Immuno-allergie alimentaire

Rapport Hcéres

agence d'évaluation de la recherche
et de l'enseignement supérieur

Section des Unités de recherche

Evaluation Report

Research unit :

Food allergy laboratory

INRA

March 2009

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Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

March 2009

Evaluation report

The research unit :

Name of the research unit : Food Allergy Laboratory

Requested label :

N° in case of renewal :

Head of the research unit : M. Jean-Michel WAL

University or school :

INRA

Other institutions and research organization:

CEA

Date of the visit :

26 January 2009

Members of the visiting committee

Chairman of the commitee :

Mr Stephan STROBEL, UCL, Plymouth, UK

Other committee members :

Mr Heimo BREITENEDER, Medical University of Vienna, Austria

Mr Henri SALMON, IASP, Nouzilly, France

Mr Jean-François NICOLAS, University Lyon 1, France

CNU, CoNRS, CSS INSERM, INRA, INRIA, IRD... representatives :

Mr Christophe DUPONT, INRA representative

Observers

AERES scientific representative:

Mr Nicolas GLAICHENHAUS

Research organization representatives :

Mr Jean FIORAMONTI, INRA representative

Mr Michel RIVA, CEA representative

Mr Christophe CREMINON, CEA representative

Mrs Anne FLURY-HERARD, CEA representative

Evaluation report

1 • Short presentation of the research unit

- Numbers of lab members : 15 including
  - full time researchers 4 including 1 DR1, 2 CR1 and 1 CR2
  - postdoctoral fellows : 2
  - PhD students : 1
  - engineers, technicians and administrative assistants : 8 including 2 on CDD
- Numbers of HDR : 1
- Numbers of postdoctoral fellows : 2
- Numbers of PhD students who have obtained their PhD : 1
- Average lenght of a PhD during the past 4 years : not applicable
- Numbers of lab members with a PEDR : 0
- Numbers of “publishing” lab members among permanent researchers : 4 out of 4

2 • Preparation and execution of the visit

Time : from 12:00 to 13 :00

Committee members

Time : from 13 :00 to 13 :30

Presentation by the head of the lab : past activity and projects

Time : from 13 :30 to 15 :45

Presentation by lab members: past activity and projects

Time : from 16 :00 to 16 :30

Two meetings at the same time

- Meeting with PhD students and postdoctoral fellows
- Meeting with engineers, technicians and administrative assistants and researchers

Time : from 16 :30 to 16 :45

Door-closed meeting : Committee members, AERES representative and Lab director

Time : from 16 :45 to 17 :00

Time length : 15 minutes

Door-closed meeting : Committee members, AERES representative, INRA and CEA representatives

Time : from 17 :00 to 17 :45

Time length : 45 minutes

Door-closed meeting : Committee members, AERES representative

3 • Overall appreciation of the activity of the research unit, of its links with local, national and international partners

The UIAA (Immuno-Allergy Unit, Food Allergy Laboratory) is a relatively small unit of 10 INRA staff scientists and technicians. It operates as a single unit. It was created 15 years ago and is located within the Pharmacology and Immunoanalysis Laboratory (SPI/LERI) at the Atomic Energy Centre (CEA) (Saclay). This close association has provided a successful base for joint projects and scientific 'critical mass'. The SPI and LERI have a large experience in the development of novel immunoassays and through collaborative projects all partners have mutually benefited. This is also apparent in the number of joint publications. The link of biochemical and immunoanalytical expertise has enabled the partners to develop 'reference' immunoassays.

Through its location (Saclay) UIAA has been able to use additional expertise and technical facilities related to biochemistry and proteomics, immunochemistry, molecular biology, cell culture and state of the art biological experimentation facilities. These include the ability to use a large range conventional and transgenic facilities. Research projects requiring germfree facilities are developed with INRA UEPSD in Jouy en Josas.

Other national collaborative partners include SPI/LERI, MRT, ANR, INRA (UEPSD, Jouy en Josas, STLO, Rennes and clinical partners in Toulouse, Paris, Nancy and Strasbourg.

International collaborations exist within in the European Union Framework Programmes (FP5, FP6) where the Head of UIAA is leader of a work package within the EUROPREVALL project relating to allergen characterisation and epitope mapping. Collaboration with industry includes scientific collaborations and contract research in France and Switzerland.

The unit is a 'pure research' unit and does not carry out any 'routine service' for hospitals or other organisations.

The UIAA is part of the Département Alimentation Humaine (ALIM-H) of INR-A.

4 • Specific appreciation project by project

Molecular basis of allergen interactions: Projects directed towards development of tools

1. This project aims to develop immuno-analytical tools for the in vitro analysis of allergens and allergen-specific antibodies by ELISA, EAST and a rat basophil mediator release assay which uses RBL SX-38 cells that stably express the human high affifinity IgE receptor. These assays are used for the analysis of cow's milk and peanut (e.g. Ara h 1) allergens.
2. Analysis of IgG and IgE responses to milk proteins. The unit has a vast experience relating to the analysis of cow's milk proteins and allergens. A interesting new line of research is the investigation of the relatively new clinical observation that there are goat milk allergic individuals who can tolerate cow's milk in contrast to most cases who are cow's milk and goat's milk allergic. Further in-detail analyses of the responsible and possible non-crossreacting caseins are likely to yield new understanding of the allergic process. However other possibilities for this observation also need to be considered. The clinical difference, for example, could be due to the different handling of goat/cow casein micelles in the penetration rate through the intestinal tract.
3. Another line of enquiry focusses on the analysis of IgE and IgG responses to peanut proteins. This is a relatively recent and new line of investigation carried out within the EUROPREVALL project which uses standard immuno-analysis, animal experiments and in vitro basophil degaranulation tests. It also addresses the influence of the food matrix and food preparation methods on potential allergenicity. The results suggest that differently glycosylated and boiled or roasted peanut allergens exhibit a different elicitatory activity than native (non-altered) peanut allergens.
4. A recent research (and PhD project) project within EUROPREVALL on hazelnut allergic patients demonstrated a country/region specific distribution of distinct hazelnut allergens responsible for the sensitisation. Cor a 8 seems to be a major allergen in the Mediterranean countries wheras individuals from northern countries are sensitised to Cor a 1.04.

Development of an experimental model of allergic sensitisation and elicitation.

1. Animal model: A rodent animal model using BALB/c mice has been developed along the models described in the literature and is used to assess the influence of allergen structure and route of application on tolerance and sensitisation. It focuses on various exposure routes and adjuvants. The main read-out systems and parameters used are IgE, IgE and IgG allergen-epitope mapping, measurement of cytokine secretion and eosinophil infiltration in the lung model. A major focus is put on the analysis of milk allergens. Immunomodulatory effects of bacterial compounds are investigated by block copolymers using polyoxyethylene and polyoxypropylen as adjuvants in the beta-lactoglobulin (BLG) model system.
2. Modulation of allergic response through administration of lactic acid bacteria: With INRA/UESPD a Lactococcus lactis (LL) strain was engineered to produce high amounts of BLG. This BLG-producing strain prevented systemic sensitisation by a skewed Th1 response after oral administration to rodents. Addition of an additional recombinant strain secreteing IL-12 did not enhance the significant effect of LL-BLG. A number of further studies to unravel the effects of LL-BLG and of other strains with gastrointestinal resistance to lysis are currently in preparation or under editorial consideration.
3. Influence of gut microbiota on the development of an allergic response: The laboratory, more recently, changed their scientific emphasis and examine the effects of 'probiotic' strains such as BLG-producing Lactobacillus casei B23 in germ free mice on the modulation (Th1 induced) of allergic responses
4. Allergic sensitisation in a gnotobiotic rodent model: These studies in collaboration with INRA/UESPD follow the principle of previously used or previously described rodent models of oral tolerance induction. In these experiments sterilised milk (UHT) was administered with cholera toxin as adjuvant followed by intraperitoneal allergic sensitisation with and without incomplete Freund's adjuvant. Early results seem to indicate that the absence of microflora influences the time course of sensitisation rather than the overall vigour of the response. These results are in contrast to other published reports and efforts are being made to reconcile these differences.

5 • Appreciation of resources and of the life of the research unit

— Management :

The director provides a competent and knowledgeable leadership for the whole team and the collaborative studies. He provides good support for all members of the laboratory and in particular for emerging young scientists. A weak aspect is that the members of the laboratory are involved in too diverse fields/projects and that the laboratory lacks a clear scientific strategy. There is no senior scientist who could take on the 'second in command' role in scientific or strategic leadership.

— Human resources :

The human resources appear well managed. Selection of candidates for positions in the UIAA is done by appropriate scientific INRA/CEA staff.

— Communication strategy :

The unit has no regular laboratory meetings. At present, meetings with the SPI/LERI are on a demand basis approximately at 4-6 week intervals. The introductory programme for new members of the UIAA could benefit from a better structure. Laboratory books (logs) should be signed by a senior individual at regular intervals. Training needs assessment for staff should form part of the regular personnel review process. The review documentation would have benefited from a structured table of content and short scientific CVs to judge the appropriateness and fit for the UIAA. More and detailed information regarding the collaborations would have been helpful.

6 • Recommendations and advice

— Strengths :

- The laboratory conducts research that is of basic scientific and clinical relevance.
- A particular strength of the laboratory is the scientific expertise of the UIAA director. He has assembled a competent and enthusiastic team of junior researchers.
- In view of the UIAA's expert knowledge on antibody epitope mapping and structural analysis of food allergens (milk), the unit is involved in many national and international collaborative projects.
- A particular emphasis is put on collaborative European research projects.

— Weaknesses :

- The high emphasis on collaborative research projects and contract research dilutes the available manpower and prevents the laboratory from following a clear and focussed research strategy.
- The size of the unit is unlikely to generate high class research output as long as its researchers are engaged in such diverse areas of scientific projects as described in the documentation provided. Consequently, the number of highly rated research publications has been low, although the output during 2008 shows encouraging signs.
- The number of PhD students is low.

— Recommendations :

- The laboratory should develop a longer-term strategy and narrower focus to enhance scientific coherence while continuing to seek and engage in fitting scientific and clinical collaborations. A focus on a smaller number of antigens/allergens and rodent models more relevant to food allergy including closer collaboration with basic and clinical immunologists would be desirable.
- New appointments of personnel should fit into the overall scientific strategy that will need to be developed.
- Identification and 'nurturing' of suitable future leaders within the UIAA or outside is absolutely necessary to maintain and further develop the unit's scientific expertise.
- Expectations related to the scientific productivity of each individual researcher should be clearly communicated, documented and the progress should be monitored.
- Recruitment of additional PhD students would enhance the scientific exchange within the unit and contribute to high(er) quality output. For this strategy to become effective, Higher Degree options and supervisory training need to be implemented

Note de l'unité	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
B	B	A	C	C