

Scientists identify strategies to conquer lifestyle and genetic factors related to chronic diseases

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A dramatic increase in the incidence of chronic inflammatory diseases such as asthma, allergy, and irritable bowel syndrome, has led to concern about how modern lifestyles may trigger physiological defense mechanisms. Now, in the context of a foresight study under the auspices of the European Science Foundation (ESF), a group of scientists has examined the challenges associated with chronic inflammatory diseases, and described 10 key areas with the highest priority for research. Their recommendations are published in a supplement to *The Journal of Allergy and Clinical Immunology* (JACI), the official journal of the American Academy of Allergy, Asthma & Immunology (AAAAI).

"Many transmissible diseases have been effectively eradicated over the last half century, yet there has been a marked increase in the incidence of chronic inflammatory diseases," says committee chair Harald Renz, MD, of the Institute of Laboratory Medicine and Pathobiochemistry, Molecular Diagnostics, Phillips University, Marburg, Germany. Strategies are urgently needed to determine the causes of these chronic diseases and identify targets for therapy and prevention."

Factors responsible for the development of chronic inflammatory diseases are not easily determined. While epidemiological evidence clearly points to an environmental influence, not all individuals in these environments develop disease. Susceptibility to chronic inflammatory disease has a clear genetic component, but genetics may not be the only

determining factor. Prenatal exposures can influence later susceptibility to disease. After birth, factors such as breastfeeding and exposure to microorganisms appear to further influence the likelihood of developing diseases such as [asthma](#) and allergy.

Dr. Renz and his colleagues on the Scientific Committee of the ESF Forward Look on Gene-Environment Interaction in Chronic Disease (GENESIS) identified the following 10 key recommendations as having the highest priority for research into chronic inflammatory diseases:

1. Research should distinguish between therapy and prevention.
2. Large prospective cohort studies including deep phenotyping should be made a priority.
3. Research should focus on the question of tolerance.
4. A global (international) approach should be taken to understanding chronic inflammatory disease.
5. Effective interdisciplinary research strategies must be established.
6. New tools and experimental models must be developed.
7. Protocols for data collection, handling, and storage need to be harmonized.
8. Substantial investment must be made in infrastructure, personnel, and development of research tools.
9. Dedicated funding must be provided for interdisciplinary research.
10. Effective public-private partnerships must be developed to ensure free exchange of information.

Furthermore, the committee pointed to a series of key strategic research targets for which significant progress in the management of chronic diseases may be achieved.

Therapy and Prevention. Given the complexity of chronic [inflammatory diseases](#), therapies must be based on deep environmental, clinical and biological phenotyping of patients. Without deep phenotyping, it is impossible to determine whether a potential therapy is clinically ineffective or simply inappropriately targeted. The committee calls for the identification of novel biological markers to enhance patient stratification, and for investments in bioinformatics and systems biology to realize the full potential of omics data.

For prevention, key issues include the selection of appropriate populations and the long-term tolerability of putative long-term protective agents. The results of clinical studies of probiotics as infant food supplements to prevent allergic disease have been mixed. The committee recommends that the term probiotic be employed with caution, and that further research be done to understand the function of gut microbes in health and disease.

Large Cohort Studies. The committee calls for large cohort studies, initiated prior to birth, to fully take into account the impact of how intrinsic and extrinsic factors determine the probability that an individual will be healthy or develop a chronic disease, given the right environmental stimuli. Such studies would analyze biological data including genomic, clinical, and environmental factors, and also psychosocial factors such as stress. It will be important to ensure international collaboration and coverage of populations with different lifestyles and environmental exposures.

Partnerships. The shifting global pattern of chronic disease to developing nations offers an opportunity to identify key factors that confer both risk and protection. The committee recommends that research projects be established in regions with low or developing risk of chronic inflammatory disease, and the establishment of parallel birth cohorts in low- and high-risk regions. Cross-disciplinary partnerships will be

essential as well, extending beyond traditional disciplines such as epidemiology and microbiology to mathematics, virology, and ecology. Finally, effective private-public partnerships, with more fluid exchanges of information between academia and industry, will be a key driving force for future research.

Research Tools, Data Generation and Management, and Infrastructure and Personnel. New research strategies that consider the diversity of the microbiome in the choice of experimental models and the potential reproducibility of results will be needed. Because of the complexity introduced by the microbiome, substantial investment will be required to develop the bioinformatics and systems biology approaches required to analyze the datasets generated. An electronic infrastructure to support integrated approaches and open collaboration will be necessary. Funding should be made by panels in which no specific discipline is over-represented to support unbiased approaches. And, a new generation of biological and medical scientists will need to be ready to exploit rapid developments in information technology. They will need to use insights from a range of scientific disciplines as well as fields as diverse as finance and engineering. The committee suggests the creation of international graduate schools to provide specific training in interdisciplinary research.

In the foreword accompanying the supplement, Lars V. Kristiansen, PhD, Science Officer, European Science Foundation, European Medical Research Councils, Strasbourg, France, and colleagues comment, "The socioeconomic costs of chronic diseases are staggering and ever increasing. There is an urgent need to prioritize resources and identify the most efficient scientific and societal initiatives to be adopted. National collaboration within the European region represents the most efficient manner in which strategies for amelioration of [chronic inflammatory diseases](#) in the western world may be achieved."

More information: The supplement is entitled "Gene-Environment Interaction in Chronic Disease – An ESF Forward Look," by H. Renz, I.B. Autenrieth, P. Brandtzaeg, W.O. Cookson, S. Holgate, E. von Mutius, R. Valenta, and D. Haller. It appears as *The Journal of Allergy and Clinical Immunology*, Volume 128, Supplement (December 2011) published by Elsevier. The supplement is freely available through the JACI website at [www.jacionline.org/issues?issu...0091-6749\(11\)X0015-5](http://www.jacionline.org/issues?issu...0091-6749(11)X0015-5)

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