



R-LRB

# Report 2019-2020



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### **SCIENCE AND SOCIETY**

## 01 PRESENTATION: INTRODUCTION

The Spanish Biomolecular Nuclear Magnetic Resonance Laboratory Network or *Red de Laboratorios de RMN de Biomoléculas* (R-LRB) is a Unique Scientific and Technical Infrastructure (ICTS) in health sciences field. The distributed ICTS consists of a network of high-field NMR instrumentation – including three 800 MHz and three 600 MHz spectrometers- placed in different locations in Spain.

This Spanish network offers coordinated open access mechanisms to improve national competitiveness in the biomolecular NMR field, through cutting edge NMR instrumentation and know-how.

The R-LRB assists internal and external users from public and private research centers and is open to both the national and the international scientific communities. The R-LRB is currently composed by three nodes:



<http://www.rmn.ub.edu/r-lrb/index.html>

### LRB

Laboratorio de RMN de la  
Universitat de Barcelona

<http://www.rmn.ub.es/lrb/>



<https://www.ub.edu>

### LMR

Laboratorio de RMN  
"Manuel Rico"

<https://lmr.csic.es/>



<https://www.csic.es>

### LRE

Laboratorio de RMN de  
Euskadi

<https://www.cicbiogune.es/research/platforms/nuclearMagneticResonance>



<https://www.cicbiogune.es/>

## 01 PRESENTATION: INAUGURATION

Words from Prof. Rosa Menéndez, President of CSIC, in the opening of the official inaugural ceremony of R-LRB (7/6/2019).

It's my pleasure to open this inaugural symposium of ICTS Network of Nuclear Magnetic Resonance Laboratories for Biomolecules.

We feel proud of this facility network becoming part of the ICTS national map. This is a significant achievement. In particular, since this is the only new CSIC installation to win entry into the map during this evaluation period. With it, there are 9 ICTS nodes in the CSIC.



But even more important is that this is a story of achievement based on the successful collaboration between three different research institutions; the CSIC, the CIC bioGUNE and the University of Barcelona. Led by the NMR facility of the University of Barcelona, which has been part of the ICTS map since the system was established, the three institutions have succeeded by working together. This "I win / you win" collaborative strategy is the best for building long term, fruitful partnerships. Complementary expertise within the NMR field, and a geographical distribution linking some of the most active regions in Spain, strengthen the network and place Spanish NMR in the right position to face the current challenges in Structural Biology. Our hope is that in coming years this ICTS will continue to grow both geographically as well as in resources and users.

This inauguration is also a recognition of the vitality of the Spanish NMR community, represented here by the president of the NMR group of the Spanish Royal Chemistry Society. Chemistry, in general, and NMR in particular have been

historically strong in our country, and they have gained a deserved international reputation.

Now that NMR is a key player in Biology and Biomedicine, this is a good moment to recognize the importance of Structural Biology in the CSIC. The increasing number of NMR spectroscopists working on biological problems, together with the flourishing community of cryoelectron-microscopists and crystallographers in the CSIC, reinforces the leading position of our institution in Structural Biology in Spain. Aware of its privileged situation, CSIC is carrying out a great financial effort to upgrade its infrastructures, and provide its researchers with the state-of-the-art equipment needed to keep performing outstanding research.



Figure 1.1 Invitation for the inauguration of the R-LRB.

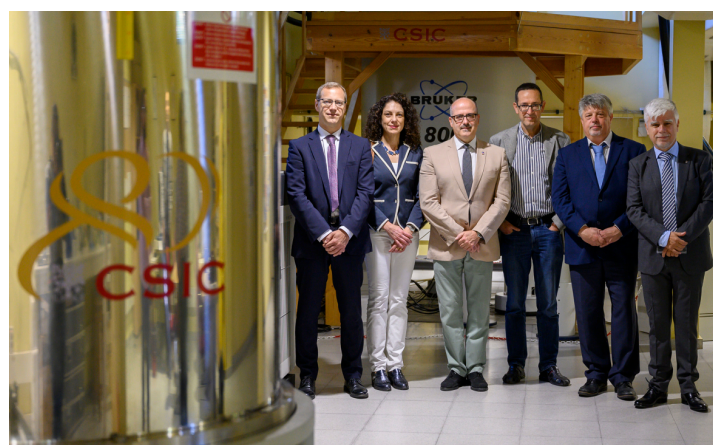
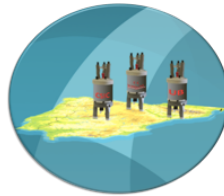


Figure 1.2 Members of The Ministry of Science and Innovation and executive committee of R-LRB.

## 01 PRESENTATION: TIMELINE

**NOV 2018**  
Updated Map of ICTS



**JAN 2019**  
Open competitive Calls

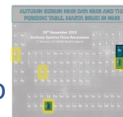
**JUN 2019**  
R-LRB Meeting

**JUN 2019**  
Official Inaguration



**NOV 2019**  
R-LRB Meeting

**NOV 2019**  
GERMN Workshop



**JAN 2020**  
Open competitive Calls

**JAN 2020**  
New Web & Logo



**MAR 2020**  
R-LRB Meeting

**FEB 2020**  
EPI Meeting



**MAY 2020**  
Installation @ LMR  
AVANCE NEO



**SEPT 2020**  
R-LRB bylaws approval

**JUN 2020**  
Signing the agreement  
(UB-CSIC-CIC bioGUNE)



**DEC 2020**  
R-LRB Meeting

**NOV 2020**  
Visit @ LMR  
Prime Minister of Spain  
Minister of Science  
President of CSIC



**DEC 2020**  
EUROMAR online  
Meeting



## 01 PRESENTATION: LOCATION

The LRB NMR facility belongs to the University of Barcelona and is integrated into the Scientific and Technological Centers of the University of Barcelona (CCiTUB) that includes a wide range of complementary infrastructures; this generates a stimulating environment and synergies for the users. Industrial companies have an important share in the use of the NMR facility and, for some of them, NMR represents an strategic tool.

The “Manuel Rico” NMR spectroscopy Laboratory (LMR) is a scientific-technical service of the CSIC is located on the Central Campus of the CSIC in a historical and privileged location, just a stone’s throw from the “Residencia de Estudiantes” and the Rockefeller building. The LMR is managed by the Rocasolano Institute of Physical Chemistry (IQFR-CSIC).

The LRE is located at the Centre for Cooperative Research in Biosciences (CIC bioGUNE) in the Technological Park of Vizcaya. CIC bioGUNE has modern scientific infrastructures, led by prestigious scientists, which allow it to compete with the main European research institutes.

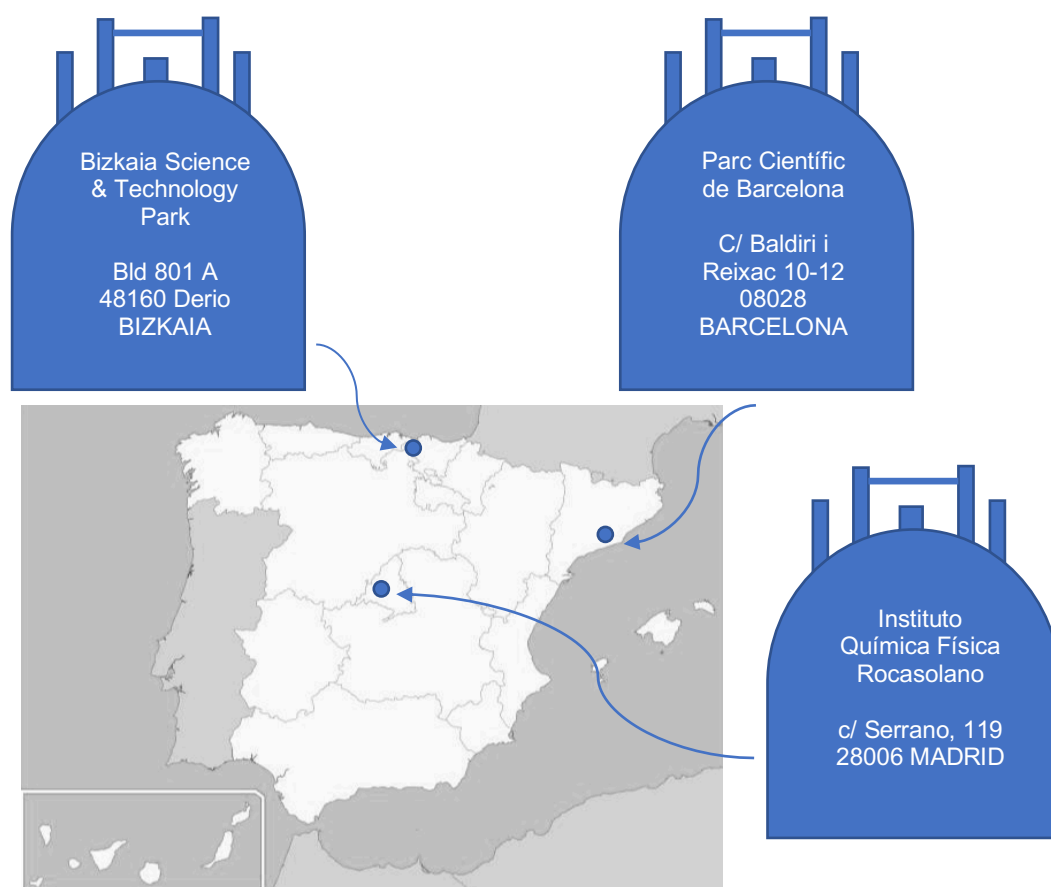


Figure1.3 Map of distributed ICTS Red de Laboratorios de RMN de Biomoléculas (R-LRB).

## 02 GOVERNING, EXECUTIVE AND SUPPORT BODIES

The R-LRB was approved by the “Consejo de Política Científica y Tecnológica y de Innovación” the 6<sup>th</sup> of November 2018 and formally established by an agreement between the University of Barcelona, the Consejo Superior de Investigaciones Científicas” and CIC bioGUNE, published on 11<sup>th</sup> September 2020. The management is regulated by the bylaws approved by the Coordination Committee on 23<sup>rd</sup> September 2020.

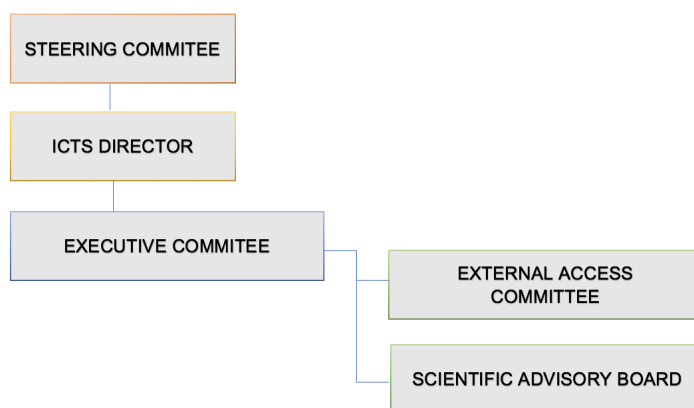


Figure 2.1 Organization chart.

The legal representatives of the institutions owning the various nodes, or the people they designate, form the **Steering Committee**, which oversee the legal and economic aspects of the distributed ICTS. The R-LRB is managed by the Coordination Committee, chaired by a coordinator, who acts as a representative of the R-LRB. The **Coordination Committee** is formed by the scientific directors and the technical facility managers of each node. The **Scientific Advisory Board** is formed by six internationally recognized experts and its role is to provide advice to the coordination committee on strategic decisions. The **External Access Committee** is in charge of evaluating the suitability of competitive access request by users. The access protocol has been approved by the coordination committee and is common to the three nodes.

### STEERING COMMITTEE

#### UB

Rector

Joan ELÍAS GARCÍA

#### CSIC

Vice-President for  
institutional Affairs and  
Organization

Rosina LÓPEZ-ALONSO

#### CIC bioGUNE

General Director

Jóse M<sup>a</sup> MATO DE LA PAZ



## EXECUTIVE COMMITTEE

### ICTS COORDINATOR

Miquel Pons  
Carlos González (Nov 2020)

### LRB

Scientific Director

Miquel PONS

Facility Managers

Margarida GAIRI

M<sup>a</sup> Teresa GONZÁLEZ

### LMR

Scientific Director

Carlos GONZÁLEZ

Facility Manager

David PANTOJA-UCEDA

### LRE

Scientific Director

Oscar MILLET

Facility Manager

Beatriz G. Valle

## EXTERNAL ACCESS COMMITTEE

Institut de Química Avançada de Catalunya,  
CSIC, Barcelona

Ignacio ALFONSO

Centro de Investigaciones Biológicas, CSIC,  
Madrid

Francisco BLANCO

Centro de Investigaciones Biológicas, CSIC,  
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Departamento de Química Orgánica  
Universidad de Sevilla

Jesús ÁNGULO

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Florence, Italy

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Max F Perutz Laboratories, University of  
Vienna, Austria

**Robert KONRAT**

Slovenian NMR center, Slovenia

**Janez PLAVEC**

Institute for Cancer and Genomic Sciences  
College of Medical and Dental Sciences  
University of Birmingham, UK

**Ulrich GÜNTHER**

Institute de Sciences Analytiques, University  
of Lyon, France

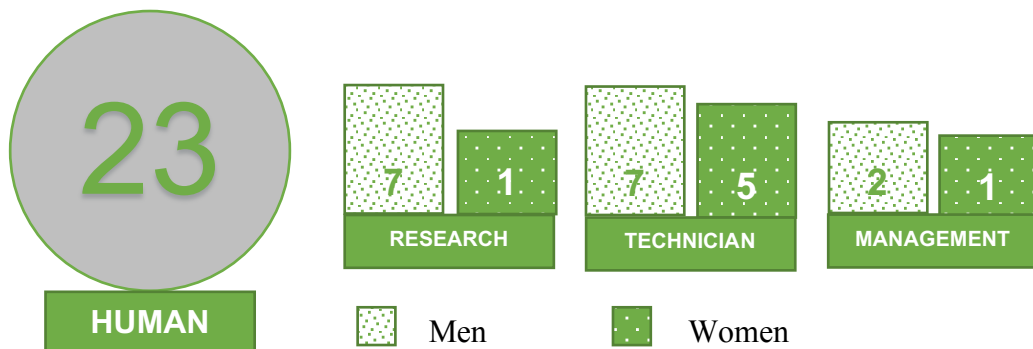
**Anne LESAGE**

Director of the Center for Biomolecular  
Magnetic Resonance, University of  
Frankfurt, Germany

**Harald SCHWALBE**

### 03 RESOURCES

The distributed ICTS consists of a network of the highest field NMR instrumentation currently available in Spain – including three 800 MHz spectrometers– placed in different locations of Spain. Additionally, this ICTS offers access to three 600 MHz spectrometers.



**ESSENTIAL EQUIPMENT**

**LRB**

**LRB-AV600**

Magnet: 14.1T Ultrashield Bruker  
Console: Avance III  
Probe: TCI cryoprobe



**LRB-AV800**

Magnet: 18.8 T Bruker  
Console: AVANCE NEO (since October 2018)  
Probe: TCI cryoprobe



**LMR**

**LMR-AV600**

Magnet: 14.1T Oxford  
Console: AVANCE NEO (since May 2020)  
Probe: TXI cryoprobe



**LMR-AV800**

Magnet: 18.8 US2 Bruker  
Console: AVANCE NEO (since May 2021)  
Probe: TCI cryoprobe



**LRE**

**LRE-AV600**

Magnet: 14.1 T US  
Console: AVANCE III  
Probe: PA-TXI, TXI for high salt, QXI (<sup>31</sup>P), QXI (<sup>19</sup>F), SEF, TBI, BBO, TXI HR-MAS  
Extras:  
6 Preamplifiers: <sup>1</sup>H, <sup>2</sup>H, <sup>15</sup>N, <sup>19</sup>F, X-BB (2x)  
HR-MAS unit (15.000 rpm)



**LRE-AV800**

Magnet: 18.8 T US2  
Console: AVANCE III  
Probe: Cryo-TCI, QXI (<sup>31</sup>P)  
Extras: 4 Preamplifiers: <sup>1</sup>H, <sup>2</sup>H, <sup>13</sup>C, <sup>15</sup>N



**LRB-LAB**

Production, Preparation NMR Samples



**LMR-LAB**

Production, Preparation NMR Samples



**LRE-LAB**

Production, Preparation NMR Samples



**HUMAN**

**LRB**

**Miquel Pons**

Scientific Director  
Research

**José Ramon Seoane**

CCiTUB Director  
Management

**Margarida Gairí**

LRB Facility Manager  
NMR technician

**M. Teresa González**

LRB Facility Manager  
NMR technician

**M Antònia Molins**

NMR technician

**M Victoria Muñoz-Torrero**

NMR technician

**Albert Gallén**

Support NMR technician

**Agustí Martínez**

Support NMR technician

**Víctor Meriel**

Lab Technician

**Oscar Nieto**

R-LRB web Manager

**Francisco Cárdenas**

NMR Facility Manager  
Management

**LMR**

**Carlos González**

Scientific Director  
Research

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**Douglas V. Laurents**

Research Advisor

**José Manuel Pérez**

Research Advisor

**David Pantoja-Uceda**

Facility NMR Manager  
Technician

**Daniel Calvo**

Support NMR Technician

**Miguel Treviño**

Facility LAB protein Manager  
Technician

**Irene Gómez Pinto**

Facility LAB ADN Manager  
Technician

**LRE**

**Jesús Jiménez-Barbero**

Scientific Director  
Research

**Oscar Millet**

Adjunct Director  
Research

**Tammo Diercks**

Facility NMR Manager  
Technician

**Beatriz G. Valle**

Project Manager  
Management

## 04 CATALOGUE OF SERVICES AND ACCESS

The facility is strongly linked to internationally recognized NMR groups that ensure that the facility remains at the leading edge of the technique and is available to offer advice to non-expert users. The dedicated staff of the facility is a team of specialists who take care of the instruments and promoting education in the area of NMR. The facility personnel guide the users according to their need, ranging from experts wishing to implement new experiments to non-expert users requiring help in experimental design and interpretation to take full advantage of the NMR facilities. Typical users come from a wide diversity of areas, including among others:

- Protein 3D structure and dynamics
- Atomic characterization of IDPs and linear peptides
- Structure and dynamics of nucleic acids and their derivatives.
- Biomolecular recognition and interactions (including carbohydrates and lipids).
- Metabolic studies (metabolomics).
- Functional Biology.
- Drug discovery and drug design (ligand screening and optimization).
- Structural elucidation in Organic and Inorganic Chemistry.
- Biologics characterization
- Food Science and Technology.
- New methodologies: NMR applications development.

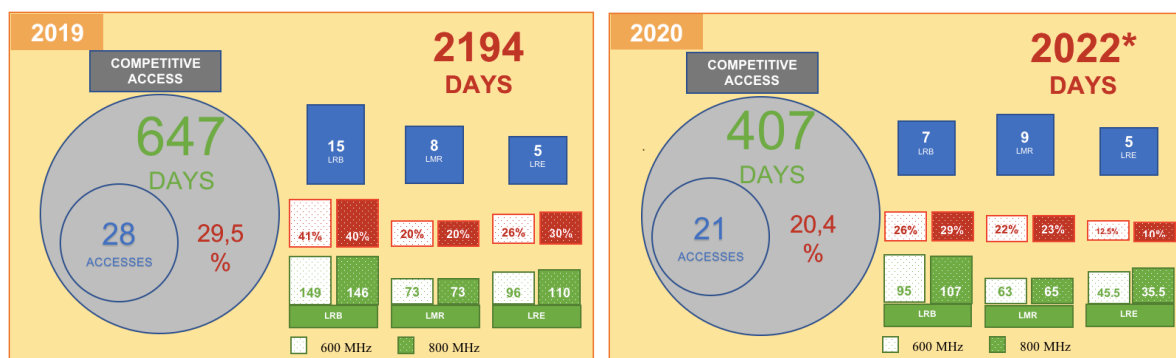
The R-LRB is open to research groups from public and private centers and offers access to the instrumentation and the know-how of scientific-technical staff responsible for NMR spectrometers. The competitive access corresponds to research projects in which an intensive use of the spectrometers is required. The access is regulated by an open competitive procedure, with an independent and transparent evaluation process. The call for competitive access is permanently open. The potential users must complete the online Access Application Form that will be evaluated by the External Access Committee (see below). A complete description of the access protocol can be found here (<http://www.rmn.ub.edu/r-lrb/pages/access.html>).

Data management protocols are being implemented to ensure open access and data traceability according to EU directives.

## 04 CATALOGUE OF SERVICES AND ACCESS: ACCESSES

The Network of Laboratories for Nuclear Magnetic Resonance of Biomolecules, R-LRB, as a distributed Singular Scientific and Technical Infrastructure (ICTS, according to its initials in Spanish) of NMR, has granted during the period 2019-2020 a total of 49 Open Accesses to the scientific community for the use of its 6 NMR spectrometers.

In all years, the percentage of competitive accesses requested and granted has been higher than 20%. On average, during the 2019-2020 period, the percentage of CAs granted was 25.0%, which represents a value of 5.0% above the committed value. It should be noted that, although in 2020 the demand for access decreased due to the state of alarm due to COVID-19, the percentage of accesses remained slightly above 20%.



\* Installation of new consoles AVNEO @ LMR

Figure 4.1 Statistics of competitive access.

Of the Open Access time granted during the 2019-2020 period (a total of 1054 days, 2500% of the total available time), 97% has been executed. The remaining 3% corresponds to ongoing projects, whose fulfillment is being carried out during the current year 2021.

The 49 Open Accesses have been used by a total of 35 different researchers. The number of new users incorporated each year has remained between 44 and 53%. On the other hand, the loyalty of users has been maintained for whom the use of the ICTS NMR spectrometers is absolutely essential for their research projects. Without these instruments, they would have been forced to request these resources in European facilities. Due to COVID-19 lockdown restrictions, travel abroad is severely restricted, so having these instruments in Spain has been indispensable for the progress of many research projects.

Figure 4.2 captures the diversity of the researchers who use the R-LRB; they come from 13 centers located in universities, research institutes and the Spanish National Research Council.

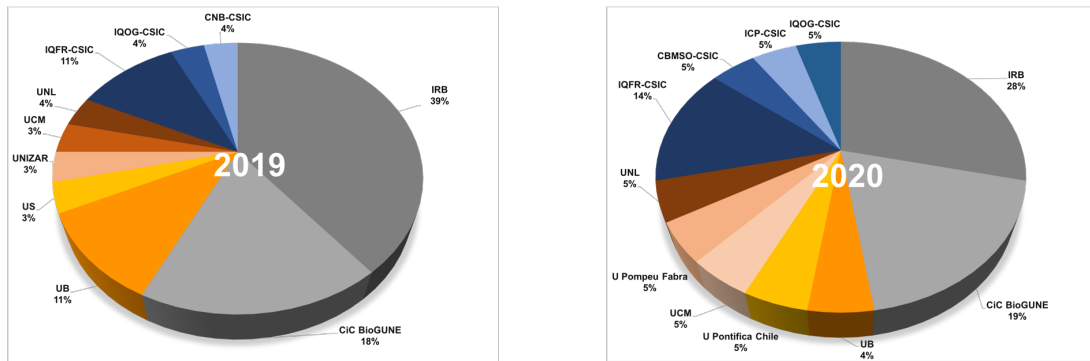


Figure 4.2 Users by type of institute and individual institutes.



## 05 KNOWLEDGE TRANSFER

R-LRB users published 104 peer reviewed articles - most of them in high-impact factor papers- and 3 book chapters. A total of 147 presentations –both oral and written- and invited lectures in prestigious national and international Congress were given where the research resulting from the use of the R-LRB was presented. Also, 9 PhD students, who used ICTS resources extensively, successfully defended their doctoral thesis during this period.

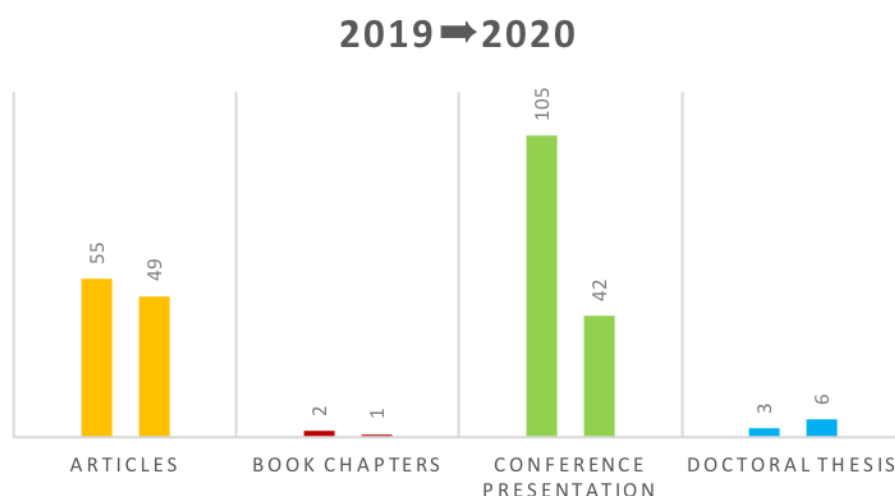


Figure 5.1 Statistics of results in R-LRB.

Furthermore, the R-LRB offers to the high-field NMR community both methodological development and application services. New methods are developed on demand. Application services are provided on the fields of IDPs, protein dynamics, biomolecular interactions, structural studies of proteins and peptides, structural studies of DNA, structural studies of carbohydrates, metabolomics, food science and in-cell NMR. In general, each node of the distributed ICTS implements and develops specific NMR methodology, according to their users main interests.

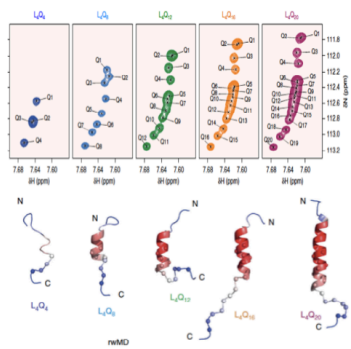
Collaboration between the LRB node from Barcelona and the chemical and pharma industry in Catalonia, previously established, have maintained throughout the 2019-2020 period. In addition, 12 industries have been new users of the NMR facility. The LRB node has an accreditation from FDA and holds ISO quality certificates that have been successfully renewed during the 2019-2020 period. The collaboration with some industries is strategic for their business plan. In addition, the LRE node from Bilbao has been actively involved in supporting several hospitals and health institutes around the country, on the identification of metabolic biomarkers of several diseases. A start-up from CIC bioGUNE is ready to begin the last clinical phases of a new drug for an orphan disease associated to protein instability initially discovered as part of an NMR project.

## 05 KNOWLEDGE TRANSFER: SUCCESS CASES

### Side chain to main chain hydrogen bonds stabilize a polyglutamine helix in a transcription factor.

*Nature Communications* 2019, 10(1), 2034

<https://doi.org/10.1038/s41467-019-09923-2>.



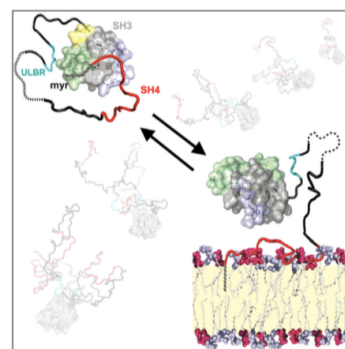
The use of the fast-NMR methods implemented at the LRB node of the R-LRB has been key for the research project led by the ICREA Research Professor Xavier Salvatella from the Laboratory of Molecular Biophysics at the Institute for Research in Biomedicine (IRB). Salvatella group has studied by NMR the structural basis of the association between polyglutamine (polyQ) tract length, transcriptional activity and polyQ disorders-based diseases, and addressed how the conformation of polyQ tract of the Androgen Receptor, associated with spinobulbar muscular atrophy (SBMA) depends on its length. Their findings suggest a plausible rationale for the association between polyQ tract length and Androgen Receptor transcriptional activity and have implications for establishing the mechanistic basis of SBMA.

### A Myristoyl-Binding Site in the SH3 Domain Modulates c-Src Membrane Anchoring.

*iScience* 12, 194–203, 2019,

<https://doi.org/10.1016/j.isci.2019.01.010>

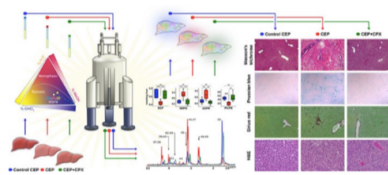
NMR spectroscopy has also been crucial for the study of intrinsically disordered proteins (IDPs) and intrinsically disordered regions (IDRs), such as those present in Src family kinases. The Pons' group has shown that the N-terminal myristoyl group binds to the SH3 domain in the proximity of the RT loop, when Src is not anchored to a lipid membrane. Residues in the so-called Unique Lipid Binding Region modulate this interaction. In the presence of lipids, the myristoyl group is released from the SH3 domain and inserts into the lipid membrane. The fuzzy complex with the SH4 and Unique domains is retained in the membrane-bound form, placing the SH3 domain close to the membrane surface and restricting its orientation. The apparent affinity of myristoylated proteins containing the SH4, Unique, and SH3 domains is modulated by these intramolecular interactions, suggesting a mechanism linking c-Src activation and membrane anchoring.



### Metabolic landscape of the mouse liver by quantitative $^{31}\text{P}$ -NMR analysis of the phosphorome.

Hepatology

<https://doi.org/10.1002/hep.31676>



$^{31}\text{P}$ -NMR provides an innovative and simple holistic view of the inherent complex metabolism in health, disease and as a response to treatment. In this context, phosphorylated metabolites occupy a prominent position in all anabolic and catabolic pathways. In Millet's laboratory, they have developed a  $^{31}\text{P}$ -NMR-based method to study the "phosphorome" in tissue samples through the simultaneous identification and quantification of multiple hydrophilic and hydrophobic phosphorylated metabolites. The methodology included the standardization and optimization of the protocol to yield a robust and quantitative measurement of the phosphorylated metabolism. They are now adapting this technique to define the metabolic landscape in several organs -including liver, brain, heart, and pancreas- of mouse models and of human tissue samples as well.



### The first DNA/ligand complex involving a G-quadruplex/duplex junction.

Chemistry. A European Journal

Cover: [doi.org/10.1002/chem.202100456](https://doi.org/10.1002/chem.202100456)

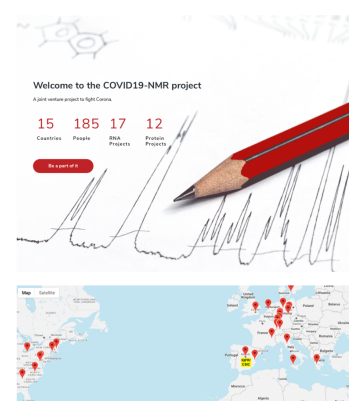
Paper: [doi.org/10.1002/chem.202005026](https://doi.org/10.1002/chem.202005026)

Researchers of two groups at CSIC used NMR to study a new designed pharmacophore based on cationic aromatic frameworks that selectively binds with high affinity to quadruplex–duplex junctions, while presenting a poorer affinity for G-quadruplex or duplex DNA alone. The structure of the complex be w een a quadruplex–duplex junction with a ligand of the HIV-1 LTR-III family has been determined. According to these data, the remarkable selectivity of this structural motif for quadruplex–duplex junctions is achieved through an unprecedented interaction mode so far unexploited in medicinal and biological chemistry: the insertion of a benzylic ammonium moiety into the centre of the partially exposed G-tetrad at the interface with the duplex.

### SARS-CoV-2 Disordered Protein Targeted for Inhibition.

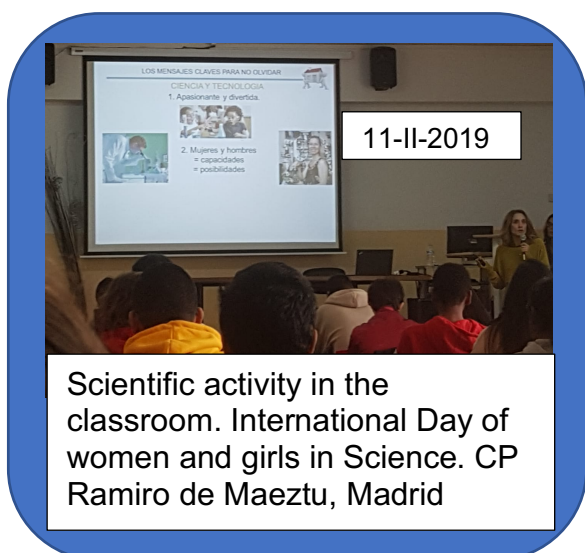
<https://covid19-nmr.de/>

The “Manuel Rico” NMR lab, LMR is characterizing SARS-CoV-2 disordered protein and collaborating as part of International Consortium COVID19-NMR in the search of inhibitors as drug leads.



## 06 SCIENCE AND SOCIETY

A total of 34 activities have been carried out to disseminate the capabilities of the R- LRB. These actions were oriented to promote cooperation with other institutions and to bring the ICTS closer to the general public. Activities included seminars, conferences, and Open Days to foster the applications of NMR among researchers and/or industry stakeholders. Many activities were disseminated through media and digital tools. When possible, on-site visits to the R-LRB were scheduled in a regular basis from a wide range of visitors: elementary, high schools and vocational training students; high school teachers; science students and future researchers; university or other research institutions management staff; industry stakeholders and policy makers.




**CIENCIA EN LA BIBLIOTECA**  
Encuentros informales (virtuales) con científicos en la biblioteca Dorotea Barrios del Instituto de Química Física Rocasolano. c/ Serrano, 119.

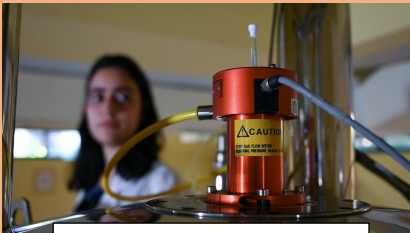
**La estructura del ADN: El poder de la hélice.**  
Encuentro con Carlos González.  
Miércoles 11 de noviembre de 2020, 18:30-19:30.



Virtual Visit of precandidates PhD @ LMR



23-X-2020



07-VI-2019

CSIC Report @ LMR

EL@MUNDO ESPAÑA OPINIÓN ECONOMÍA INTERNACIONAL DEPORTES CULTURA TELEVISIÓN

PERSONAS QUE SUMAN

**El investigador que busca descifrar el misterio de la ELA**


Miguel A. Mompeán trabaja sobre cómo ocurre las secuencias erróneas de la esclerosis lateral amiotrófica antes de que estas ocurran



20-I-2020

Press "El Mundo" @ Dr. Miguel Mompeán

TVE 24h @ Dr. Miguel Mompeán



19-X-2020

Welcome to the COVID19-NMR project

15 185 17 12

Quantities Peaks NMR Products Peaks Products



13-VI-2020

Press CSIC : COVID19-NMR @