European Initiatives in Food Allergy Research

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Concerns about food allergies have increased over the last 20 years, and in response to this the European Commission, through the Directorate Géneral for Research, has funded a series of projects focused on food allergy under successive tranches of funding known as Framework Programmes (FP). The lack of good quality data on how many people suffer from food allergies, which foods they react to, how much of a food can cause a problem, has been hampering the development of effective management strategies to optimize the quality of life for allergic patients. There is also no data on the impact of food allergies on quality of life or an estimate of its cost to society. The EuroPrevall project[1], funded through FP6, brings together a multidisciplinary partnership to address these issues. Cohorts spanning the main climatic regions of Europe have been developed in infants through a birth cohort, community surveys in school-age children and adults and an outpatient clinic study. Confirmatory double-blind placebo controlled food challenge diagnosis is being undertaken using foods as they are eaten with titrated doses to allow no-effect and lowest-observable effect levels for allergenic foods to be determined. The cohorts will also facilitate validation of novel *in vitro* diagnostics through the development of the EuroPrevall serum bank. Complementary studies in Ghana, Western Siberia, India and China will allow us to gain insights into how different dietary patterns and exposure to microorganisms affect food allergies. This also builds on networks developed through an allied project, Glofal, led by Maria Yazdanbakhsh which is taking tools and approaches developed in EuroPrevall and other EU-funded projects, to study food allergies in Ghana, Gabon and Indonesia with particular reference to the role parasitic infections and parasitic diseases may play. New instruments to assess the socioeconomic impact of food allergy have been developed and are now being applied in the EuroPrevall cohorts, which will allow an assessment to be made of the burden this disease places on allergy sufferers and their communities.

Two new projects have been funded under FP7 related to food allergy, FAST, co-ordinated by Ronald van Ree and FORALLVENT, co-ordinated by Erika von Mutius. FORALLVENT has been set up to create a platform for the development of innovative strategies and therapeutic approaches in the area of asthma and allergy. One of its key goals is to bridge the gap between the various strands of research on allergic diseases and the practical application of their results. FAST is a research project, due to begin later in 2008 which over a seven year period focused on the development of safe and effective treatment of food allergies. It targets persistent and severe allergy to fish and fruit, specifically peach. FAST will develop a safe alternative by replacing food extracts with hypo-allergenic recombinant major allergens, the active ingredients of specific immunotherapy. After pre-clinical testing (toxicology testing and efficacy in mouse models), Phase I and II randomized double-blind placebo-controlled multi-center clinical trials will be performed. Two routes of administration will be evaluated, subcutaneous in case of fish and sublingual in case of fruit, the primary read-out to assess efficacy being double-blind placebo-controlled food challenge.

The new information coming from these projects is going to fill many of the gaps in our knowledge. In addition international collaborations, spanning Europe, N. America, Africa, India and the Far East, is giving us new insights into how environmental and lifestyle factors may affect patterns of allergies. This is especially relevant in an era of the global market place where industries must manage hazards across complex supply chains spanning continents. Furthermore, our knowledge of how environmental factors, including climate change, may affect patterns of food allergies and hence how we develop effective knowledge-based means of predicting and preventing food allergies. ***In view of the new data and tools and this emerging picture of food allergies on a global scale how do we move forward***

to protect allergic consumers from existing hazard, develop effective preventive strategies and move towards the ultimate goal of a cure for this important disease? Can we build European-North American initiatives to address these issues? Some topics and questions that may form the basis for such interactions are:

1. Development of holistic approaches to managing allergens in foods: Data becoming available from EuroPrevall, programmes such as FARRP, form the foundation of risk assessment and management, but are not sufficient on their own. Appropriate tools are required to use these data optimally but there is a need to develop robust objective risk assessment processes enabling risk assessors and risk managers to protect allergic consumers, based on transparent and consistent criteria. Our understanding of factors governing the way in which foods sensitise and elicit allergic reactions is still poor. This hampers the risk assessment processes, especially for novel foods, including GMOs. There remains a pressing need to understand why some foods and not others, why some proteins and not others, cause food allergies. Fundamental mechanistic studies, coupled with development of new tools are required to support the risk assessment of novel proteins. There is a need to develop robust risk monitoring processes which address current short-comings in measuring the parameters upon which the risk from allergenic foods depends. These include analytical methodology for the allergenic components of foods, as well as the clinical methodology for assessing reactivity and the effect of different confounding factors (exercise, alcohol, medication, allergic status, stress) on thresholds of elicitation.

2. How are patterns of food allergies changing and what are the environmental factors involved? Effective tools and cohorts are being established for defining the patterns and prevalence of food allergies across Europe. It will be important to follow these up in order to understand how patterns are changing and whether food allergies, like other types of allergy such as allergic asthma, are really increasing. The cohorts also offer the opportunity to understand how food consumption patterns, widely different environments and migrating populations may all affect patterns and prevalence of food allergies and to effectively identify risk factors. Having established the patterns of food allergy across Europe it is important to capitalise on past investment through EuroPrevall and the pre[1]decessor projects (ECHRSI and ECRHSII) in order to define whether rates are changing and if the patterns of food allergies are shifting. This will help risk managers to prioritise resources allocated to different health issues (it is recognised that allergic diseases, while rather minor in terms of mortality, have significant economic implications through their effects on well-being). Effective cohorts have been developed in Africa, Indonesia, India and China for studying food allergies using common approaches to those used in the pan-European studies. It will therefore be timely to investigate how population migration influences both rates of food allergies and confounding lifestyle factors by studying, for example immigrant populations form Indonesia, Africa, India and China in Europe, extending this to European populations that have migrated to Africa, N. America and Australia.

3. Mechanisms and prevention of food allergies: Even if the incidence of food allergies remains static it still represents a considerable burden to society in terms of quality of life and cost to allergic individuals, their families and social networks [also see above]. Ultimately the goal of any research should be to develop knowledge-based means of prevention, coupled with development of the ultimate goal – a cure. New developments are underway with regard to application of immunotherapy but these are likely to take many years to come to fruition and have shortcomings. The development of validated quality of life and economic impact questionnaires through EuroPrevall offer the opportunity to assess the impact of future interventions aimed at prevention or cure of food allergies. New approaches are still required based on a fundamental understanding of the mechanisms of food allergies, which are likely to be related to those involved in development of allergic disease in general. The role of infections, and the dialogue between food, the gut microbiota and the human immune system that affects sensitisation (and food allergy) or induction of oral tolerance needs to be defined. This is a

[1]Mills EN, Mackie AR, Burney P, Beyer K, Frewer L, Madsen C, Botjes E, Crevel RW, van Ree R. (2007) The prevalence, cost and basis of food allergy across Europe.Allergy 62(7):717-22.

major gap that needs to be addressed to address issues regarding food allergy, allergic disease in general, and non-IgE mediated adverse reactions to food.