Molecular Imaging of Cancer

Keywords
EMIL, molecular imaging, drug development, guided therapies, tumour diagnosis, in vivo imaging of gene expression

Summary
The general objective of EMIL is to bring together the leading European research teams in molecular imaging in universities, research centres and small and medium enterprises to focus on early diagnosis, prognosis and therapeutic evaluation of cancer.

The 58 partners of EMIL work around a common activity programme including:

• Integration activities: creation of a network of technological and training facilities favouring the mobility of researchers and the integration of small and medium enterprises

• Dissemination activities: training, communication, common knowledge management and intellectual property rights

• Research activities: a common research programme making use of methodological tools of physics, biology and chemistry for the further development of molecular imaging (instrument techniques, molecular probes, biological engineering), and bringing together cancer imaging applications (early diagnostic imaging, development of new therapies, imaging for drug development).

Problem
Cancer is characterised by an uncontrolled proliferation of cells. For normal cells, controls operate at spatial level – a cell’s location is defined by its integration in an organised tissue and temporal level – and a cell undergoes controlled division and death corresponding to its programmed life cycle.

The last two decades have witnessed enormous advances in our understanding of cancer at the molecular level and demonstrated that it results from abnormal gene expression in cell clones. Gene expression analysis techniques are now witnessing systematic compilation of molecular data that can be used to provide accurate diagnosis and prognosis. These techniques are well established and widely applied to in vitro biological samples, but they destroy the sample during analysis and are not applicable to whole body and longitudinal explorations. Hence they fail to recognise the essential character of cancer development across time and space.

On the other hand, in vivo imaging is a repeatable and non-invasive localisation technology with the potential to become the preferred means for cancer diagnostic and follow-up. However, imaging is based on evidencing a contrast between cancer and normal tissue, and this is quite challenging to perform in vivo in view of the fact that cancer cells are a clone of normal cells. Even though anatomic imaging can occur in vivo at sub-millimetre resolution, imaging techniques based on gross physical differences, such as density or water content, perform poorly in producing a contrast which must be based on specific imaging agents targeting tumour cells.

Molecular imaging is a new science bridging together molecular biology and in vivo imaging with the aim of detecting the expression of specific genes. Imaging science has made sufficient progress in the last decade to bridge the gap between physiology and molecular biology, and is now at the stage where it can perform molecular imaging of gene expression in vivo. Significant advances have occurred in molecular imaging modalities, including the nuclear medicine techniques of SPECT and PET, MRI and spectroscopy, which have attained resolution sufficient for small animal imaging, and optical imaging, which can now reach unprecedented sensitivities.

Aim
The potential of molecular imaging is considerable:

• In fundamental research, it allows the visualisation of cell function and molecular processes in living organisms – in particular the monitoring of the stages of growth and ageing, the response to environmental factors, the exploration of cell movements, etc.

• In experimental medicine it identifies the molecular determinants of pathophysiological processes in situ, evaluates new molecular therapies (such as gene therapy), and accelerates drug development (delivery of active compounds, efficacy of vectors, etc.).
With the evolution of imaging techniques and the capacity to transfer animal data directly into clinical applications, molecular imaging is a promising technique to tackle cancer detection, following the rule of the three Ps: Precocious, Precise and Predictive.

- **Precocious**: several successive mutations are necessary to make a cell cancerous. By detecting genetic anomalies at the very first mutation, molecular imaging could permit early diagnosis and prompt intervention at the start of the cancer-forming process.
- **Precise**: molecular imaging makes it possible to detect precisely, in space and time, the gene or genes that are dis-regulated in the cancer cell. A tumour can be characterised with molecular precision.
- **Predictive**: the fineness of the information obtained by molecular imaging allows it to determine the tumour type and to predict its evolution, adapt the treatment and monitor its efficacy.

This is essential to:

- Validate, in the context of living organisms, the targets and drugs designed by genome data mining and *in vitro* gene expression analysis through non-invasive methods;
- Acquire fundamental knowledge about the patterns of gene expression in normal tissues and define the changes in specific gene expression in cancer;
- Design and develop drugs targeting cancer-related gene expression;
- Allow precise evaluation of new treatments and new anti-cancer drugs that are required for progress in cancer management, through reliable measures of the cancer burden.

The general objectives of EMIL are:

1. to coordinate the current effort in molecular imaging of Cancer in Europe by merging 43 groups from universities, research centres and SMEs coming from different scientific and technical fields into ONE virtual excellence centre with dedicated technological training platforms and integrated dissemination and management activities;
2. to advance molecular imaging of cancer to the scientific, technical and economical status that should be expected from its value for European citizens, in order to improve cancer diagnosis follow-up, to promote and assist in the development of new targeted therapies, and translate science and technology progress into economical benefits;
3. to act as leverage for a strong technological development that can be fuelled through specific research and development projects.

And more precisely:

- to optimise hardware and software for the integration of radiotracer, magnetic resonance and optical imaging data;
- to develop so called ‘smart’ imaging probes which are specific for a given molecular process and which can be detected and localised by at least one imaging modality;
- to use further developments of mouse models of human cancer to: (i) improve early detection of small cancer by advanced imaging, (ii) directly study alteration of gene expression, tumour cell proliferation and migration *in vivo* over an extended period of time in the same animal;
- to identify *in vivo* molecular targets of cancer and metastasis enabling early diagnosis, assessment of disease progression and response to therapy;
- to establish imaging-guided patient-tailored therapies;
- to develop imaging technologies for *in vivo* drug screening using animal models;
- to apply molecular imaging of apoptosis to cancer.

**Expected results**

The present initiative is taken to capitalise on the extraordinary opportunity for studying non-invasively gene expression and function in cancer, due to recent advances in molecular imaging modalities. Because molecular imaging is fundamentally multi-disciplinary by nature, the instrument for this goal is a Network of Excellence bringing together genome-oriented scientists with various actors of imaging science and clinicians dedicated to formulating novel diagnostic methods based on imaging. The EMIL Information System called EMIL Net (www.emilnet.org) will both facilitate the information flow between the partners and contribute to promoting molecular imaging of cancer. Therefore EMIL Net will be dedicated to two different groups of users: the EMIL partners and the public:

- The public section will allow the free flow of information towards the end-users through the Internet site that will be used as a ‘shop-window’ of EMIL, the aim being to provide the molecular imaging community as well as the public with a tool that will spread excellence.
- The private section will be protected and accessible only to the 58 registered members. It will be used for management, knowledge and the Image database.

The EMIL Net private section:

The day-to-day management of the website will be secured by the management board to inform the EMIL partners on:

- Research activities within the EMIL network
- Research outcomes: publications, common protocols, regulatory issues
- Career opportunities
- Training courses
- Education courses
- Knowledge management (consultation of documents, registrations to EMIL events, on-line reporting, consultation of work packages documents, discussion forum, etc.).

This will have an integrating action on the EMIL members who will visit the website to gather information on the network’s events and activities. Members’ access will be enforced progressively, with different levels of security.
Once the EMIL website is operating in good conditions, it will be upgraded with the final objective to create the EMIL database. This database will function as a reference server for molecular imaging of cancer. The web is a unique means to disseminate image information and more particularly animated data which cannot be shown on paper. EMIL will provide unique pharmacokinetics information visible on the website.

Potential applications

- Tumour diagnosis
- Follow-up of tumour progression
- Therapeutic evaluation

Project website: www.emilnet.org

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