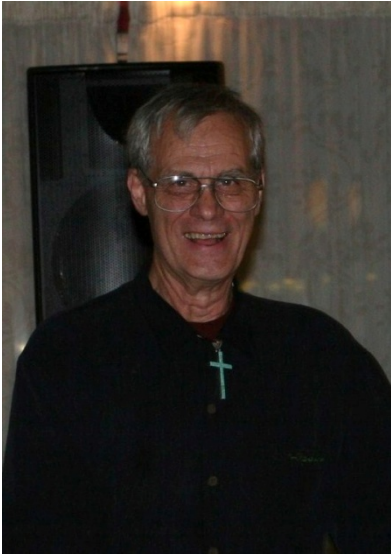


# 13<sup>th</sup> European NF Association Meeting Killarney, Ireland 29 October – 2 November 2008

## Paddy Griffin, Organizer

### Summary Report

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This piece is not a recounting of individual presentations as itemized and described in the Meeting's published program. Rather, it is a distillation and celebration of the event as a whole. This piece is the written, perhaps refined, rendition of what I presented orally at the wondrous session we shared Sunday morning, the 2<sup>nd</sup> of November.

The meeting began unofficially in the late afternoon of Thursday, 30 October 2008, with the General Meeting of NF Europe in one setting and, in another setting, a workshop to clarify the nomenclature and classification of neurofibromas, deemed to be especially important now that several rational treatments of these masses are being considered. While no specific system was identified or advanced, progress was nonetheless made toward the goal of a more consistent way of specifying these hallmarks of NF1. The next morning, Friday, the 31<sup>st</sup>, concurrent sessions of the "Scientific Conference Programme" and the "Lay Person Conference Programme" began at 9:00 a.m.

These parallel sessions, which continued through the early evening of Saturday, 1 November, though separated by walls, were punctuated by the presence and attentive listening by many members of both groups, "Scientific" and "Lay," with excellent interactions. On Sunday morning, 2 November, the distinctions between "Scientific" and "Lay" were abandoned and a joint session, with presenters from all of Europe and Brazil, was a rousing success as determined by the uniform sense that we had all learned something vital over the meeting's four days.

No small contributor to the outcome was the opportunity for all attendees to mix and interact during the meals and breaks. The Celtic music and folk dancing at the dinner on the 31<sup>st</sup> and the more casual entertainment and dancing on the 1<sup>st</sup> were additional highlights that underscored the fraternity and camaraderie that so characterized the meeting as a whole.

The scientific faculty was excellent, with the best of Europe well represented and a number of individuals from the United States, emphasizing again the sharing and fraternal nature of the meeting.



I found there to be five summary points:

- Partnership
- Heterogeneity
- The Interactome
- Mice
- Quality of Life

## **PARTNERSHIP**

In this age of high technology and a focus on genes and devices like MRI and CT scans we often forget that science and medicine on the one hand are really in partnership with the patients, families and other interested members of the lay community on the other hand. In general I have found that the “European NF Meetings” have consistently blurred that distinction and in Killarney this was so to the extreme. In particular, the interdigitation during either sets (“Scientific” or “Lay”) of presentations was heartening and fruitful. Among other things, members of the “Lay” participants showed themselves to be especially sophisticated about NF – whether NF1 or NF2 or schwannomatosis – and they were not there simply to hear for the umpteenth time about the features of this disorder or that disorder. They showed themselves to be sophisticated members of the NF community who wanted to contribute as much as to learn. The “Docs” on the one hand constantly commented on how much they had learned from the other attendees. My own engagement with patients and family members gave me the impression that they had both learned and been an influence. Indeed, the Killarney meeting manifested partnership for other NF organizations to envy and emulate.

## **HETEROGENEITY**

NF is more than one disorder. This meeting thus emphasized heterogeneity – a mixture replacing a singular, homogeneous entity. On the one hand, there are distinct disorders on the basis of being caused by totally different genes on different chromosomes. Thus, during the conference we discussed and examined in detail NF1, NF2, schwannomatosis and the newly named Legius syndrome (previously known as the NF-like disorder due to SPRED1 mutations). And then there was extensive discussion about the different types of NF1, whether apparent in terms of the clinical picture (e.g., “Spinal NF,” with or without café-au-lait spots) or in terms different genetic changes, that is mutations. And even within a particular type of NF1, the pattern and timing of features is heterogeneous, leading some who were present to rely more on imaging approaches, with discussions about the attendant need for routine brain and whole-body MRI scans, the former focusing on optic pathway gliomas and the latter focusing on “spinal” neurofibromas. Even the neurofibromas of NF1 are apparently heterogeneous – so much so that a consensus could not be reached as to what defines the differences. And finally, the NF1 gene itself turns out to be heterogeneous: from one part to another, the NF1 gene does multiple things. It is a very large gene and it is highly conserved in evolution, which means that fruit flies and mice have NF1 genes very similar to that of humans. So far, we have been trying to explain all of NF1 and its features, consequences and complications on just that 10% of the NF1 gene that controls the tumor suppressor molecule, Ras.

## **THE INTERACTOME**

Much of the technical discussion about how the change in the genetic material – the mutation – actually causes the clinical problems focused not on the genetic material itself, but rather the interaction of the gene product (i.e., neurofibromin for NF1, merlin or for NF2, schwannomin for schwannomatosis) with other proteins. In short, there has been a remarkable shift away from the “Genome” (the genetic code and its translation) to the “Interactome,” the multiple and complex pathways in which the gene products participate. This requires an appreciation of another level of sophistication in understanding mechanisms of disease. I was impressed both by the shift to the Interactome being made by those doing the research and the shift to understanding the elements of the Interactome by the other attendees.

## **MICE**

Mice are being used to study all four current forms of NF – NF1, NF2, schwannomatosis and the Legius syndrome – and to great advantage. This especially true in devising treatment approaches, especially in terms of tumors, such as neurofibromas, gliomas, schwannomas and neurofibrosarcomas, as well as bone abnormalities and learning or school performance problems of NF1. In particular, with the mouse it is possible to study the time of onset of the disorder’s specific lesions. By looking at different stages of embryologic development the timing of the onset of (mouse) neurofibromas seems to be long before birth.

## **QUALITY OF LIFE**

Neurofibromatosis is not just about tumors and skin coloring or bones or learning disability or cancer. It is also about people and of course there are increasing efforts to study the “people” aspect of persons with NF. Over the last several years I have been concerned that efforts to study the “quality of life” or

“self-concept” or “self-esteem” of patients with NF1 are biased to document a compromise of those elements of the life of persons with NF1. My impression has always been that, to the contrary, persons with NF1 are often extraordinary, without the presumed compromise of “quality of life” or “self-esteem.” And I saw such at this meeting. I saw firsthand – again – that persons with NF1, and NF2 for that matter, do very well in spite of whatever compromises or limitations that each of them might have. I heard and saw at this meeting – during formal presentations and during more casual interludes – that many persons with NF1 have a most wholesome, perhaps even enviable, quality of life and sense of self-esteem. What we all shared at this meeting as peers was a