

## **Fondation Neurodis**

### **Report of the International Scientific Council**

**November 24, 2009**

#### **Members of the International Scientific Council:**

Professor Colin Blakemore (Chair)	University of Oxford, UK
Professor John Duncan	UCL Institute of Neurology, London, UK
Professor Francesc Graus	Institut d'Investigació Biomèdica August Pi i Sunyer, Barcelona, Spain
Professor Pierre Magistretti	Université de Lausanne, Switzerland
Professor John Parnavelas	University College London, UK
Professor Giacomo Rizzolatti	Università degli Studi di Parma, Italy

## Background

The first meeting of the International Scientific Council (ISC) of the Fondation Neurodis was held at the offices of Merck Serono in Lyon on 24 November 2009. Unfortunately, Professors Magistretti and Rizzolatti were unable to attend.

The members of the ISC and all the participants in this meeting were grateful to Merck Serono for providing excellent facilities for the plenary sessions, the meetings of the ISC with various groups, and for the pleasant lunch.

Fondation Neurodis was officially created in August 2007, after a successful tender in response to a call for proposals issued jointly by the Ministry of Health and the Ministry of Universities and Research.

Neurodis is a foundation that supports research in neuroscience, with an initial budget for 5 years of 6.4 M€, comprising 4.0 M€ from the two ministries and 2.4 M€ from the institutions associated with the foundation (the four teaching hospitals of the Rhône-Alpes area, Lyon 1 and Grenoble 1 Universities, INSERM and CEA). The funding did not commence until 2008, so the ISC was essentially reviewing the first year of progress.

28 research teams and 4 university teaching hospitals in the Rhône-Alpes area are associated with Fondation Neurodis. All the researchers, engineers, technicians and graduate students of these research laboratories and hospital departments - some 800 people - are nominally classed as members of Neurodis. However, apart from those laboratories that are fortunate enough to host research teams or postdoctoral researchers funded by the Foundation, there has, so far, been rather little impact on the rest of the community.

The ISC was impressed by the enormous effort that Professor François Mauguière has invested in the establishment and direction of the Foundation. We also commend the administrative staff, Claire Rigaud-Bully (General Secretary) and Isabelle Rondy (Direction Assistant) for their dedication and efficiency.

The broad goal of the Neurodis Foundation is to stimulate neuroscience research in the Rhône-Alpes area, with the eventual objective of improving the prevention, diagnosis and treatment of neurological and neurosensory disorders. There is a similar Foundation for the Paris-Île de France region, with a bias more towards fundamental neuroscience than translational.

The application for support for Neurodis identified considerable strength for training and high-quality research in the Rhône-Alpes region. There is world-class fundamental research in such areas as neuronal proliferation and

differentiation, neural networks, cognition, motor control and systems neuroscience in animals. And there is strength in research related to the following clinical conditions:

- Epilepsy;
- Parkinson's disease;
- Movement disorders;
- Neuropathic pain; and
- Myelin pathologies.

Neurodis directs funds to support new research appointments in areas of high competitiveness in the Rhône-Alpes area. It provides salaries for three categories of support:

- Establishing new senior research teams through appointment of Chairs of Excellence;
- Creation of young research teams through the appointment of team leaders or young independent researchers; and
- Individual postdoctoral researchers.

There are also plans to fund the deployment of clinical transfers, to reinforce European & International cooperation, and to widen the scope of research to include more work on Alzheimer's disease, post-stroke cognitive impairments and schizophrenia

At the presentation on 24 November, the ISC was told about the first round of appointments (two senior researchers for the team of excellence; a junior research team; and three postdoctoral researchers). We were also given early information about the second round of appointments

## **Administrative Board and Steering Committee**

The Administrative Board of the Foundation has 15 members, mainly representatives of the donor organisations. It nominates the Director and the members of the Steering Committee and is responsible for approving the strategic plans of the Foundation and allocating the budget.

The Steering Committee (Comité de Pilotage) consists of 21 representatives from the member institutions of the Fondation Neurodis. Their role is to define the strategy, suggest new research orientations to be supported, carry out recruitment and assess the quality of the actions of the Foundation.

After the presentations by Professor Mauguière and the researchers supported by the Foundation, the ISC had a discussion with all those members of the Steering Committee who were able to attend.

## Chair of Excellence

Neurodis has committed a substantial fraction of its total budget (1.6 M€ for five years) to establish a Chair for Functional Neuroimaging at the CERMEP (Lyon). Alexander Hammers, a German clinician scientist who was Head of the PET Epilepsy Group at the MRC Clinical Sciences Centre at the Hammersmith Hospital, London, was appointed to this Chair. The funding also supports a second clinical scientist, Rolf Heckemann, who came with Dr Hammers from the same unit in London.

Alex Hammers brings a wealth of neuroimaging experience and expertise that should contribute greatly to the success of Neurodis. His particular strengths are in the methodology of PET and of data and image processing, which he brings from his decade in London. Fondation Neurodis is to be congratulated for attracting him to Lyon.

Professor Hammers arrived only in mid-August 2009, but he had made an impressive start in setting up his research, helped by the fact that he had spent time previously on a research visit to Lyon. He has already written four grant applications for additional research support.

Professor Hammers described his continuing interest in techniques for neuroimaging data analysis. It will clearly be of benefit to the neuroimaging community in the Rhône-Alpes region, especially the clinical neuroscientists, for him to implement established techniques such as SISCO and voxel-based analyses of FDG PET. However, such work is time-consuming, is unlikely to yield a substantial output of high-impact publications and will generate even more demand on the time of Alex and Rolf, because of expectation that they will also provide software support to others who use these techniques.

### **The IAC recommends that Professor Hammers is encouraged and enabled to protect time for his own specialised research.**

Professor Hammers' research interests include the use of novel PET ligands that can be investigated in patients with epilepsy, who will proceed to surgical excision and hence provide tissue for follow-up *in vitro* studies. This is a promising area of research, which fits well with one of the major clinical strengths in the Rhône-Alpes area.

The multimodal imaging display and automated labelling of anatomical structures are important tools that can be clinically very useful, especially when planning surgical treatment. Integration with MRI-based neurosurgical navigation would be an important aspect to develop. A caution is not to expend excessive time developing techniques that are already available from other sites, such as BrainLAB.

Alex Hammers and Rolf Heckemann need to decide how much effort to expend on further development of their anatomical atlas approaches. They (and the Neurodis Steering Committee) need to consider the implications of this work. While there is no doubt about the general value of the provision of this service, serious thought needs to be given to the time needed and the business model for supporting the use of these tools by researchers at other Centres, recognizing the commitment that this would entail, and that there are already similar facilities available for free use.

**Integration with the local Academic and Clinical Institutions in Lyon is crucial. To this end it is recommended that Alex and Rolf become part of the Centre of Neuroscience at its inception.**

**The ISC feels that it is also very important that he be granted a clinical contract by HCL, so that he can function fully as a Consultant Neurologist. Without this he will become distanced from the clinic, and will risk losing clinical relevance in his research.**

## **Young Research Team**

344 K€ over three years, awarded to Inserm U836 of the Grenoble Institute of Neurosciences, has funded the first Young Research Team for work on 'Pathophysiology of dopamine dysregulation syndrome in Parkinson's Disease'. The team leader, Dr Sébastien Carnicella, previously held an appointment at the Ernest Gallo Clinic and Research Center, University of California San Francisco.

The aim of the team is improve the understanding of the non-motor symptoms of Parkinson's Disease, in particular apathy, and exaggerated appetitive behaviours. The team will test the hypothesis that such symptoms are due to dopamine depletion in the mesolimbocortical system. They will attempt to induce selective dopamine depletion of the ventral tegmental area by bilateral injection of 6-OHDA in rats. They will then use behavioural tests to assess symptoms in this animal model.

There was some discussion about the question of how the selectivity of the lesions would be assured and assessed. But, in general, the ISC thought that Dr Carnicella has settled in well since his appointment only at the start of October.

## Post-Doctoral Researchers

For the 2008 contingent of post-docs, three contracts of 86 K€, each for two years, have been awarded as follows:

- GReD (Clermont-Ferrand), Director: Professor Odile Boesplug-Tanguy. Méлина Bégou (French), who was appointed on 1 December 2008 is working on '*Gene therapy in a mouse model of leucodystrophy*'.
- UMR Inserm 842 (Lyon), Director: Professor Jérôme Honnorat. Anne Wierinckx (Belgian) appointed 1 December 2008, working on '*Myeloid progenitors in Multiple Sclerosis; Gene & transcriptome profiling of low grade gliomas*'
- Inserm U864 (Lyon), Directors: Dr A Farne & M Meunier. Elisabetta Monfardini (Italian), recruited 2 June 2009, working on '*fMRI of multisensory perceptive tasks activation in non human primates*'

Drs Bégou, Wierinckx and Monfardini gave short talks on their progress. After only a year (or less than 5 months in the case of Dr Monfardini) it was impossible to evaluate fully the work of these researchers. However, the ISC did feel that their projects were closely related to existing work in the groups in which they worked. The projects may be of high quality, but cannot be said to have brought new research to the Rhone-Alpes area.

The ISC noted that Dr Wierinckx, who had already been working with Professor Lachuer in Inserm U842 before her appointment to a Neurodis post-doc, was appointed as an Assistant Professor in the same group on 1 September 2009.

Dr Monfardini, who has a background in social behaviour in humans and monkeys, and in cognitive behavioural therapy, will help to develop facilities for neuroimaging (fMRI) in awake monkeys at Inserm U864 in Lyon. She will be working on sensory integration and sensory competition in perception. Monkey fMRI is a technically demanding but topical area of work, with great potential, when coupled with electrophysiological techniques, to illuminate the basis of cognitive behaviour. The ISC were, though, concerned that there were no immediate plans for parallel electrophysiological methods, and were uncertain of the advantages of doing this work on monkeys rather than humans.

## Future plans

Professor Mauguère described the process for selection of topics and recruitment for the second round of appointment, 2009-10.

Two appointments have been made as leaders of Young Research Teams:

- Alain Buisson in GIN (Inserm U836), Grenoble; and
- Céline Amiez at Inserm U846, Lyon.

Three appointments have been made to Post-doctoral appointments:

- Esteban Fridman (Argentina) working with Angela Sirigu on the Neural Basis of Social Pain at UMR 5229 CNRS-UCBL, Lyon;
- Guy Gingras (Canada), working with Howard Cooper at Inserm U846, Lyon, on Rescue of vision by adeno-viral mediated ectopic expression of melanopsin in the non-human primate; and
- Charlie Wilson (UK) working at Inserm U846, Lyon, with Emmanuel Procyk on Chronic neurophysiology of early non-motor symptoms induced by slow dopaminergic lesion and evaluation of cell therapy.

Professor Mauguère reported that the process used to select topics for all these posts was less 'top-down' than for the first round. Nevertheless, it took fully one year between the call for research proposals from the groups associated with Neurodis and the eventual appointment of the two successful candidates, and this process involved external peer review of the proposed research topics before the candidates were interviewed.

**The ISC thought that the process used for making appointments has, so far, been strongly biased towards the needs of the host research groups. While they understood that this approach has enabled Neurodis to direct additional support to projects assessed competitively, it is not necessarily an ideal way of attracting to the Rhône-Alpes area bright young scientists who would bring new ideas and new approaches.**

**The ISC recommends that the Steering Committee consider using, for at least some rounds of appointments, a much more open process, in which the team leader and post-doctoral positions are advertised without reference to specific projects but simply with a list of the range of research interests of the potential host groups. The Committee could then select the very best candidates and allow them to negotiate with which groups they preferred to work.**

**The ISC was impressed with the numbers of applicant for Neurodis posts, and their geographical spread. However, a more 'bottom-up' selection process might be more attractive to independently-minded candidates and might attract an even wider range of excellent young researchers.**

## **Discussion with researchers supported by Neurodis**

The ISC asked for an opportunity to talk in private with all the young researchers supported by Neurodis, giving them an opportunity to raise issues that they might have been embarrassed to discuss in the plenary session.

The young researchers were grateful for the support that they have received from Neurodis, and they praised the administrative staff. They all felt that they had integrated easily into the groups with which they are working. They talked about the difficulty for young researchers obtaining support during the transition between doctoral training and a tenure-track position.

The post-docs agreed with a concern of the ISC that two years is a short period of time for young researchers to establish themselves and complete a significant project.

There was particular concern about the difficulty of gaining and paying for places on training courses offered by Inserm. It appears that these courses are made available only to Inserm employees, at least without a very substantial fee. They also pointed out that they have no consumable funds of their own, and are entirely dependent on their host research group, not only for the costs of their research but also for funding for participation at conferences etc.

There was also a specific request for help with the cost of courses in English

Even though the number of people currently supported by Neurodis is very small, it was clear that some of them had not yet met each other, and they said that they would value the creation of a Neurodis 'community' of young researchers.

## **General Comments and Recommendations**

The ISC presents the following additional recommendations for consideration by the Administrative Board and the Steering Committee of Neurodis

1. At present, the benefits of the funding provided by Neurodis have accrued almost exclusively to those groups that have been fortunate enough to win support for positions. Thought should be given to ways in which the broader community of neuroscientists in the Rhône-Alpes area can benefit from the existence of Neurodis. The Foundation might sponsor small workshops, or visiting speakers, or an annual conference, open to all members. The excellent website might provide a vehicle for communication between members, advertising positions and

studentships, describing facilities available for collaboration, seeking collaborative funding etc.

2. The ISC was surprised by the large size of the Steering Committee and wonders whether it was established as a 'stakeholder group', to provide full representation of all the associated organizations, rather than a management committee. The ISC suggests that the Steering Committee might work more efficiently, and give more executive help to François Mauguière, if it were reconstituted with fewer members – perhaps only 6, with membership rotating every two or three years. The larger group could still be involved in reviewing proposals and candidates.
3. Stakeholder representation for all the institutions associated with Neurodis could be provided by a different mechanism, such as an annual conference in which progress is reported and future strategy discussed.
4. The ISC hopes that Neurodis will consider providing a small personal allowance to each post-doc, to be used as they wish to support training, visits to conferences or to other labs etc.
5. Fluent English is essential for any researcher and the ISC recommends that support for courses in spoken and written English should be funded for those young researchers who request it.
6. The ISC is particularly concerned about the short duration of the post-doctoral appointments and recommends that at least some of the positions should be offered for three years rather than two.
7. The ISC recommends that an annual retreat or other form of conference should be organized for all Neurodis employees, together with colleagues from the member groups. These annual meetings could be used as the vehicle for 'brain-storming' about future collaborations, grant applications etc.
8. The ISC believes that the excellent Neurodis website could also be used as a vehicle for communication between neuroscience researchers in the Rhône-Alpes region.

**The ISC addresses the following opinions, questions and suggestions specifically to the ministries and other funding organizations for Fondation Neurodis:**

1. The ISC applauds the funding initiative that has created Neurodis and the flexibility that has been given to Professor Mauguière and his colleagues in determining the strategy of Neurodis. Neurodis should play a significant part in stimulating neuroscience in the Rhône-Alpes region, in promoting the recruit and career development of good young scientists, in fostering new collaborations, in facilitating interaction between basic researchers and clinicians, and in promoting the translation of high-quality fundamental research into clinical application.
2. Although the total of 6.4 M€ initial funding is significant, it is not a large amount of money to cover 5 years of work for a community of some 800 individuals. The expectations for what this funding can achieve must be realistic.

3. If Neurodis proves its worth and if it is to have lasting impact, it will need continuity of funding beyond the first five years. Although Professor Mauguière and his colleagues are making serious efforts to solicit private funding to enhance the work of Neurodis, the ISC believes that it is unlikely that sufficient donations will be attracted to replace completely the public funding at the end of the initial 5-year period. Therefore the ISC recommends that the two ministries and the other public funds of Neurodis give serious consideration to whether and how longer-term funding can be provided.
4. We suggest that a comprehensive review of the progress of Neurodis should be conducted after the first 3 or 4 years of operation and that further funding beyond the 5-year period should be considered at that time.
5. The ISC did not understand the reasons for requiring Neurodis to retain 1 M€ of the total funding as 'frozen assets'. It was not clear whether this substantial amount of money will be available for use by the Foundation, and whether there are restrictions on how it can be used. The ISC hopes that this reserve can be deployed to benefit Neurodis. In that case, the ISC recommends that Professor Mauguière and his colleagues should be invited to propose use for this money to generate 'added value' for the Neurodis community. Possible uses of the 'frozen assets' funds include:
  - Retreats and workshops for members of Neurodis and invited external speakers, to plan future collaborations;
  - Purchase of equipment to provide new technical platforms of value to the Neurodis community;
  - Funding the personal research allowances for postdoctoral researchers that are recommended above;
  - Establishing a scheme to which Neurodis postdoctoral employees can apply, competitively, for the extension of their own salaries for up to one extra year, if a strong case can be made for such continuation of funding.