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EuroBoNeT

European Network to Promote Research into Uncommon Cancers in Adults and Children:
Pathology, Biology and Genetics of Bone Tumours

Network of Excellence

Life sciences, genomics and biotechnology for health
LSH-2004-2.2.0-1: Uncommon cancers in adults and children

Publishable executive summary

Period covered: from 01-02-2006 to 01-02-2007

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Version [1]

Publishable executive summary



Within Europe high standards are found in the research of bone tumours, which is however scattered over several institutes. A major goal of EuroBoNeT is to integrate the different laboratories performing this research thereby increasing the sample size of these rare tumours and to profit from the different expertise in the different labs. By creating standard operating protocols for the different techniques used in this field and staff exchange to visit the different labs and learn new skills we hope to create a good environment that will lead to new discoveries, which can help in the diagnosis and treatment of these tumours.

The network aims to extend existing expertise and resources to facilitate the European discoveries and spreading of knowledge in the field of bone tumours by the creation of guidelines for diagnosis and training courses on the pathology of these bone tumours will give less skilled institutes a helping hand in the recognition of these mostly rare tumours. The consortium focuses on cartilaginous tumours (both benign and malignant), osteogenic tumours, giant cell tumours and Ewing family tumours, as well as processes involved in chondrogenesis and osteoclastogenesis. This consortium has successfully negotiated within FP6 of the European Union for a grant of 13.2 M€ to establish a 5 year joint program of activities (JPA), composed of integration, spreading of excellence, research and management activities. The EuroBoNeT NoE started officially in February 2006, and is coordinated by P.C.W. Hogendoorn at the Leiden University Medical Center (for further information please visit www.eurobonet.eu or contact the coordination office EuroBoNeT, c/o L Rozeman, LUMC, department of Pathology L1Q, PO box 9600, 2300RC Leiden, The Netherlands or email to eurobonet@lumc.nl).

Major goals of EuroBoNeT NoE

- Coordinated European research on bone tumours
 - o Increase the number of samples available for research
 - o Perform a variety of tests on identical sample groups
 - o Creation of standard operating procedures for the different laboratory techniques
 - o Staff exchange
- Reduce fragmentation by sharing samples, which will be documented in the virtual BioBank
- Raise the standing in the field by the creation of guidelines and training courses
- Promote the research of these rare tumours

Major goals in a more global context

- Identify new candidate molecules for
 - o Diagnostics
 - o Prognostics
 - o Drug development

In total 24 institutions and SMEs from 12 different countries share the workload of the sub-programs to strengthen the collaboration between the groups. The entire JPA is subdivided in five segments (four for research and one for integration and spreading of excellence) containing 18 work packages (WP). Most goals described in the technical annex are on track.

The main accomplishments of EuroBoNeT in the first 12 months are:

1. the establishment of the management structure of EuroBoNeT
2. the set-up of core facilities
3. the development of Standard Operating Procedures
4. the development of new collaborations between groups that were originally not planned
5. new plans were generated that integrate the techniques and knowledge of different partners
6. the organization of a successful first annual meeting where further plans were made for collaboration, staff exchange, and RL meetings
7. the organisation of 4 researchline meetings to detail ongoing program and future plans

Changes to the JPA:

1. addition of a Bioinformatics technology platform in the next period
2. termination of redundant technology platforms

Management

In order to monitor the progress of the EuroBoNeT project, a management team capable of coordinating and executing the different tasks has been formed.

Management office

The Scientific coordinator P.C.W. Hogendoorn has employed a full-time assistant coordinator, a part-time financial officer and a part-time administrative assistant to coordinate the office. Leida Rozeman, a former cartilage tumour researcher, has been hired for the day-to-day administrative managerial aspects of the network. She is assisted in her task by a part-time secretary (Pauline de Graaf) and part-time financial officer (Wytse van Ingen-Bouwsma). All the documents related to the EuroBoNeT network are centralised in the EuroBoNeT management office.

Management of JPA

For the coordination of the JPA the tasks were divided in research lines (RL1-4) and one integration/spreading of excellence line. These sub-segments of the project are coordinated by scientists of international reputation who function as spokespersons for their lines. Together these five research line leaders/coordinators form the Steering Committee, which has held regular contact and meetings to discuss and decide on various issues concerning the network.

Integration

Overall integration of the EuroBoNeT is coordinated by A.P. Dei Tos (Treviso Hospital, Italy). However, the different research line leaders decide on the allocation and the distribution of the staff exchange funding to the partners, making sure that this budget is distributed equally amongst the partners.

BioBank

A virtual BioBank containing information on tumour samples is being developed. This database will contain anonymised clinical and histological information, but also on the fixation type. These samples can be requested by partners of the EuroBoNeT consortium, and used in their research. At the moment the database, a tailor-made extension on a previously developed database (TuBaFrost) for Erasmus MC, is constructed and is currently tested to search for bugs. The BioBank is expected to be ready for use within a few months.

Technology platforms

Standardisation of protocols is taking place through use of technology platforms (WP5.2). Different platforms have been established, such as expression arrays (LUMC), array CGH (LUMC and Radium Hospital), siRNA (WWU Münster), proteomics (CIC Salamanca), etc. In some cases the technology platform leader is available for support, whereas in the case of expression arrays, array CGH and proteomics a core facility is appointed to ensure that all results are comparable. Currently 25 SOPs (standard operating procedures) are available and these will be placed online shortly.

Staff exchange/training

Staff exchange is strongly encouraged, especially under the young scientists, to benefit from the expertise of the other partners, to learn new techniques and to use specialized equipment. In the first 12 months already several exchanges have taken place. In the first year, the collaborations were still new and some of the research projects were not yet planned in such ways that techniques other than the ones used at the own locations were included. In the coming period the number of staff exchanges will be increased.

Meetings

A kick-off meeting and the first annual meeting were organised for the total network assembly and its researchers and for the four research lines independently. Especially at the first meetings new collaborations were started and information was exchanged on the different topics of interests. At the research line meetings especially extensive discussion was held on the joint research projects, SOPs, staff exchange and development of standards for diagnosis (e.g. on chondrosarcomas, fibrosarcomas of bone and malignant fibrous histiocytoma of bone).

Spreading of excellence

In order to spread excellence beyond the consortium, specific activities will be open to researchers and clinicians from non-participating institutions. The coordination of this section is in the hands of AP Dei Tos (Treviso Hospital, Italy). Patient organisations, supporting the network, have been informed.

Courses

In the first year one course was organised in collaboration with EuroBoNeT. This was held in Birmingham (Royal Orthopaedic Hospital): Bone and Soft Tissue Tumour Pathology Course, for registrars and consultants in pathology. Speakers from within EuroBoNeT were involved (ROH and ULUND). Preparations for a course in Bologna (20th course on musculoskeletal pathology, February 2007) and a course in Leiden (practical clinico-pathological diagnosis of tumours of the skeleton, October 2007) were initiated. Also a course will be organised in the next year covering molecular techniques used in research on bone pathology. These courses are open to all interested researchers from within and outside the EuroBoNeT consortium and will have speakers with specific expertise coming from the network and beyond.

Website

The EuroBoNeT website will be fully operational shortly. A prototype of the website was shown at the first annual meeting in January 2007. It will contain information on bone tumours, the EuroBoNeT project, upcoming courses and congresses that are of interest and links to other relevant web pages. The website will contain a closed section designated to the EuroBoNeT participants, on which management related subjects and reports, SOPs and datasets not available to outsiders will be placed.

Publications/presentations

The EuroBoNeT so far has already generated several publications (articles and presentations). As collaborations will continue to evolve, many more joint publications will be generated by authors from the different EuroBoNeT groups.

Research

The scientific topics that EuroBoNeT will address during the lifetime of this network have been subdivided based upon tumour type. Each research line addresses (a group of) tumour type(s) in which previous excellence was shown, as can be observed by publications in peer-reviewed journals.

- Research line 1: Cartilaginous tumours
Coordinator: P.C.W. Hogendoorn (LUMC, The Netherlands)
- Research line 2: Osteogenic tumours and related sarcomas
Coordinator: H. Bürger (WWU Münster, Germany)
- Research line 3: Osteoclastogenesis and Giant cell tumours of bone
Coordinator: N.A. Athanasou (University of Oxford, United Kingdom)
- Research line 4: Ewing's sarcoma family of tumours
Coordinator: P. Picci (IOR, Italy)

The research is mainly focussed on obtaining a better understanding in the tumourigenesis of these bone tumours and to identify molecular targets for diagnostic, prognostic and therapeutic purposes. Four research line meetings are held annually, in which exchange of scientific ideas, presentation of technical facilities, discussion of approaches, and detailed planning of the WP is addressed.

Research line 1: Cartilaginous tumours

This research line contains the tumours that have a cartilaginous histology, and encompass the various subtypes of chondrosarcomas and their benign counterparts (enchondromas and osteochondromas), chondroblastomas, and chondromyxoid fibromas. Also in vitro models of cartilage are included, derived from primary tumours, mesenchymal stem cells and articular cartilage.

In July 2006, a research line related meeting was held in Leiden, The Netherlands, in which all involved partners presented their current interests to familiarise each other with the work and research techniques available. One of the main conclusions of the meeting was that it is essential for the genome-wide analysis to combine and integrate the results of all different partners in order to achieve a substantial dataset to study clinicopathological parameters. The plans for the integration of results were presented

in more detail at the first annual meeting. Substantial progress has been made in this research line and some of the deliverables set at later time points have already been met, resulting in published and submitted articles. There is some delay in WP 1.4, but the partners working within this workpackage currently have the experiments running. In this workpackage also several phone conferences have taken place to coordinate the research. Several new ideas and deliverables are implemented in the new plans for the upcoming period.

Research line 2: Osteogenic tumours and related sarcomas

This research line focuses on the osteosarcomas and osteolytic lesions (chordomas, malignant fibrous histiocytomas and fibrosarcomas of bone). In June 2006, a research line meeting was held in Münster, Germany, in which all involved partners presented their current interests to familiarise each other with the projects, techniques and facilities available at the different centres. The work in this research line is generally on track, although the deliverable concerning the histologic review and guidelines for the diagnosis of malignant fibrous histiocytomas and fibrosarcomas of bone are delayed. This is currently in progress and results are expected at the beginning of the second half of the second year. Some other deliverables on expression arrays experience some delay due to the production/introduction of a newer version of arrays. These are currently available and work is expected to continue, without too much delay in the deliverable endpoint.

Also for this research line, the intensified collaboration among partners has led to many novel ideas, which has resulted in the addition of several new deliverables and the addition of two other tumour types to be added to the WP2.3, vascular tumours of bone and Langerhans cell histiocytosis.

Research line 3: Osteoclastogenesis and Giant cell tumours of bone

The work of research line 3 is focussing on osteoclastogenesis, giant cell tumours of bone and Paget disease of bone. In October 2006, a research line related meeting was held in Oxford, United Kingdom, in which all involved partners presented their current interests to familiarise each other with the work and research techniques available at the different laboratories. The research deliverables in this research line are producing results, and seem to meet the set deadlines. Only the deliverable to collect samples from a cohort of first degree relatives of patients with Paget disease of bone has not met the deadline yet, but effort is given to complete this deliverable as soon as possible.

Again in this research line lots of ideas are arising and some of these have been described in deliverables for the coming period, for instance the role of vascularisation in Giant cell tumours of bone and the process of osteoclastogenesis.

Research line 4: Ewing's sarcoma family of tumours

Ewing sarcomas are the focus point of research line 4. In May 2006, a research line related meeting was held in Bologna, Italy at the Rizzoli institute, in which all involved partners presented their current interests to familiarise each other with the work and research techniques available at the different laboratories. All research projects proposed for the first 18 months of the NoE are ongoing and a few have been finalised, such as the first deliverables on PRAME research. New plans have been made and deliverables are added to all workpackages in this research line.

Final conclusions

The EuroBoNeT project has made a good start. One point of attention is the pursuit of more integration of the different partners. During the first year partners got to know each other and each other's ideas and possibilities, which takes some time. However, many new collaborations have been outlined and started during this first year and these will obviously lead to a further increase of integration and staff exchange in the next few years. In fact, during the first annual meeting in Treviso many visits from one laboratory to the other have been planned in order to exchange material, personnel, knowledge and laboratory techniques. Also the consortium has many ideas regarding research beyond the budget of EuroBoNeT. Expected is that partners will look together to obtain additional funding.