area, this rate reaches over 60%. This can be explained by the fact that endogamy is culturally favoured. In consequence of the high rate of inbreeding, there is an increase in the prevalence of recessive genetic disorders. During the last 10 years our research unit contributed to the molecular characterisation of several genetic diseases in Tunisia including Fanconi anaemia, idiopathic BCGitis, type I megaloblastic anaemia, epidermolysis bullosa, palmo-plantar hyper-keratosis. Although different diseases are studied, a standardized strategy has been adopted. In a first step, patients and their families are typed with microsatellite markers flanking the already known genes to assess linkage to these candidates using homozygosity mapping. In a second step mutation screening is performed by direct sequencing of the coding region of the gene of interest. Despite the relatively small size of the Tunisian population, clinical and genetic heterogeneity is generally observed. One of the major achievements was circumventing liver biopsies in infants for the diagnosis of glycogenosis by developing a simple molecular tool.
More recently we started investigation of multifactoriel diseases, including type II diabetes. We have shown familial aggregation and excess maternal transmission of type 2 diabetes (T2D) in the Tunisian population and we investigated involvement of genetic variations in susceptibility to type II diabetes or its complications. Through a New Partnership for Africa's Development/ North African Biotechnology Network (NEPAD/NABNet) project, on investigation of T2D in North African Population, we aim to exchange experience with other colleagues and develop capacities in the field of genetics of non communicable diseases.

In the post-genomic era and taking into account the geographical, historical, socio-cultural and economic context of southern Mediterranean countries, development of strategies for better prevention of genetic diseases should be discussed and set up not only at the national but also at the regional level.

Information content of connections determines network topology: The case of transcriptional gene regulatory networks and outlook for microRNA.

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Many of the presently observed complex patters and structures in living beings have emerged spontaneously, without the need for evolutionary selection pressure, merely as a consequence of the possibilities offered by the laws of physics, chemistry and combinatorics, with subsequent selection leading to the fine tuning of these already

complex formations. We have demonstrated that the topological properties of transcriptional gene regulatory networks can be reproduced on the basis of a random sequence-matching rule, given the appropriate length distributions corresponding to the information content of the binding sequences. We argue that RNA interference and the role played by micro-RNA in gene regulation can also be understood on purely probabilistic grounds.