

# Molecular Diagnostics Core Unit

## Summary

For the past five years, the Molecular Diagnostics Unit has supplied Spanish National Health System hospitals with a wide range of specific and sensitive methods to monitor response to therapy and to improve diagnosis, prognosis, and personalised medicine.

Our role is to determine changes in sequences and/or levels of expression of genes involved in the cancer process. The Unit adopts a multidisciplinary, built-in and cutting-edge approach offering histological, molecular, and genetic techniques – frequently not employed by most hospitals.

## Main Objectives

- Provide robust and time-efficient diagnostic tests for: (1) the early detection of cancer before its clinical manifestation; (2) discovering Minimal Residual Disease in patients in clinical remission; and (3) monitoring response to therapy
- Develop, implement and supply the very latest technologies available in order to perform more reliable and reproducible assays in a more time-efficient and cost-effective fashion to facilitate the molecular diagnosis of cancer
- Provide support to Clinical Units of the recently created CNIO Clinical Research Programme with state-of-the-art facilities and technical expertise

## Luis J. Lombardía *Unit Head*

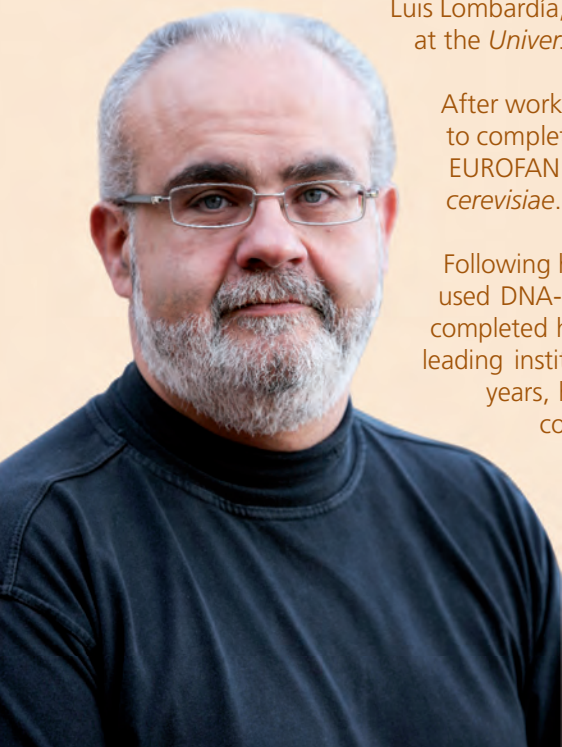
Luis Lombardía, born in Nimes, France, in 1967, obtained his degree in 1991 in Biological Sciences at the *Université des Sciences et Techniques du Languedoc*, Montpellier, France.

After working within the agro-chemical industry for more than three years he moved to Spain to complete his PhD studies at the *Universidade Da Coruña*, La Coruña, Spain. Funded by the EUROFAN EU project, he worked on transcription analysis of orphan ORFs in *Saccharomyces cerevisiae*.

Following his thesis in 1998, he collaborated in the second phase of the EUROFAN project and used DNA-microarray technology to pioneer yeast transcriptome studies in Europe. He then completed his post-doctoral studies at the *Commissariat à l'Énergie Atomique*, Paris, France – a leading institution in the implementation of microarray technology in France. For almost two years, he participated in the BIOCHIP-CEA project collaborating in the first studies ever to compare the transcriptome versus the 2D-gel proteome in yeast.

In 2001 he joined the CNIO Genomics Unit as a Staff Scientist, responsible for the implementation, development, and support of large-scale gene expression studies in partnership with basic and applied research groups at the CNIO.

Since June 2007 he has organised and managed the CNIO Molecular Diagnostics Unit and coordinated the Molecular Diagnostic Service.





Technicians: Cristina Alubreros (since July), Diana Romero.

## Highlights

For 2009 the Molecular Diagnostics Unit has witnessed a 25% increase in the number of tests required by hospitals. We have also added 3 new molecular diagnostic tests to our catalogue: (1) detection of mutations in the NPM1 gene to help determine prognosis in Acute Myeloid Leukemia (AML) patients with a normal karyotype and no mutations detected in the FLT3 gene, (2) detection of mutations in the PI3K gene to predict clinical outcome in patients with lung (excluding

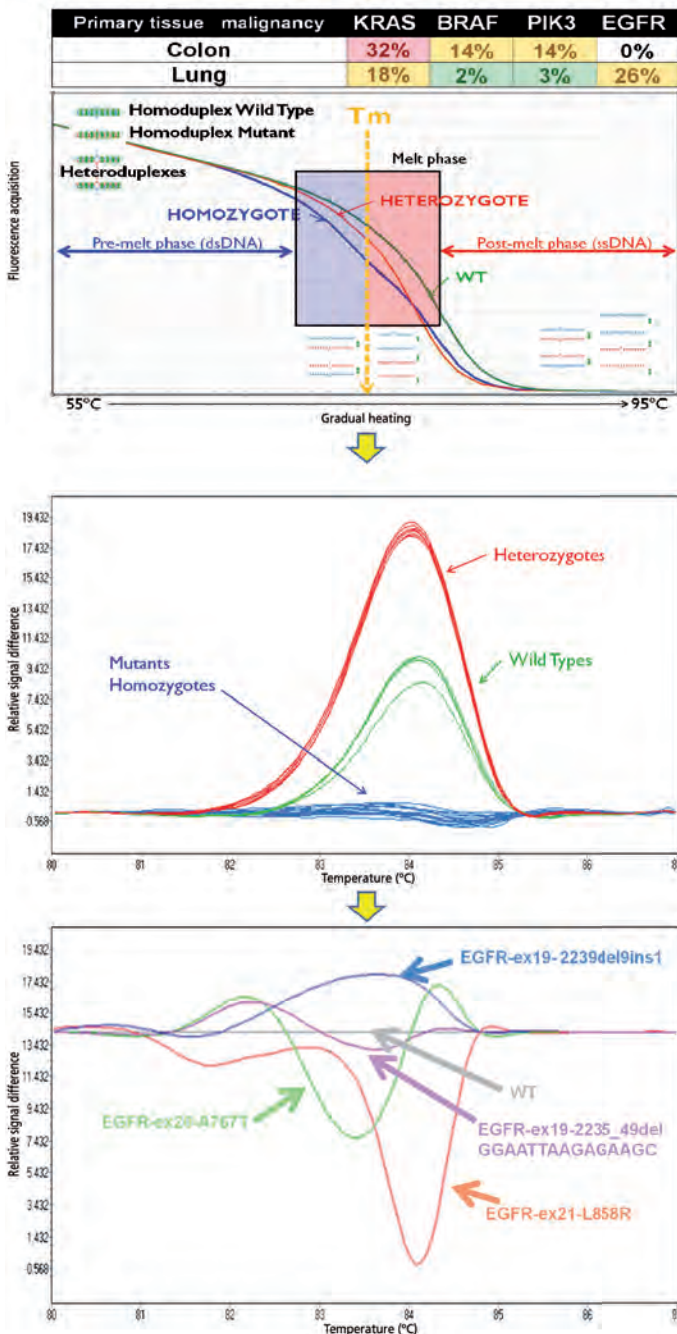


Figure: The growing number of gene mutations related to different cancers and their corresponding treatments has increased the necessity to apply new diagnostic tools. High Resolution Melting (HRM) technology will allow for more sensitive screening in each patient through a full comprehensive range of diagnostic markers without delaying the delivery of results to clinicians.

EGFR mutations) or colorectal cancer (resistant to anti-EGFR treatment), and (3) identification of rearrangements in the IgK genes to complement the screening of malignant B cell proliferations.

Moreover, we have embarked on the development and implementation of two new molecular diagnostic platforms. We have already completed the pilot phase and almost finished collecting and extracting a large sample series to develop a low density array for quantification of the expression of a panel of microRNAs likely to be predictors of metastasis in breast cancer. In parallel – to strengthen and update the current tests – we are in the preliminary stages of implementing new technology (High Resolution Melting) to detect mutations with greater sensitivity and speed, both in genes already included in our catalogue as well as in others with diagnostic utility (Figure).

We are active members in international (<http://euroclonality.org/QualityControl.html>) and national (<http://grupobmh.onmedic.net/>) groups dedicated to standardising and improving molecular diagnostic tests in cancer. We have also supported training and education by welcoming undergraduate students, technicians, and medical residents to our laboratory.

## Publications

Lorenzo Y, Provencio M, Lombardía L, Díaz R, Silva J, Herrera M, García JM, Peña C, García V, Romero J, Domínguez G, Bonilla F. (2009). Differential genetic and functional markers of second neoplasias in Hodgkin's disease patients. *Clin Cancer Res* 15, 4823-4828.

Martínez I, Lombardía L, Herranz C, García-Barreno B, Domínguez O, Melero JA (2009). Cultures of HEp-2 cells persistently infected by human respiratory syncytial virus differ in chemokine expression and resistance to apoptosis as compared to lytic infections of the same cell type. *Virology* 388, 31-41.

Olivares I, Ballester A, Lombardía L, Domínguez O, López-Galíndez C (2009). Human immunodeficiency virus type 1 chronic infection is associated with different gene expression in MT-4, H9 and U937 cell lines. *Virus Res* 139, 22-31.