Francois Cambien

Institut National de la Sante et de la Recherche Medicale (INSERM), France

CV

Epidemiologist, geneticist, Director of INSERM Unit 258 "Molecular and Epidemiological Genetics of Cardiovascular Diseases" and of INSERM SC7 "INSERM DNA Bank for Cardiovascular Research".

CONTACT INFORMATION

Francois Cambien, M.D., Ph.D.
INSERM U525
Faculte de Medecine Pitie-Salpetriere
96 bd de l'HOPITAL
Paris, France
cambien@idf.inserm.fr

Genetics of multifactorial diseases

The etiology of mutifactorial diseases is characterized by a complex interplay between genetic and environmental determinants. Atherothrombosis, diabetes, hypertension, obesity, cancer, rheumatologic, neurodegenerative, pulmonary, digestive and most other common disorders are multifactorial; even infectious diseases are known to be strongly influenced by genetic predisposition. A number of environmental factors contributing to these conditions have been identified, such as infectious agents, smoking, excess or specific patterns of food intake, sedentarity, stress of different nature ... The conviction that genetic factors contribute to most common disorders is based on the observation that these diseases aggregate in families in a specific way that is compatible with genetic transmission and on the discovery of associations between particular gene variants and the risk to develop the disease. Identifying the precise genetic determinants of multifactorial diseases is considered important for 2 reasons: 1. On the short term, from a clinical perspective, it may help identify individuals at increased risk and provide a rational to tailor drug prescription, providing better efficacy and reduced risk of adverse effects; 2. For the long term, from a more basic perspective, a global understanding of the contribution of gene variability to etiology and pathophysiology through the study of major biological functions may be a prerequisite to ultimately control diseases and maintain health and well-being of human until an advanced age. Obviously, the first reason above constitutes the major stimulus for present research. Genetic factors having strong effects may be identified by a systematic exploration of the genome; however many expectations may not be fulfilled, because many genes may be involved, the genetic effects may be weak, important interaction may exist ... In several research programs, the assumed models linking genes to multifactorial diseases may be much too simplistic (as for example in the proposals for whole genome associations studies) or the question of which model to assume may even not be considered. Despite the availability of the almost complete human genome sequence, we still know very little of the distribution and structure of polymorphisms across the human genome. An important goal for the next few years will be to generate (in an appropriate way that needs to be discussed !) a catalogue of 'all' common polymorphisms of functional sequences (genes and non-gene) in

the human genome. A second goal which is implicit for the global understanding mentioned above will be to develop models of relevant functions that will allow the direct evaluation of naturally occurring gene variants reliably and with high throughput using proteomic tools and cellular arrays. Interestingly biological systems and the functions to which they contribute are not specie-specific; there is therefore good reasons to investigate them in relation to the genetic variability of their protein components in different species simultaneously. The evolutionary and functional information gained from these comparative-genomics studies is expected to provide a powerful source of inspiration for drug development or other rational ways to maintain health. As recently stated by Richard Lewontin "The greatest methodological challenge that population genetics now faces is to connect the observations between outcome of evolutionary processes to the tradition of experimental functional biology". We believe that it is not only the challenge of population geneticists but of most scientists trying to understand multifactorial diseases. Epidemiology and Mendelian genetics may be helpful in this context but may also obscure the specificity of this area of research which has to develop its own concepts and tools.