SCIENTIFIC RESEARCH REPORT

BANC DE SANG I TEIXITS I 2010

Generalitat de Catalunya
Departament de Salut

Banc de Sang i Teixits

INDEX

PRESENTATION OF MANAGING DIRECTOR

The year 2010 marked the start of a new strategic plan, drawn from a broad process of reflection and which has culminated in new challenges for an organization that is and intends to continue being a leader in its field of action. The new plan emphasizes the desire to maintain the BST as an innovative, modern, efficient and excellent company towards increasing the knowledge to maximize value creation. For this reason, research and innovation are one of the cornerstones of this new road layout in 2010.

A year in which we have achieved another major challenge: the transfer of basic research institutions of the BST to the new building located in the 22@, with the qualitative leap that this represents. New art facilities and more square feet available for research and to take advantage of the synergies of different teams that share the common goal of continuing to generate social value.

The scientific report 2010 shows the main data of the scientific activity of BST in 2010: 14 new research projects, 43 publications in refereed journals, 8 patents in process, among other milestones achieved. These and other data show that the research is part of the daily activity of BST and that all divisions have incorporated it into their day to day.

In a context of economic uncertainty, a human team like the one of the BST has been the best warranty, best asset in order to continue and advance in a way essential to the life of the organization.

Ramon Pau Pla Illa

INTRODUCTION BY THE SCIENTIFIC DIRECTOR

It is a pleasure to present the research report of 2010 of the Blood and Tissue Bank. It is the first time, as Scientific Director of BST, I write to people inside and outside the organization. I take this opportunity to appreciate to the Board of Directors and to the Direction, the confidence awarded. I will do my best not to disappoint the expectations.

I would not like to continue this introduction without acknowledging the great work and the outstanding achievements of my predecessor in the charge, Dr. Ricardo Pujol, as well as those who have collaborated with him in the field of research in recent years. Proof of what I say is the objective information contained in this report, competitive grants obtained, publications, collaborations with other institutions and agreements with industry, amongst other. It is fair to say that the scientific path of BST is consolidated thanks to the efforts of his researchers.

Despite the crisis that surrounds us, we have a future full of opportunities. It is true that we live in a strong budgetary adjustment. Nevertheless, there remains a 90% investment in health and a significant proportion in research. The current situation forces us to be even more competitive and innovative. I'm sure we can be it, because I fully trust in the BST, his Divisions, his Centers and, above all, in his people. We must concentrate our efforts in doing investigation in our natural field, blood and tissues, given that it has to be especially applied and useful to society. Our area of knowledge experiences continuous and spectacular advances, opening possibilities up to now unsuspected. We have to take advantage of all our capacity and our imagination to investigate and do it with sustainability, responsibility and focused in the citizens who we give service, especially in those that need us more because they are sick.

I am confident that together we will cross an exciting way in the coming years.

Jordi Sierra Gil

1. BANC DE SANG I TEIXITS

The Banc de Sang i Teixits (Blood and Tissue Bank - BST) is the public company of the Catalan Ministry of Health whose mission is the management and administration of the donation, transfusion and analysis of blood and blood plasma. It also acts as a centre for obtaining and processing tissues and develops other lines of activity as a centre specialized in immunobiology, molecular analysis, cell therapy and regenerative medicine.

- BST is the backbone of the hemotherapy system in Catalonia
- Its activity extends to all public and private centres in Catalonia as well as others in Spain
- BST aims to be a first level centre in management, innovation and hemotherapy and tissue research

Among the projects recently implemented by the organisation are the Biobank and the Human Milk Bank.

The BST participates in its own research projects or in collaboration with all the centres of the Catalan Health Institute, a large part of the Public Hospital Network and Catalan Universities and also promotes strategic alliances with research centres and industry.

1.1 GOVERNING BODIES

The Governing Bodies of the Banc de Sang i Teixits are the Board of Directors and the Delegated Commissions.

1.1.1 Board of Directors

President: Antoni Esteve Cruella
First Vice-president: Enric Argelagués Vidal
Second Vice-president: David Elvira Martínez
Secretary: Josep Ramon Arisa Clusella
Members: Enric Argelagués Vidal, Francesc Brosa Llinares, Enric Contreras Barbeta, Lourdes Girona Brumós, Josep Fité Benet, Joan Profitós Tuset, José Luis de Sancho Martín, Jordi Teruel Boladeras, Jordi Varela Pedragosa, Marc Ibars Badia, Francesc Guerra Maestre, Ana Veiga and Josep Maria Piqué Badia

1.1.2 Delegated Commissions

Science and technology: Enric Argelagués Vidal
Internal Audits: David Elvira Martínez
Economics: Francesc Brosa Llinares / Jordi Teruel Boladeras
Human Resources: Enric Contreras
Quality: Lourdes Girona Brumós / Josep Maria Fité Benet
Works: Jordi Varela Pedragosa
Communication: Joan Profitós Tuset

1.2. DIRECTION AND MANAGEMENT BODIES

1.2.1 Steering Committee

Managing Director: Ramon Pau Pla Illa
Assistant to Managing Director: Isabel López Asión
Economic/financial Director: Gabriela Marín Cobo
Director of People and Values: Esther Solà Saplana
Marketing Director: (vacant)

Director of Information and Communication Technologies: Albert Herrero Espinet
General Services Director: Joan Ovejo Cortes
Director of the Blood Division: Lluís Puig Rovira
Director of the Tissues Division: Aurora Navarro Canturella
Director of the Advanced Therapy Division (Xcelia): Joan Garcia López
Director of the Immunohematology Division: Eduardo Muñiz-Díaz
Director of the Immunobiology Division: Ricardo Pujol Borrell
Director of the Congenital Coagulopathy Division: Rafael Parra López

1.2.2 Healthcare Management Committee

Director of the Blood Division: Lluís Puig Rovira
Director of the Tissues Division: Aurora Navarro Canturella
Director of the Advanced Therapy Division (Xcelia): Joan Garcia López
Director of the Immunohematology Division: Eduardo Muñiz-Díaz
Director of the Immunobiology Division: Ricardo Pujol Borrell
Director of the Congenital Coagulopathy Division: Rafael Parra López

1.2.3 Directors Committee

Barcelona. Vall d'Hebron and Clínic: Dolors Castellà Cahíz
Barcelona. Sant Pau: Pedro Madoz Resano
Badalona. Germans Trias i Pujol: Joan Ramon Grífols Ronda
L'Hospitalet. Bellvitge: Lluís Massuet Bosch
Manresa. Fundació Althaia/Terrassa. Mútua de Terrassa: Ramon Salinas Argente
Girona. Dr. Josep Trueta: Joan Profitós Tuset
Lleida. Arnau de Vilanova: Juan Manuel Sánchez Villegas
Tarragona. Joan XXIII/Tortosa. Verge de la Cinta/Reus. Sant Joan: Enric Contreras Barbeta

1.3 ADVISORY BODIES

The External Scientific Committee and the Committee of Innovation will be the advisory bodies of the BST in the field of research and innovation.

1.3.1 External Scientific Committee

The objective of this committee is to inform and advise the managfement of BST on the importance of the various research projects and to alert the company about the development of new technologies that are relevant to our processes (technological monitoring).

This committee should also analyze the situation in which the BST is in research and innovation and issue a series of recommendations with a view focus from 5 to 10 years.

Its composition must be reviewed and updated for slaughter all the products and services offered by BST and that BST wants to offer. It is the responsibility of the Scientific Director and the Management to review the composition of this committee.

1.3.2 Committee of Innovation

This committee's main objective is the selection of ideas that will become the research and innovation projects of the company. Also carry out the external and internal analysis of the situation of the company in terms of innovation (from a more functional perspective than the one made by the External Scientific Committee).

Will be responsible for search technology partners and collaboration agreements with public and private entities that promote the generation of new products and services. Assume the technological monitoring and reporting to other innovative staff of the organization.

Composition:

- A member of the Directorate-Management
- BST Scientific Director
- The head of each of the divisions of activity and scientific officers
- A member / manager of the Information and Communication Technologies / General Services Divisions (when appropriate).
- A member / manager of the Marketing Division
- A representative from the Area of Innovation and Projects
- A representative from the Regional Centres (when necessary)

1.4 LOCATION

The new corporate headquarters of the Banc de Sang i Teixits are located on the corner of Passeig Taulat and Lope De Vega, in the new 22@ technological district of Barcelona which combines economic and training activity with campuses and residential areas. The building centralises the various lines of activity and a large part of the 600 professionals of the organisation who were located in different facilities in the province of Barcelona.

The project was designed by the architects Joan Sabaté and Horacio Espeche Sotailo and adheres to criteria for maximum energy efficiency.

The new corporate headquarters was recognised in the III edition of the ENDESA Awards for the most sustainable real-estate promotion in 2009 in the category of more sustainable promotions exhibited in Barcelona Meeting Point '09.

Banc de Sang i Teixits
Dr. Frederic Duran i Jordà
Passeig Taulat, 106-116
08005 Barcelona
Phone: 93 557 35 00

1.5 SUMMARY OF RESEARCH ACTIVITY

1.5.1 Research and technical staff

	Number	FDA
Research staff	52	34.79
Principal investigators	23	9.62
Senior physicians	10	8.57
Junior physicians	19	16.60
Technical staff	11	11
TOTAL	63	45.79

1.5.2 Contracts to investigators and technicians funded by different organizations and programs

Contracts to investigators	Number	Research area:
Agency for Administration of University and Research Grants AGAUR	2	Diagnosis
CIBER Liver and Digestive Diseases	2	Blood technology
Torres Quevedo, Ministry of Science and Innovation	2	Advanced cell therapies
Carlos III Health Institute	2	Diagnosis

1.5.3 Economic data

Breakdown of BST research income for 2010	Euros
Projects funded by public agencies	1,356,030
Projects funded by private agencies	30,498
Agreements with industry	596,053
Own funds	2,233,473
TOTAL	4,216,054

1.5.4 Research projects

The ongoing research projects funded by public organisations and private bodies are shown below. A total of 14 projects received grants in 2010. There were 36 ongoing research projects on 31 December 2010.

Funding organisations	Ongoing projects in 2010	
	principal investigator BST	collaboration
Public Agencies		
Carlos III Health Institute	6	5
Spanish Ministry of Science and Innovation, MICINN	2	
ACC10		1
Catalan Health Service	1	
European Comission	3	
AGAUR	1	
MICINN + Industry (Diagnostic Grífols)	1	
Non-profit Private Agencies		
Marató TV3 Foundation	1	
BST+Anthony Nolan Trust+Nottingham Trent Univ	1	
Mutua Madrileña		1
Agreements with industry		
ABBOTT	1	
Wyeth Farma, S.A.	1	
Laboratorios Salvat, S.A.	1	
Bayer	1	
Asahi Kasei Kuraray	1	
Gamida	1	
Own funds		
BST	2	
Other		1
TOTAL	**36**	

Ongoing projects by research areas

Advanced cell therapies	9
Diagnosis and biomarkers	15
Blood technology and transfusion medicine	12

1.5.5 Doctoral theses

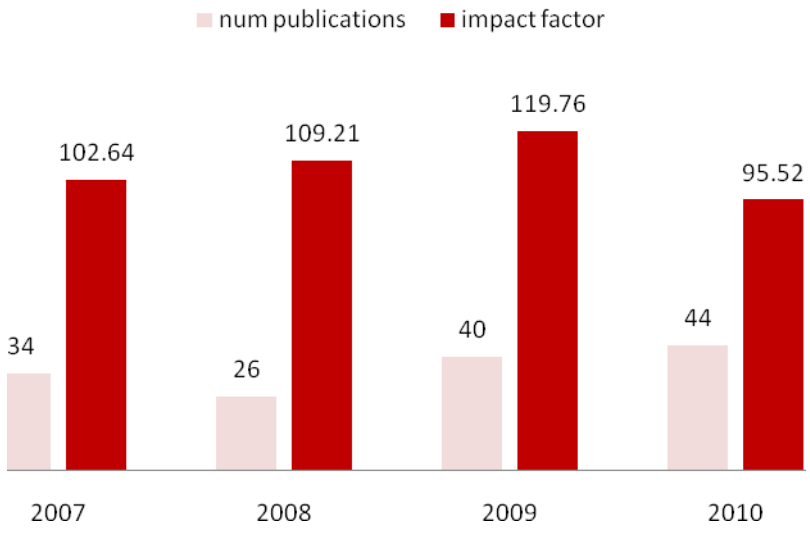
Three doctoral theses were read or directed by BST investigators in 2010.

PhD student	Thesis title	Directors	Department	Grade
Raquel Planas Bas	Gene expression profiles and immunologic alterations identified at the target organ of diabetes type I	Marta Vives Pi	Department of Cellular Biology, Physiology and Immunology (UAB)	Excellent Cum Laude
Nuria Alonso Pedrol	Immunological and hormonal gastric parameters in patients with diabetes mellitus type I	Eva Martínez Cáceres, Anna Sanmartí Sales	Medicine Department (UAB)	Excellent Cum Laude
Marta Ruiz Riol	Analysis of the central and peripheral tolerance mechanisms implicated in the pathogenesis of autoimmune thyroid diseases	Ricardo Pujol Borrell	Department of Cellular Biology, Physiology and Immunology (UAB)	Excellent Cum Laude

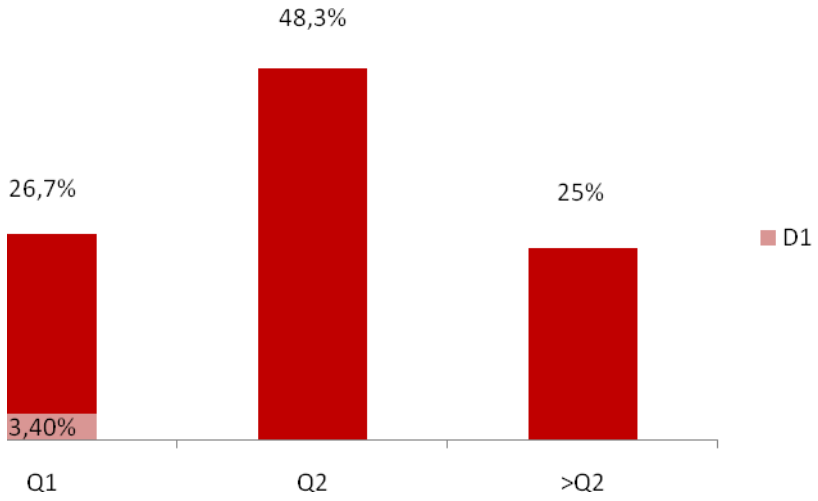
1.5.6 Publications

A total of 43 articles were published in scientific magazines by BST investigators in 2010 with an impact factor of 95.52 and a weighted impact factor of 31.89.
The impact factor for 2010 was calculated using Journal Citation Reports (JCR) for 2008. The calculation included original articles, revisions and editorials. Presentations to congresses were excluded.

Evolution of the scientific production of the BST over the last 4 years:



It is important to emphasise that 27.6% of the publications in scientific magazines by BST investigators in 2010 fall into the first quartile depending on their category and impact factor. The 3.4% of these publications are in the first decile.



2010 publications by research areas:

Diagnosis and biomarkers	21
Advanced cell therapies	14
Blood technology and transfusion medicine	8

1.5.7 Patents

The BST currently has 8 patents in different stages of processing. Four of them are being processed in Spain and six are in process abroad. One of the patents is currently being exploited.

1.6 TEACHING IN RESEARCH

The central element of teaching at the BST is the master of Transfusion Medicine and Cell Therapy, organised through the Autonomous University of Barcelona (UAB) with the support of the Doctor Robert Foundation. Even though this master is not research oriented, some students become interested in presenting their doctoral thesis. The master degree, begun in 2003, has improved in format and internationalisation. Its purpose is specialised training in all processes that take place in a blood bank (donation, processing, transfusion, immunohematology, management and certification) and a tissue bank with a far-reaching cell therapy program.

LIRAD professionals act as lecturers for the pre- and post-graduate immunology courses for the UAB degree of Medicine and in various courses of the Master in Immunology of the University of Barcelona-Autonomous University of Barcelona (UB-UAB). In addition, the BST gives classes of the Transfusion Medicine module to residents in Hematology-Hemotherapy in different teaching hospitals in Catalonia and is certified to teach Immunology residents.

The BST participates in directing professionals who are writing dissertations and doctoral theses. These programs include collaboration with nursing schools, laboratory technicians and the postgraduate and ongoing training schools of the UB, the UAB, the UPF, The Universitat Internacional de Catalunya and the Rovira and Virgili University.

The BST organizes stays of training for diverse professional through collaboration agreements with most Latin American countries (Argentina, Uruguay, Colombia, Mexico…) and other European countries like the United Kingdom, Portugal, Sweden, Italy, etc.

Other related projects

Chair of Transfusion Medicine and Cell and Tissue Therapy

The Autonomous University of Barcelona, the Blood and Tissue Bank and the Doctor Robert Foundation, created in 2008, the Chair of Transfusion Medicine and Cell and Tissue Therapy (CMT3).

The Mission of the Chair is to promote, assist and strengthen the training, research and consultancy in the field of Transfusion Medicine and Cell and Tissue Therapy, promoting collaboration between researchers and teachers of biomedical, health and welfare.

Since its inception, the CMT3 has led a project included in the sub-European Erasmus Education, Audiovisual & Culture Executive Agency. It has also participated in the project Eurocord-ED, within the subprogram Leonardo da Vinci.

On the other hand, in terms of postgraduate training, is currently underway the third edition of "Master in transfusion medicine and cellular and tissue therapy." A master for nurses in transfusion medicine and a european master in transfusion medicine and advanced cell therapy are under accreditation.

1.7 THE BANC DE SANG I TEIXITS WEB SITE

The Banc de Sang i Teixits has two web sites with the following addresses: www.bancsang.net and www.donarsang.gencat.cat.

The first, www.bancsang.net, is five years old and institutional in character. The contents are divided into four access routes depending on the user profile: Donors, Professionals, Receivers and Suppliers, together with a section with Corporate Information. Through this web page orders can be managed online.

The page www.donarsang.gencat.cat was created in 2009 to publish all the information of interest in relation to blood donations. It was conceived as an act of solidarity and citizen participation.

Its main objectives are to provide arguments on the social importance of giving blood and simplify donation as much as possible by providing information about up-coming campaigns. It includes a postcode or town search engine together with the exact location using Google maps.

Another purpose of the web site is to simplify contact with the donor through specialised query systems and the option of updating personal details using an online form. There is also direct access to social networks Twitter and Facebook.

2. RESEARCH ACTIVITY OF THE BANC DE SANG I TEIXITS

2.1 AREA OF RESEARCH IN ADVANCED CELL THERAPIES

PERSON IN CHARGE
Joan Garcia Lopez

2.1.1 Xcelia

Based on the conviction that cell therapies will be one of the main exponents of medicine in the future, the Banc de Sang i Teixits has promoted its Advanced Cell Therapy Division under the name of Xcelia. The purpose of this division is to develop personalised, safe cell medicines and tissue engineering to improve people's health. In accordance with this purpose and taking into account that the products of advanced cell therapy are considered drugs, Xcelia research is centred on four basic lines:

A. The development of candidates for cell drugs.

B. The development of bioprocesses under GMP standards.

C. The performance of non-clinical studies under GLP regulations.

D. The performance of clinical studies under GCP regulations.

The "MEDCEL" and "FACTOCEL" projects have been the driving forces behind this research activity. The first has enabled developing a pipeline composed of four products called Xcel-m-condro-alpha (mesenchymal cells for the treatment of arthrosis), Xcel-p-hemato-alpha (expanded hematopoietic stem cells for the treatment of myeloid aplasia), Xcel-mt-osteo-alpha (product of tissue engineering for the treatment of bone injuries) and Xcel-t-immuno-alpha (CMV-specific T-cells for the treatment of post transplant infections). At present these products are in different stages of development ranging from non-clinical studies to clinical phases I/II.

On the other hand, the "FACTOCEL" project has enabled the development of the specialised infrastructures and teams to work in compliance with the requirements of GMP. As a result of this project new production facilities, with a capacity to manufacture up to 600 batches/year, are now completed.

PERSON IN CHARGE

Joan Garcia Lopez

INVESTIGATORS

Carlos Torrico Leon
Joaquim Vives Armengol
Luis Vidal Conde
Nuria de la Fuente Oliva
Marta Caminal Bobet
Alba Casamayor Genescà
Margarita Codinach Creus
Arnau Pla Calvet
Ruth Coll Bonet
Jose Ramon Lopez Esquerdo
Irene Oliver Vila

ONGOING RESEARCH PROJECTS

Principal investigator: Joan Garcia Lopez

FACTOCEL – Enlargement of the production facilities of a factory for producing cell drugs for regenerative medicine.
Funding organisation: Spanish Ministry of Science and Innovation
File N°: PLE2009-0092
Duration: 2009 to 2011

Principal investigator: Joan Garcia Lopez

REDONTAP-Continous Proliferation&Simultaneous Maturation of Haematopoietic Stem Cells into Blood Cell Lineages
Funding organisation: European Commission
File N°: FP7-NMP-2008-SMALL-2
Duration: 2010 to 2014

Principal investigator: Joan Garcia Lopez

MEDAVAN – Advanced cell therapies: celular products and tissue engineering
Funding organisation: Spanish Ministry of Science and Innovation
File N°: IPT-300000-2010-17
Duration: 2010 to 2013

Principal investigator: César García Fontecha (Bioengineering, orthopaedics and pediatric surgery, H Vall d'Hebron), Margarita Codinach Creus (BST)

Application of stem cells obtained from amniotic fluid for neural and bone repair of myelomeningocele in ovine fetus
Funding organisation: Mutua Madrileña
Duration: 2008 to 2011

PUBLICATIONS

Garcia J. Allogeneic unrelated cord blood banking worldwide: An update. TRANSFUS APHER SCI 42; 257-263, 2010. QUARTILE 4, DECILE 10, IMPACT FACTOR: 0.95

Today Cord Blood (CB) Transplants are accepted as a therapeutic resource for the treatment of a variety of disorders, comparing in some cases, with transplants performed with other sources of progenitors. Unrelated Cord Blood Banks (CBBs) have significantly contributed to this improvement by the improvement on the knowledge of the CB biology and technical developments. Today, there are more than 100 active Cord Blood Banks

(CBB), with an inventory of more than 400,000 units, which have generated more than 10000 cord blood transplants all around the world. Access to the world-wide CB inventory, as well as the hemopoietic progenitors inventory from adult donors, is a rather complex task which is continuously subject to improvements and consolidations. The growing numbers of CBBs and the search for efficiency has driven them to constitute or adapt consolidated data bases and access systems, and to develop a number of registries or networks to improved the access to inventories. The purpose of the present article is to provide a general overview on the number of CB units stored around the word, the quality accreditation systems and how the CB networks and their national and international inventories and registries are organized in order to support the, every time more efficient search for suitable CB units for patients lacking family donors.

Uhde CW, Vives J, Jaeger I, Li M. Rmst Is a Novel Marker for the Mouse Ventral Mesencephalic Floor Plate and the Anterior Dorsal Midline Cells PLOS ONE Jan 8; 5(1): e8641, 2010

2.1.2 Cord blood and stem cells line

Hematopoietic stem cells are used in clinical situations to reconstitute bone marrow function. These cells can be obtained from bone marrow or mobilised peripheral blood of an adult, but also from the umbilical cord blood after giving birth. The administration of these cells to a patient regenerates haemapoietic and immune functions, contributing to the saving of many lives of patients suffering from cancer or acquired or genetic medullar insufficiency. The mission of the cell processing area of the Banc de Sang i Teixits is to transform the haemapoietic products collected in order to produce a therapeutic product with the expected qualities: safe and functional. The availability of high quality haemapoietic tissue is an essential factor for transplant and therefore investigating its improvement could contribute to therapeutic success.

A. Design and develop new products derived from cord blood and adult stem cells.

B. Introduce new predictive assays of the haemapoietic potency of the products developed (facilitation of the graft).

C. Study the product factors that condition the transplant immune function (donor-host reactions and immuno-vigilance).

D. Improve the efficiency of the production process to make it more sustainable, guaranteeing its high quality.

All this is performed in BST laboratories using techniques for volume reduction, cell selection, cryopreservation and storage, and assays of product quality based on cell cultures and cytometric analysis. In addition, collaboration agreements have been established with centres of excellence that complement our own tools, including the Anthony Nolan Research Institute in the United Kingdom, as well as transplant centres to evaluate application of the products at a clinical level.

PERSON IN CHARGE

Lluís Puig Rovira

INVESTIGATORS

Sergi Querol Giner
Marta Torrabadella Reynoso
Gregorio Martín-Henao
Carmen Azqueta Molluna

ONGOING RESEARCH PROJECTS

Principal investigator: Sergi Querol Giner

Biomarkers of Stem Cell Circulating in Plasma of Cord Blood
Funding organisation: BST, Anthony Nolan Trust and Nottingham Trent University
Duration: 2009 to 2011

Principal investigator: Marta Torrabadella de Reynoso

CBUs StemEx Separations
Funding organisation: Gamida Cell-Teva Joint Venture Ltd.
Duration: 2010 to 2012

PUBLICATIONS

Giorgetti A, Montserrat N, Rodriguez-Piza I, Azqueta C, Veiga A, Izpisúa Belmonte JC. Generation of induced pluripotent stem cells from human cord blood cells with only two factors: Oct4 and Sox2 NAT PROTOC 5(4); 811-820, 2010. QUARTILE 1, DECILE 2, IMPACT FACTOR 4.17.

Gamez J, Carmona F, Raguer N, Ferrer-Sancho J, Martín-Henao GA, Martí-Beltrán S, Badia M, Gratacós M, Rodriguez-Gónzalez E, Seoane JL, Pallero-Castillo M, Burgos R, Puiggros C, Pasarin A, Bori-Fortuny I. Cellular transplants in amyotrophic lateral sclerosis patients: an observational study. CYTOTHERAPY, 12; 669-677, 2010. QUARTILE 2, DECILE 4, IMPACT FACTOR 3.47.

Katz G, Mills A, Garcia J, Hooper K, McGuckindC, Platz A, Rebulla P, Salvaterra E, Schmidt A, Torrabadella M. Banking cord blood stem cells: attitude and knowledge of pregnant women in five European countries TRANSFUSION 2010, Dec 3. QUARTILE 2, DECILE 4, IMPACT FACTOR 3.47.
OBJECTIVE: This study explores pregnant women's awareness of cord blood stem cells and their attitude regarding banking options in France, Germany, Italy, Spain and the UK. METHODS: Questionnaires were distributed in six maternities. This anonymous and self-completed questionnaire included 29 multiple choice questions based on: 1/ socio-demographic factors; 2/ awareness and access to information about cord blood banking;

3/ banking option preferences; 4/ donating cord blood units (CBU) to research. RESULTS: 79% of pregnant women had little awareness of cord blood banking (n=1620). 58% of women had heard of the therapeutic benefits of cord blood, of which 21% received information from midwives and obstetricians. 89% of respondents would opt to store CBU. Among them, 76% would choose to donate CBU to a public bank to benefit any patient in need of a cord blood transplant. 12% would choose a mixed bank and 12% a private bank. 92% would donate their child's CBU to research when it is not suitable for transplantation. CONCLUSION: The study reveals a strong preference for public banking in all five countries, based on converging values such as solidarity. Attitudes of pregnant women are not an obstacle to the rapid expansion of allogeneic banking in these EU countries. Banking choices do not appear to be correlated with household income. The extent of commercial marketing of cord blood banks in mass media highlights the importance for obstetric providers to play a central role in raising women's awareness early during their pregnancy with evidence-based medical information about banking options.

Querol S, Gomez SG, Pagliuca A, Torrabadella M, Madrigal JA. Quality rather than quantity: the cord blood bank dilemma BONE MARROW TRANSPL Jun 45; 970-978, 2010. QUARTILE 2, DECILE 4, IMPACT FACTOR 3.4.

Martín-Henao GA, Resano PM, Villegas JM, Manero PP, Sánchez JM, Bosch MP, Codins AE, Bruguera MS, Infante LR, Oyarzabal AP, Soldevila RN, Caiz DC, Bosch LM, Barbeta EC, Ronda JR. Adverse reactions during transfusion of thawed haematopoietic progenitor cells from apheresis are closely related to the number of granulocyte cells in the leukapheresis product VOX SANG May 19; 2010. QUARTILE 2, DECILE 5, IMPACT FACTOR 2.75.

Romero-Pinel L, Pujal JM, Martínez-Yélamos S, Gubieras L, Matas E, Bau L, Torrabadella M, Azqueta C, Arbizu T. HLA-DRB1: genetic susceptibility and disability progression in a Spanish multiple sclerosis population EUR J NEUROL; 2010. QUARTILE 2, DECILE 4, IMPACT FACTOR 2.73.
BACKGROUND AND OBJECTIVE: The association of HLA-DRB1*15 with susceptibility to multiple sclerosis (MS) has been consistently reported although its effect on the clinical phenotype is still controversial. The objectives of this study are to investigate the influence of the HLA-DRB1 alleles on the genetic susceptibility to MS and to study their impact on disability progression in a Spanish population. METHODS: HLA-DRB1 typing was performed by PCR-SSP in 380 patients with sporadic MS and 1088 unrelated healthy controls. Allelic frequencies were compared between groups. We studied the correlation between the different alleles and the progression of MS. RESULTS: The HLA-DRB1*15 allele in patients with MS had a statistically significant higher frequency when compared with controls (18.9% in patients vs. 10.1% in controls, Odds ratio (OR) = 2.07, 95% CI = 1.64-2.60, P < 0.001). In the univariate analysis, the DRB1*01 and DRB1*04 alleles were associated with a worse prognosis when considering the time to reach an EDSS of 6, whereas the DRB1*03 was correlated with a better outcome. In the multivariate analysis, the alleles*01 and *04 were demonstrated to be independent factors to have a worse prognosis. CONCLUSIONS: HLA-DRB1*15 is associated with MS when comparing patients with unrelated healthy controls in a Spanish population. The HLA-DRB1*01 and HLA-DRB1*04 alleles are related to a worse prognosis when considering the time taken to reach severe disability.

Romero-Pinel L, Pujal JM, Martínez-Yélamos S, Gubieras L, Matas E, Bau L, Torrabadella M, Azqueta C, Arbizu T. Epistasis between HLA-DRB1 parental alleles in a Spanish cohort with multiple sclerosis J NEUROL SCI; 2010. QUARTILE 2, DECILE 5, IMPACT FACTOR 2.40.
BACKGROUND AND OBJECTIVE: Multiple sclerosis (MS) has been consistently associated with the HLA-DR2 haplotype and particularly with the HLA-DRB1*15 allele. Epistatic interactions between both parental alleles in the DRB1 loci have been shown to modify the MS susceptibility risk. This study investigated the frequencies of various HLA-DRB1

genotypes, their impact on MS susceptibility and their correlation with the clinical severity in a Spanish population. METHODS: A genotype was considered as the combination of the two parental DRB1 alleles. We compared the frequencies of the genotypes in a sporadic MS population (n = 380) with those of an unrelated healthy control cohort (n = 1088). We correlated the different genotypes with the age at onset, gender distribution, symptoms at onset, course of the disease and progression severity by means of the time to reach the progressive phase and EDSS scores of 3 and 6. RESULTS: We found 81 different genotypes. There were four different MS-predisposing genotypes. Three of them contained the DRB1*15 allele (DRB1*03/15, DRB1*04/15, and DRB1*08/15) and the fourth was homozygote for the DRB1*03 allele. The highest odds ratio was found with the genotype DRB1*08/15 (OR = 3.88, 95% CI = 1.83–8.26, p < 0.01), followed by DRB1*03/03 (OR = 3.15, 95% CI = 1.93–5.14, p < 0.01), DRB1*03/15 (OR = 2.72, 95% CI = 1.88–3.94, p < 0.01) and DRB1*04/15 (OR = 2.54, 95% CI = 1.64–3.98, p < 0.01). The DRB1*01/04 and the DRB1*15/15 genotypes were associated with a shorter time to reach an EDSS score of 6. CONCLUSIONS: Our results show the importance of epistatic interactions among the HLA-DRB1 alleles, modifying the risk for MS as well as its clinical severity. KEYWORDS: Multiple sclerosis; Genetics; HLA-DR; Genotypes; Epistasis; Susceptibility; Prognosis

Güell JL, Gris O, Manero F, Calatayud M, Torrabadella M, Morral M. Cornea, 3rd Edition, Chapter 146: Indications for and uses of Amniotic Membrane; 2010.

Martín-Henao G. Hematopoietic stem cells purging. Chapter 3.13. Hemopoietic Transplant Manual 2010, 4th edition

Martín-Henao G. Elimination of T cells of the inoculum. Chapter 3.14. Hemopoietic Transplant Manual 2010, 4th edition

Querol S, Torrabadella M. Collection and management of progentiors of umbilical cord blood. Chapter 3.10. Hemopoietic Transplant Manual 2010, 4th edition

2.1.3 Tissues line

The Tissue Bank is a division of the BST that is in charge of obtaining, processing and shipping tissues from living and dead donors. The bank's Unit for Research, Innovation and Development is based on the three main processes of the division:

A. Obtaining tissue for research: the tissue bank has an extraction team specialised in obtaining multiple tissues (ocular, cutaneous, osteo-tendinous and cardiovascular). They also obtain specific tissues for research groups as is the case of the diabetes group of the Vall d'Hebron Research Institute that has studied the neurodegeneration mechanisms of diabetes pathogenesis in the eyeballs of corneal tissue donors. Obtaining tissues from cadavers for research is always done with the knowledge and approval of the family, the purpose being to have a source of specific tissue to meet the needs of the study, according to the characteristics of the extracted tissue.

B. Processing: we collaborate with research teams to improve the final viability of our tissues and reduce, whenever possible, the deterioration that occurs between the moment of extraction and implant. Along these lines, we have developed a protocol in conjunction with Laboratorios Salvat to control the corneal endothelium and evaluate the possibility of reducing its mortality during the period of preservation prior to implant.

C. Implant professionals: the tissue bank actively participates in the research projects of tissue implant professionals attempting to develop new tissue formats and therapeutic products that better suit specific requirements, as is the case of platelet rich plasma (PRP) in tympanoplasties. We participate in the development of projects to validate the efficiency of some products such as PRP in osteoarticular disease.

PERSON IN CHARGE
Aurora Navarro Canturella

INVESTIGATORS

Luciano Rodríguez Gómez
Xavier Genís Planella

ONGOING RESEARCH PROJECTS

Principal investigator: Aurora Navarro Canturella

Evolution of corneal endothelium in hypothermia in the presence of anti-apoptotic agents.
Funding agency: Laboratorios Salvat S.A.
Duration: 2009 to 2010

Principal investigator: Daniel Pacha Vicente (Traumatology H Vall d'Hebron), Luciano Rodríguez Gómez (BST)

Randomized prospective clinical trial comparing the subacromial injection of platelet rich plasma with betamethasone and bupivacaine in the rotator cuff tendinopathy.
Funding agency: Carlos III Health Institute
File Nº: F08/00284
Duration: 2009 to 2011

Principal investigator: Maria Luisa Navarrete Alvaro (Otorhinolaryngology H Vall d'Hebron), Luciano Rodríguez Gómez (BST)

Pilot Study on the Efficiency of the Platelet Growth Products (PRP) in otologic surgery (tympanoplasty type I).
Duration: 2010 to 2011

PUBLICATIONS

Navarro A. Deceased Donors of Tissue Essentials of tissue banking; Essentials of tissue banking. Editorial Springer. 23-40, 2010

2.2 Area of research in diagnosis and biomarkers

PERSON IN CHARGE
Ricardo Pujol Borrell

2.2.1 Immunohematology line

The Immunohematology laboratory is a national and international reference in the diagnosis of immune cytopenia and the typing and characterisation of blood groups. The two ongoing research projects are in line with the objectives and areas of our professional activity in healthcare and teaching.

The project "Implementation and development of a new strategy for the prevention of foetal and neonatal alloimmune thrombocytopenia including a protocol of pre-implantation diagnosis", represents an important step forward along our line of diagnosis, prevention and treatment of neonatal alloimmune thrombocytopenia by making it possible to propose a therapeutic strategy that no other group in Spain can offer to couples suffering this problem. Far beyond the therapeutic benefits and social service this treatment provides, completion of the project and success in achieving its aims once again confirms us as one of the leading countries in the management of this complex complaint.

The project "Expression of low frequency erythrocyte antigens in erythroleukemia cells" forms part of the objective of seeking new techniques and strategies for typing blood groups and research into anti-erythrocyte antibodies that improve the sensitivity, and especially the specificity, of the techniques now being used. These techniques are based on the use of reactive red blood cells obtained from donors extensively typed for different erythrocyte antigens. Our proposal considers an alternative consisting of having a combination of cells each of which expresses a single erythrocyte antigen through transfection of cell lines that express an antigen variant of a particular erythrocyte protein. This system enables simplifying and clarifying the results obtained. Furthermore, in a second phase, a suitable support must be found for these cells so that they can be used as a routine test in all transfusion and immunohematology laboratories.

PERSON IN CHARGE
Eduardo Muñiz Diaz

INVESTIGATORS
Núria Nogués Galvez

Cecilia González Santesteban
Laia Freixa Puig

TECHNICAL STAFF
Marcel Tarrago Lamelas
Raquel Fores Aquilue

ONGOING RESEARCH PROJECTS
Principal investigator: Eduardo Muñiz Díaz
Implementation and development of a new strategy for the prevention of foetal and neonatal alloimmune thrombocytopenia including a protocol of pre-implantation diagnosis
Funding organisation: Carlos III Health Institute
File N°: PI070758
Duration: 2008 to 2010

Principal investigator: Núria Nogués Gálvez
PANAREC- Development of an alternative to the use of RBC panels for the detection of erythrocyte antibodies
Funding organisation: Spanish Ministry of Science and Innovation and Diagnòstic Grífols
File N°: TRA2009_0331
Duration: 2010 to 2012

PUBLICATIONS
Middelburg RA, van Stein D, Zupanska B, Uhrynowska M, Gajic O, Muñiz-Diaz E, Galvez NN, Silliman CC, Krusius T, Wallis JP, Vandenbroucke JP, Briët E, van der Bom JG. Female donors and transfusion-related acute lung injury TRANSFUSION May 28; 2010. QUARTILE 2, DECILE 4, IMPACT FACTOR 3.47

Reesink HW, Panzer S, Gonzalez CA, Lena N, Muntaabski P, Gimbatti S, Wood E, Lambermont M, Deneys V, Sondag D, Alport T, Towns D, Devine D, Turek P, Auvinen MK, Koski T, Lin CK, Lee CK, Tsoi WC, Lawlor E, Grazzini G, Piccinini V, Catalano L, Pupella S, Kato H, Takamoto S, Okazaki H, Hamaguchi I, Wiersum-Osselton JC, van Tilborgh AJ, Zijlker-Jansen PY, Mangundap KM, Schipperus MR, Dinesh D, Flanagan P, Flesland O, Steinsvåg CT, Espinosa A, Letowska M, Rosiek A, Antoniewicz-Papis J, Lachert E, Koh MB, Alcantara R, Corral Alonso M, Muñiz-Diaz E. Haemovigilance for the optimal use of blood products in the hospital VOX SANG ; 2010. QUARTILE 2, DECILE 5, IMPACT FACTOR 2.75

Barba P, Pallarés P, Nogués N, Canals C, Gracia M, Vinyets I, Muñiz-Diaz E. Post-transfusion purpura caused by anti-HPA-3a antibodies that are only detectable using whole platelets in the platelet immunofluorescence test TRANSFUSION MED 20; 200-202, 2010. QUARTILE 3, DECILE 7, IMPACT FACTOR 2.05

Novelli S, Canals C, Nogués N, Julià MR, Gracia M, Vinyets I, Muñiz-Diaz E. Severe neonatal alloimmune thrombocitopaenia with anaemia TRANSFUSION MED 20(2); 125-126, 2010. QUARTILE 3, DECILE 7, IMPACT FACTOR 2.05

2.2.2 Immunobiology line (LIRAD)

LIRAD research is centred on autoimmunity.
Basic lines:

A. Generation of new biomarkers in the field of autoimmunity (autoimmune thyroidopathy, diabetes, multiple sclerosis).

B. Design and testing of new (cell) therapies applied to multiple sclerosis and diabetes.

C. Clinical immunology.

The LIRAD brings together healthcare, teaching and research professionals in the area of immunology who are not only associated with the BST but also to the Germans Trias i Pujol Health Sciences Research Institute (IGTP), the Autonomous University of Barcelona (UAB), and the Vall d'Hebron University Hospital Vall d'Hebron Research Institute (VHIR). This diversity of environments all come together in LIRAD thus increasing and enriching the research possibilities.

Historically the problem being treated by LIRAD is autoimmunity, with studies being performed on two fronts: 1) Gain an understanding of the mechanisms leading to loss of tolerance (a phenomenon found at the origin of these diseases). 2) Improve knowledge of the immunopathological process underlying autoimmune diseases. Diabetes type 1, autoimmune thyroidopathy and multiple sclerosis have been the main focus point of the studies on autoimmune diseases.

In the last ten years two advances have taken place in the understanding and approach to these diseases:

1. On the one hand, and in part as a result of applying genomics and genetic mice models (transgenic), significant advances have taken place in understanding the control mechanisms (tolerance) of the autoimmune response whose failure leads to onset of the disease and associated damage to the effector mechanisms. Many of the mediators (like cytokines) and ways of control (through the use of transcriptome profiles, among other

methods) and even new lineages of immunological cells involved in these processes, have all been identified. LIRAD has participated in these advances as shown by the projects and publications related to chemokines and their polymorphisms, the transcriptomic analyses of human autoimmune diseases and their animal models, and the description of the new cell populations involved such as plasmacytoid dendritic cells (pDCs) and the use of animal models.

2. On the other hand, so-called immunomodulatory treatments have appeared either using monoclonal antibodies or cell therapies based on adoptive transfer of specific lymphocytes or dendritic cells. The use of these new treatments brings about a need to have better biomarkers to evaluate these new therapeutic approaches and this creates an opportunity for LIRAD to delve deeper into these aspects as it has prior knowledge of the technical methods and the relationship with basic groups and clinics. At present, one of the lines of research in LIRAD is the identification of biomarkers for the diagnosis and follow-up of these autoimmune diseases. In collaboration with the Advanced Therapies Division of the BST, LIRAD is developing pre-clinical projects and preparing clinical trials for the use of tolerogenic dendritic cells in multiple sclerosis and diabetes.
Apart from these two basic lines, there is a constant flow of collaboration projects with clinical groups of the hospitals that LIRAD supports, all of them enriching and combining with the two main lines described above and grouped under the clinical immunology section. These projects have resulted in outstanding publications (for example in *Science* magazine).

The association of LIRAD with the Department of Cell Biology, Physiology and Immunology of the UAB also contributes to generating collaboration projects, in this case more basic, especially in the study of the lymphocyte T physiology. These more basic projects make a significant contribution to the strength of the most prevalent lines.
The LIRAD HLA typing laboratory has made good use of its knowledge of new technologies for amplification of nucleic acids and contact with the other laboratory teams for the design of patented in-house typing protocols, especially in applications for the diagnosis of autoimmune diseases, and which are now about to be marketed. This example shows the capacity of the LIRAD to cover all aspects of this research, from the study of basic mechanisms and the generation of knowledge, to application of the results in the laboratory and their extension to a commercial application.

PERSON IN CHARGE
Ricardo Pujol Borrell

INVESTIGATORS
Eva Martínez Cáceres
Marta Vives Pi
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Mar Naranjo Gómez
Begoña Pérez Cabezas
Dalia Raich Regue
Maria Jose Herrero Matas
Patricia Bastos Amador
Raquel Planas Bas
Irma Pujol Autonell
Marta Ruiz Riol
Edurne Pedrosa Berrio
Paula Andrea Correa Vanegas
Estíbaliz Ruiz Ortiz de Arrizabaleta

ONGOING RESEARCH PROJECTS

Principal investigator: Ricardo Pujol Borrell

Physiopathology and Diagnosis of autoimmune diseases: thyroid, diabetes and multiple sclerosis, an approach inspired by systems biology.
Funding organisation: Carlos III Health Institute
File N°: PI08405
Duration: 2009 to 2011

Principal investigator: Ricardo Pujol Borrell

Consolidated immunology research group
Funding organisation: AGAUR
File N°: 2009 SGR 1442
Duration: 2009 to 2013

Principal Investigator: Ricardo Pujol Borrell

ENTIRE Definition and characterization of the "immunotype" of healthy individuals and IMID patients before, during and after targeted immunomodulation. Cost Program
Fundign organisation: COST- European Cooperation in the fiels of Scientific and Technical Research
Duration: 2010 to 2012

Principal investigator: Eva Martínez Cáceres

TOLERVIP-MS: Induction of tolerance in multiple sclerosis with dendritic cells treated with vasoactive intestinal peptide loaded with myelin peptides.
Funding organisation: Marató de TV3 Foundation
File N°: 07/2410
Duration: 2008 to 2010

Principal Investigator: Marta Vives Pi

Treatment of T1D by immunotherapy with dendritic cells and apoptotic bodies
Funding organisation: Carlos III Health Institute
File N°: PS09/00253
Duration: 2010 to 2012

Principal Investigator: Francesc Borràs Serres

Evaluation of exosomes obtained from biological fluids as alloantigens to induce tolerance un allogeneic transplantation
Fundign organisation: Carlos III Health Institute
File N°: PS09/00229
Duration: 2010 to 2012

Investigador principal: Francesc Borràs Serres

Study of extracellular microvesicles (exosomes) in human biological fluis (serum and urine) for the identification of non-invasive biomarkers
Funding organisation: BST
Duration: 2010 to 2012

Principal investigator: Jaume Coll Cantí (IGTP), Eva Martínez Cáceres (BST)

Paralysis of the critical patient: a clinical, electrophysiological, biochemical and pathological study.
Funding organisation: Marató de TV3 Foundation
File N°: 06/1510
Duration: 2007 to 2009

Principal investigator: Beatriz E Bayés Genís (IGTP), Ricardo Pujol Borrell (BST)
The role of autoimmunity in the development of post-renal transplant diabetes mellitus (PRTDM): humoral markers, genetics and regulatory T lymphocytes.
Funding organisation: Carlos III Health Institute
File N°: PI070349
Duration: 2008 to 2010

Principal investigator: Javier Martínez Picado (Fundació IrsiCaixa), Eduard Palou Rivera (BST)
CoRP. Viral and host factors contributing to rapid disease progression in HIV-1 infected individuals.
Funding organisation: iscIII, RETIC-RIS RD06/0006
Duration: 2009 to 2013

PUBLICATIONS

Ballana E, Senserrich J, Pauls E, Faner R, Mercader JM, Uyttebroeck F, Palou E, Mena MP, Grau E, Clotet B, Ruiz L, Telenti A, Ciuffi A, Esté JA. ZNRD1 (zinc ribbon domain-containing 1) is a host cellular factor that influences HIV-1 replication and disease progression CLIN INFECT DIS 50(7); 1022-1032, 2010. QUARTILE 1, DECILE 1, IMPACT FACTOR 8.26

Brckalo T, Calzetti F, Pérez-Cabezas B, Borràs FE, Cassatella MA, López-Botet M. Functional analysis of the CD300e receptor in human monocytes and myeloid dendritic cells EUR J IMMUNOL 40(3); 722-32, 2010. QUARTILE 1, DECILE 2, IMPACT FACTOR 4.86

Trallero-Araguás E, Labrador-Horrillo M, Selva-O'Callaghan A, Martínez MA, Martínez-Gómez X, Palou E, Rodriguez-Sanchez JL, Vilardell-Tarrés M. Cancer-associated myositis and anti-p155 autoantibody in a series of 85 patients with idiopathic inflammatory myopathy MEDICINE 89(1); 47-52, 2010. QUARTILE 1, DECILE 2, IMPACT FACTOR 4.33

Soldevila B, Alonso N, Martínez-Arconada MJ, Morillas RM, Planas R, Sanmartí AM, Martínez-Cáceres EM. A prospective study of T- and B-lymphocyte subpopulations, CD81 expression levels on B cells and regulatory CD4CD25CD127FoxP3 T cells in patients with chronic HCV infection during pegylated interferon-alpha2a plus ribavirin treatment. doi:10.1111/j.1365-2893.2010.01317.x. J VIRAL HEPATITIS May; 10, 2010. QUARTILE 1, DECILE 3, IMPACT FACTOR 3.32

Colobran R, Pedrosa E, Carretero-Iglesia L, Juan M. Copy number variation in chemokine superfamily: the complex scene of CCL3L-CCL4L genes in health and disease CLIN EXP IMMUNOL; Oct; 162 (1): 41-52, 2010. QUARTILE 2, DECILE 5, IMPACT FACTOR 2.85
Summary Genome copy number changes (copy number variations: CNVs) include inherited, de novo and somatically acquired deviations from a diploid state within a particular chromosomal segment. CNVs are frequent in higher eukaryotes and associated with a substantial portion of inherited and acquired risk for various human diseases. CNVs are distributed widely in the genomes of apparently healthy individuals and thus constitute significant amounts of population-based genomic variation. Human CNV loci are enriched for immune genes and one of the most striking examples of CNV in humans involves a genomic region containing the chemokine genes CCL3L and CCL4L. The CCL3L-CCL4L copy number variable region (CNVR) shows extensive architectural complexity, with smaller CNVs within the larger ones and with interindividual variation in breakpoints. Furthermore, the individual genes embedded in this CNVR account for an additional level of genetic and mRNA complexity: CCL4L1 and CCL4L2 have identical exonic sequences but produce a different pattern of mRNAs. CCL3L2 was considered previously as a CCL3L1 pseudogene, but is actually transcribed. Since 2005, CCL3L-CCL4L CNV has been associated extensively with various human immunodeficiency virus-related outcomes, but some recent studies called these associations into question. This

controversy may be due in part to the differences in alternative methods for quantifying gene copy number and differentiating the individual genes. This review summarizes and discusses the current knowledge about CCL3L-CCL4L CNV and points out that elucidating their complete phenotypic impact requires dissecting the combinatorial genomic complexity posed by various proportions of distinct CCL3L and CCL4L genes among individuals.

Planas R, Pujol-Borrell R, Vives-Pi M. Global gene expression changes in type 1 diabetes: Insights into autoimmune response in the target organ and in the periphery IMMUNOL LETT ; 2010. QUARTILE 2, DECILE 5, IMPACT FACTOR 2.85

Type 1 diabetes (T1D) is an autoimmune disease caused by the selective destruction of the insulin-producing beta cells. Research into the pathogenesis of T1D has been hindered by the lack of detection of the autoimmune process during the asymptomatic period and by the inaccessibility to the target tissue. Therefore current understanding of the immunological phenomena that take place in the pancreas of the patients is very limited and much of the current knowledge on T1D has been obtained using animal models. Microarray technology and bioinformatics allow the comparison of the gene expression profile - transcriptome - in normal and pathological conditions, creating a global picture of altered processes. Microarray experiments have defined new transcriptional alterations associated with several autoimmune diseases, and are focused on the identification of specific biomarkers. In this review we summarize current data on gene expression profiles in T1D from an immunological point of view. Reported transcriptome studies have been performed in T1D patients and Non-Obese Diabetic mouse models analyzing peripheral blood, lymphoid organs and pancreas/islets. In the periphery, the distinctive profiles are inflammatory pathways inducible by IL-1beta and IFNs that can help in the identification of new biomarkers. In the target organ, a remarkable finding is the overexpression of inflammatory and innate immune response genes and the active autoimmune response at longstanding stages, contrary to the pre-existing concept of acute autoimmune process in T1D.

Ortiz-Santamaria V, Olive A, Martinez-Caceres E, Coll M, Codina X, Suris X. Neonatal lupus erythematosus: a possible role for anti-Sm antibodies LUPUS 19(5); 659-661, 2010. QUARTILE 3, DECILE 6, IMPACT FACTOR 2.24

Alonso N, Granada ML, Soldevila B, Salinas I, Joaquin C, Reverter JL, Juncà J, Martínez Cáceres EM, Sanmartí A. Serum autoimmune gastritis markers, pepsinogen I and parietal cell antibodies, in pattients with type 1 diabetes mellitus: a 5-year prospective study J ENDOCRINOL INVEST; 2010. QUARTILE 4, DECILE 8, IMPACT FACTOR 1.88

BACKGROUND AND AIM: To determine the temporal evolution of serum markers of autoimmune gastritis, mainly pepsinogen I (PI) and parietal cell antibodies (PCA) in patients with type 1 diabetes mellitus (DM1). MATERIAL/SUBJECTS AND METHODS: A 5-year prospective follow-up study of 186 DM1 patients (93 men, aged 32.4+/-8.7 yrs) attending the endocrinology outpatient clinic of a university hospital evaluated in 2001, 168 of whom were re-evaluated in 2006. Serum PI, gastrin, haemoglobin, cobalamin concentrations, PCA and antibodies to intrinsic factor were measured. Results In 2001, 11 patients had low PI concentrations and positive PCA (group I), 11 had only low PI concentrations (group II) and 33 had only positive PCA (group III). After 5 years, PI remained low and PCA positive in all patients from group I. In group II, PI remained low in 4 and normalized in 7. In group III, 4 patients presented low PI concentrations after 5 years remaining normal in the other 29. PCA became negative in 17 patients from group III. In 2001, 3 of the 11 patients of group I had low cobalamin concentrations. In 2006, 2 additional patients from this group presented low cobalamin concentrations. CONCLUSIONS: These results show the importance of determining PI together with PCA, since the presence of abnormal results in both tests, that is low PI and positive PCA, is the association that best identifies patients with a higher risk to decrease cobalamin concentrations during follow-up.

Lucas A, Julián MT, Cantón A, Castell C, Casamitjana R, Martínez-Cáceres EM, Granada ML. Undiagnosed thyroid dysfunction, thyroid antibodies, and iodine excretion in a Mediterranean population ENDOCRINE 38(3); 391-396, 2010. QUARTILE 4, DECILE 8, IMPACT FACTOR 1.84

The prevalence of thyroid dysfunction varies in different populations. The aim of this cross-sectional study was to analyze the prevalence of undiagnosed thyroid dysfunction and thyroid antibodies and their relationship with urine iodine excretion in a representative sample of 1,124 (55.5% women; mean age: 44.8 ± 15.2 years) non-hospitalized Mediterranean adults, in Catalonia (Spain). Free thyroxine, thyroid-stimulating hormone, thyroperoxidase and thyroglobulin antibodies, and urine iodine were measured. Undiagnosed thyroid dysfunction was 5.3% (hypothyroidism 3.8%; 56.66% of these subjects were women). The total (diagnosed + undiagnosed) thyroid dysfunction was 8.9% (71.15% women). Thyroperoxidase antibodies were positive in 2.4% of men and 9.4% of women and thyroglobulin antibodies, in 1.3% of men and 3.8% of women. No differences were observed in urine iodine between groups with thyroid dysfunction and euthyroidism, or between subjects with positive or negative antibodies. In subjects over 60, undiagnosed thyroid dysfunction was 9.8% (hypothyroidism 6.9%, hyperthyroidism 3.3%; 36.36% women) and total thyroid dysfunction 13.61% (53.12% women). Women and men over 60 had similar thyroid dysfunction prevalence. Thus, aggressive case-finding should be recommended in both, over 60.

Balibrea del Castillo JM, Arias-Díaz J, García Martín MC, Vives-Pi M, García Pérez JC, Cantero Cid R, Vara Ameigeiras E, Balibrea Cantero JL. Cytoprotective effect of low-dose tacrolimus on islets of Langerhans in cultures subjected to stimulation by acute rejection cytokines CIRUGIA ESPAÑOLA 87(6); 372-377, 2010

INTRODUCTION: The improvement in pancreatic islet transplantation results is due to immunosuppression protocols that include, among others, low-dose tacrolimus. Both anti-inflammatory and anti-oxidant effects of tacrolimus could be useful in preventing primary rejection. AIM: To evaluate in vitro islet low-dose tacrolimus response after pro-inflammatory stimulation. MATERIAL AND METHODS: Isolated rat islets were cultured in RPMI medium in the presence of IL-1 (50 UI/mL) plus IF-gamma (1000 UI/mL) and tacrolimus (5 ng/mL). The 24 h production of lipoperoxide (LPO) and nitric oxide (NO) were measured as oxidative stress markers. Determination of apoptosis markers (nucleosome content and Bcl-2) was also performed. RESULTS: Oxidative stress (LPO 10.1+/-1.16 pmol/islet x 24; NO 19.1+/-3.28 pmol/isletx24 h) and apoptosis (nucleosome 0.24+/-0.04 UI/islet; Bcl-2 0.69+/-0.212 UI/islet) markers showed a very significant increase after cytokine stimulation ($p<0.01$). Both effects improved by adding tacrolimus to the medium. Protective effect was complete when lipoperoxide (1.58 pmol/isletx24 h), nitric oxide (9.81 pmol/isletx24 h) and Bcl-2 (1.37+/-0.23 UI/islet) were determined. CONCLUSION: In vitro cytoprotective effect of low-dose tacrolimus on isolated rat islets decreases both oxidative stress and apoptosis markers after stimulation of pro-inflammatory mediators.

Grau-López L, Sierra S, Martínez-Cáceres E, Ramo-Tello C. Analysis of the pain in multiple sclerosis patients NEUROLOGIA Dec 16; 2010

INTRODUCTION: Despite pain being a disabling symptom in patients with multiple sclerosis (MS), its prevalence and characteristics are not well established. The aim of this study is to describe the characteristics and prevalence of pain in patients with MS, and to assess the associated clinical variables and radiological findings. METHODS: We prospectively studied patients with MS. A structured questionnaire which evaluated depression symptoms, type of pain, location, intensity (defined according to a visual analogue scale (VAS) as severe (VAS 7-10), moderate (VAS 4-6) and mild (VAS 0-4), and pain therapy was recorded in patients who referred to pain at the time of interview. Protocol variables were demographic data, MS clinical forms (remitting-relapsing, progressive-secondary and progressive-primary), neurological dysfunction (defined according to EDSS scale), symptoms at onset, attack frequency, illness duration, disease

modifying treatment, fatigue, spasticity, oligoclonal bands in CSF, visual evoked potentials, depression symptoms (Hamilton test) and presence of lesions in spinal cord MRI. RESULTS: A total of 134 MS patients were included, and MRI was performed on 105 of them. Pain was reported by 74 (55%) patients and was most frequently neuropathic, located in limbs, severe and burning/spiky. Of these 28 (38%) received therapy for their pain, based predominantly in anti-inflammatory drugs. Patients with pain had a worse functional state (EDSS score, 4.5 [3-6] vs 1.5 [1-2], p<0.001), higher number of relapses (7.13±3.4 vs 3.75±2.9, p<0.001), progressive forms of MS (86.7% vs 13.3%, p<0.001), depression (91.9% vs 8.1%, p<0.001), spinal cord involvement at onset (79.2% vs 20.8%, p=0.009), spinal cord lesions by MRI (84.3% vs 15.7%, p<0.001) and longer duration of disease (14.6±7.8 vs 8.43±5.9 months, p<0.001). In a logistic regression model, the presence of lesions in spinal cord MRI (OR 3.5 [1.5-24.5]) and higher EDSS score (OR 1.7 [1.1-2.7]) were independently associated with pain. CONCLUSIONS: Pain is a frequent disabling symptom in MS and is associated with disability and spinal cord lesions.

Herrero MJ. ABC of the Toll-like receptors: relationship with the development and progression of autoimmune diseases SEMINARS OF THE SPANISH FOUNDATION OF RHEUMATOLOGY 11(4); 135-143, 2010

The Toll-like receptor family is an important group of pattern-recognition receptors whose ligands include a wide range of molecules with strong adjuvant activity (such as lipopolysaccharide, lipopeptides and bacterial DNA). These ligands can activate dendritic cells, macrophages and other antigen presenting cells that allow the effective presentation of microbial antigens to cells of the adaptative immune system. Nowadays, the identification and characterization of endogenous ligands for these receptors has provided a novel perspective for examining the etiology of some autoimmune diseases. Instead of being considered as an aberrant response to host antigens by the adaptive immune system, autoimmunity can be viewed as arising from a response to exogenous or endogenous ligands by the innate immune system, at least in some cases. This review summarizes recently published data that indicate an important connection between DNA- and RNA-containining immune complexes, activation of Toll-like receptors, production of type I interferons (INF- α, INF-β) and the development of some systemic autoimmune diseases.

Izquierdo-Useros N, Naranjo-Gómez M, Erkizia I, Puertas MC, Borrás FE, Blanco J, Martinez-Picado J. HIV and mature dendritic cells: Trojan exosomes riding the Trojan horse? PLOS PATHOG 6(3); e1000740, 2010

vanZyl B, Planas R, Ye Y, Foulis A, de Krijger R, Vives-Pi M, Gillespie K. Why are levels of maternal microchimerism higher in type 1 diabetes pancreas? CHIMERISM 1 (2); 1-6, 2010

Maternal microchimerism (MMc) results from transfer of maternal cells to the fetus in pregnancy. These cells have been shown to persist into adulthood in healthy individuals and an increased frequency of MMc has been associated with autoimmune disease. Female (presumed maternal) islet beta cells have recently been identified at higher levels in pancreas from a child with T1D compared to three controls. There was, however, no evidence that these cells were the targets of autoimmune attack. The aim of this study was to analyze well-characterized T1D pancreases encompassing a spectrum in age at diagnosis, and duration of diabetes, for the presence of maternal microchimerism compared to control pancreases.
Pancreas samples were available from six males with T1D and four male controls. Fluorescent-labeled probes were used to detect X and Y chromosomes. At least 1,000 cells, usually 4,000–8,000 cells underwent confocal imaging for each pancreas. The frequency of MMc was higher in T1D pancreases (range 0.31–0.80%, mean 0.58%) than in controls (0.24–0.50%, mean 0.38%) (p = 0.05). Intriguingly, clusters of 2–3 MMc were occasionally found in the pancreases, particularly T1D pancreases, suggesting replication of these cells. Concomitant FISH and immunofluorescence staining for insulin

or CD45 was performed to phenotype cells of maternal origin. Insulin positive and insulin negative MMc were identified indicating that MMc contribute to the exocrine and endocrine compartments. No CD45 positive MMc were observed. These data confirm the presence of maternal cells in human pancreas and support previous observations that levels of MMc are higher in T1D pancreas compared to controls. MMc do not appear to be immune effector cells and those that stain positive for insulin within intact islets in T1D tissue appear healthy with no evidence that they are the focus of immune attack. This study adds support to the hypothesis that maternal stem cells have the capacity to cross the placental barrier and differentiate into both endocrine and exocrine cells but more detailed characterization of MMc in the pancreas is required.

Vives-Pi M, Sabater L. Stiff person syndrome and cerebellar ataxia associated with glutamic acid decarboxylase antibodies and type 1 diabetes: What is the link between neurological diseases and autoimmunity to the beta cell? INMUNOLOGIA 29(4); 119-124, 2010

Stiff person syndrome is a rare CNS disorder characterized by progressive muscular rigidity (trunk muscles), with superimposed spasms. High titres of antibodies to glutamic acid decarboxylase (GAD-Ab) are present in more than 70 % of patients. Adult-onset cerebellar ataxia (CA) is the second most frequent disease associated with high titers of GAD-Ab, and characterized by an almost isolated cerebellar syndrome. Both syndromes are frequently associated with autoimmune type 1 diabetes (T1D). The immunogenetic basis of SPS is supported by the DQB1*0201 allele, a susceptibility allele for T1D. Several T1D autoantigens are related to proteins of the nervous system. The concordance of both neurological diseases with T1D and the presence of anti-GAD antibodies suggest a common aetiology.

2.2.3 Coagulopathy line

The line of research into congenital coagulopathies of the Banc de Sang i Teixits has had a dual character since its foundation in 1998: support for the diagnosis of congenital coagulation disorders and other hereditary diseases; and the investigation and development of new perspectives in the diagnosis and therapeutic field. A large part of the current objectives is innovation of technological tools and their transfer into laboratory routine.

The main lines are centred on the study of hereditary diseases or blood defects of enormous clinical, economic and social relevance such as haemophilia or von Willebrand's

disease, as well as other aspects derived from these, and other, coagulopathies. In detail, the research objectives of the unit can be described as:

A. Identification of the mutations responsible for haemophilia A and B in the Spanish population.

B. Applications to therapeutic orientation, genetic advice, prenatal and pre-implantation diagnosis.

C. Molecular diagnosis of von Willebrand's disease: study of genotype-phenotype relationship and their application to clinical diagnosis.

D. Establishment of protocols and the genetic study of rare monogenic bleeding disorders: FXI deficit, FXIII deficit, combined FV and FVIII deficit, FVII deficit, Glanzmann's thrombasthenia, etc…

E. Examination of alternatives for the recombinant human factor VIII expression using new expression systems in yeast.

F. In-depth studies of the molecular events found in some affected individuals and the genotype-phenotype relationship constituting the most basic area of the team's objectives.

G. Clinical epidemiological studies aimed at the exhaustive identification of the clinical characteristics of patients with congenital coagulopathies and their response to different therapeutic options. These studies often entail the creation of different types of registers.

It is important to emphasise that epidemiological studies are reflected on the Hemobase web site (http://www.hemobase.com), dedicated to haemophilia and von Willebrand's disease. It includes the first register of characterised mutations of haemophilia patients in the Spanish population. It is a dynamic register with permanent updates. It includes general information on haemophilia, its classification, clinical characteristics and diagnosis difficulties, as well as the biochemical and molecular characteristics of the genes. Hemobase is recognised by the NCBI and Orphanet as a specific database of mutations of the FVIII, FIX and VWF loci.

The research activity is associated with the commitment of the Haemophilia Unit of Vall d'Hebron Hospital (reference centre for congenital coagulopathies in Catalonia) to the development of molecular protocols, applicable genetic advice and prenatal diagnosis. The Haemophilia Unit offers specialised healthcare to patients with hemorrhagic congenital coagulopathies such as haemophilia, von Willebrand's disease, thrombopathies and other coagulation factor deficits. Congenital coagulopathies, and especially haemophilia, are rare complex diseases. Achieving effective treatment requires a program of integral therapy. The Haemophilia Unit has an experienced multidisciplinary team that develops integral patient care, carries out daily healthcare control through clinical sessions, and has become a reference centre for congenital coagulopathies on a national and international level. Equally outstanding is the participation of the unit in numerous international multicentre studies (ITI, RODIN, HIGS and EUHASS).

PERSON IN CHARGE
Rafael Parra López

INVESTIGATORS
Francisco Vidal Pérez
Irene Corrales Insa

Júlia Ayats Blanch
Lluis Martorell Cedrés

TECHNICAL STAFF
Lorena Ramírez Orihuela
Sofia Alonso Mateos

ONGOING RESEARCH PROJECTS
Principal investigator: Rafael Parra López
Post-authorisation safety surveillance study of patients who have changed from ReFacto or other factor VIII products to ReFacto AF in the context of normal medical care.
Funding organisation: Wyeth Farma, S.A.
Duration: 2009 to 2011

Principal investigator: Rafael Parra López
Catalan coagulopathy register
Funding organisation: Catalan Health Service
Duration: 2008 to 2010

Principal investigator: Francisco Vidal Pérez
Application of optimised technologies to the molecular diagnosis of von Willebrand's disease: analysis of genetic heterogeneity.
Funding organisation: Carlos III Health Institute
File N°: PI080385
Duration: 2009 to 2011

Principal investigator: Francisco Vidal Pérez
Exploration of alternatives for the heterologous expression of human recombinant factor VIII using new expression systems in yeast.
Funding organisation: Química Farmacéutica Bayer, S.L.
Duration: 2007 to 2011

PUBLICATIONS
Corrales I, Ramirez L, Ayats J, Altisent C, Parra R, Vidal F. Integration of molecular and clinical data of 40 unrelated VWD families in a Spanish locus-specific mutation database. First release including 58 mutations HAEMATOL-HEMATOL J 95(11); 1982-1984, 2010. QUARTILE 1, DECILE 2, IMPACT FACTOR 5.97
Von Willebrand disease (VWD) is the most common congenital coagulopathy in humans. Nonetheless, the great complexity of the von Willebrand factor (VWF) gene has hindered routine molecular diagnosis. We designed and developed a technique based on complete VWF sequencing that has led to continuous identification of putative VWD mutations. To compile and update the molecular data produced, a new online publicly accessible VWF mutation registry (http://www.vwf.hemobase.com) was designed. In this first release of the database, 93 individuals from 40 unrelated families are included. Among the 58 mutations identified, 19 were first described by our group and are distributed over the entire gene. It is also provided additional data, such as coagulation parameters, STR tracking and pedigree representation of mutation and disease inheritance. This online registry will contribute to a better understanding of the mechanisms involved in the pathophysiology and provide a dynamical view of the molecular epidemiology of VWD in our population.

Ramírez L, Altisent C, Parra R, Vidal F. The "Royal Disease" Mutation in a Spanish Patient J THROMB HAEMOST 8; 2316-7, 2010. QUARTILE 1, DECILE 2, IMPACT FACTOR 6.29

Vidal F. Capítol 2: Diagnose of hemophilia carrier. In Hemophilia carriers. What need to know? Barcelona: Catalan Association of Hemophilia; 11-20, 2010

2.3 Area of research in blood technology and transfusion medicine

PERSON IN CHARGE
Lluís Puig Rovira

2.3.1 Blood transmitted diseases line (LST)

The Transfusion Safety Laboratory (LST) is comprised of the Healthcare Unit for Validation of Blood and other Components, and the R&D&I Unit for transmissible agents. The R&D&I activity of the LST can be classified in the following main lines:

A. Viral hepatitis and co-infection with HIV.

B. Epidemiological research and development of new tools for the detection of emerging infectious agents (Chagas disease, HTLV-I/II, Chikungunya virus, malaria, XMRV).

The final end-point of these lines is to improve physiopathological and epidemiological knowledge and the detection of infectious agents relevant to the safety of blood products, cord blood and tissues.

It is also important to highlight the activity undertaken to improve knowledge of the presence of pathogens coming from other countries among the BST Catalan reference population. The objectives of studies performed along these lines is to plan and establish strategies to guarantee the safety of blood products based on the correct selection of blood donors and the application of diagnostic tests. It must be born in mind that the BST is the only centre that distributes blood products in Catalonia and is directly responsible for maintaining and promoting research along these lines.

PERSON IN CHARGE
Sílvia Sauleda Oliveras

INVESTIGATORS
Natàlia Casamitjana Ponces
Maria Piron
Marta Bes Maijo

TECHNICAL STAFF

Angeles Rico Blázquez
Anna Oliveira Tercero

ONGOING RESEARCH PROJECTS

Principal investigator: Sílvia Sauleda Oliveras

Serological, immunological and molecular characterisation of blood donors with occult infection by hepatitis B virus.
Funding organisation: Carlos III Health Institute
File N°: PI070754
Duration: 2008 to 2010

Principal investigator: Sílvia Sauleda Oliveras

Botia - Improving the safety of blood and organ supply by creating the research infrastructure to monitor emerging pathogens and develop new screening tests.
Funding organisation: European Commission
File N°: SP23-CT-2006-006487
Duration: 2006 to 2010

Principal investigator: Sílvia Sauleda Oliveras

Pilot study of malaria markers in high-risk blood donors.
Funding organisation: BST
Duration: 2006 to 2010

Principal Investigator: Sílvia Sauleda Oliveras

Study of the retrovirus XMRV prevalence in blood donors and patients with chronic fatigue
Funding organisation: BST
Duration: 2010 to 2011

Principal Investigator: Maria Piron

Evaluation of sensitivity and specificity of the Chagas ARCHITECT reagent for screening of anti-Trypanosoma cruzi antibodies in blood donors
Funding organisation: Abbot científica
Duration: 2010 to 2011

Principal Investigator: Maria Piron

Development of a technique for the detection of West Nile Virus by real time PCR and field study to determine the seroprevalence of West Nile Virus in Catalonia
Funding organisation: BST
Duration: 2010 to 2012

Principal investigator: Maria Piron

Development of real time protocols for PCRs (Dengue, Chikungunya, HTLV-I, HTLV-II, etc) as screening tools or supplementary analyses of emerging infectious pathogens and a field study of emerging pathogens in high-risk travellers and immigrant donors.
Funding organisation: BST
Duration: 2009 to 2012

PUBLICATIONS

Buti M, Homs M, Rodriguez-Frias F, Funalleras G, Jardi R, Sauleda S, Tabernero D, Schaper M, Esteban R. Clinical outcome of acute and Chronic Hepatitis Delta: A long term follow-up study J VIRAL HEPATITIS Jun 08, 2010. QUARTILE 1, DECILE 3, IMPACT FACTOR 3.33

Devine DV, Sher GD, Reesink HW, Panzer S, Hetzel PA, Wong JK, Horvath M, Leitner GC, Schennach H, Nussbaumer W, Genoe K, Cioffi JM, Givisiez FN, Rogerson M, Howe D, Delage G, Sarappa C, Charbonneau, Fu Y, Sarlija D, Vuk T, Strauss Patko M, Balija M,

Jukić I, Ali A, Auvinen MK, Jaakonsalo E, Cazenave JP, Waller C, Kientz D, David B, Walther-Wenke G, Heiden M, Lin CK, Tsoi WC, Lee CK, Barotine-Toth K, Sawant RB, Murphy W, Quirke B, Bowler P, Shinar E, Yahalom V, Aprili G, Piccoli P, Gandini G, Tadokaro K, Nadarajan VS, de Kort W, Jansen N, Flanagan P, Forsberg PO, Hervig T, Letowska M, Lachert E, Dudziak K, Antoniewicz-Papis J, de Olim G, Nascimento F, Hindawi S, Teo D, Reddy R, Scholtz J, Swanevelder R, Rovira LP, Sauleda S, Carasa MA, Vaquero MP, Ania MA, Gulliksson H, Holdsworth S, Cotton S, Howell C, Baldwin C, Cusick RM, Geele GA, Paden C, McEvoy P, Gottschall JL, McLaughlin LS, Benjamin RJ, Eder A, Draper NL, AuBuchon JP, León de González G. Inventory management VOX SANG 98(3 Pt 1); e295-363, 2010. QUARTILE 2, DECILE 5, IMPACT FACTOR 2.75

Reesink HW, Panzer S, Wendel S, Levi JE, Ullum H, Ekblom-Kullberg S, Seifried E, Schmidt M, Shinar E, Prati D, Berzuini A, Ghosh S, Flesland Ø, Jeansson S, Zhiburt E, Piron M, Sauleda S, Ekermo B, Eglin R, Kitchen A, Dodd RY, Leiby DA, Katz LM, Kleinman S. The use of malaria antibody tests in the prevention of transfusion-transmitted malaria VOX SANG 98(3 Pt 2); 468-478, 2010. QUARTILE 2, DECILE 5, IMPACT FACTOR 2.75

2.3.2 Blood donation and use of blood products line

This area includes projects whose purpose is to improve blood donation, the production of blood components, and their use in transfusions and other applications.

PERSON IN CHARGE
Lluis Puig Rovira

INVESTIGATORS
Pilar Ortiz Murillo
Joan Ramon Grífols Ronda
Alba Bosch Llobet
Lluís Massuet Bosch

ONGOING PROJECTS:

Principal Investigator: Lluís Puig Rovira
Randomized, controlled, parallel clinical trial to asses the efficacy of an allogenic fibrin sealant in the treatment of wounds secondary to laminectomy of degenerative etiology
Funding organisation: BST
Duration: 2010 to 2011

Principal Investigator: Lluís Massuet Bosch
Double filtration plasmapheresis in patients with chronic hepatitis C with genotype 1 and high viral load
Funding organisation: Asahi Kaseu Kuraray Medical Company Ltd.
File N°: AM-HC-SP-2008
Duration: 2009 to 2011

Principal investigator: Lluís Orozco Delclos (Teknon), Alba Bosch Llobet (BST)
Randomised, multicentre, controlled, parallel, double blind clinical trial to assess the efficiency of autologous platelet-rich plasma in the treatment of "tennis leg" muscle sprains.
Funding agency: Carlos III Health Institute

File N°: P08/0724
Duration: 2009 to 2011

Principal investigator: Joan Francesc Julián Ibánez (IGTP), Joan Ramon Grífols Ronda (BST)
Evaluation of volumetric reconstruction using platelet gel from healthy donors in the conservative treatment of breast cancer.
Funding agency: ACC10
File N°: VALTEC09-2-0098
Duration: 2009 to 2011

PUBLICATIONS

Bosch MA, Contreras E, Madoz P, Ortiz P, Pereira A, Pujol MM. The epidemiology of blood component transfusion in Catalonia, Northeastern Spain TRANSFUSION; 2010. QUARTILE 2, DECILE 4, IMPACT FACTOR 3.47

BACKGROUND: Epidemiologic information on blood component usage can help improve the utilization of transfusion resources. STUDY DESIGN AND METHODS: Crosssectional survey in 2007 that included every hospital in Catalonia. Clinical data of blood recipients, including the four-digit International Classification of Diseases, 9th Revision, Clinical Modification codes and the indication for transfusion, were prospectively collected according to an established protocol. RESULTS: In total, 19,148 red blood cell (RBC) units, 1812 platelet (PLT) doses, and 3070 plasma units, transfused into 8019 patients (median age, 71 years; 52% males), were surveyed. Half the RBC units were used by patients older than 70 years. Specific diagnosis and procedures with the highest RBC use were lower limb orthopedic surgery (10.6% of all units) and gastrointestinal hemorrhage (6%). Therapeutic plasmapheresis (8.1%) and heart valve surgery (7.2%) were the procedures with the highest plasma use. Oncohematology patients accounted for 73% of transfused PLTs, more that two-thirds being administered for hemorrhage prophylaxis. Acute hemorrhage was the most common indication for RBC and plasma transfusion. Among all blood recipients, 80% received only RBCs and 6.9% received only plasma and/or PLTs, without concomitant RBCs. The population transfusion incidence rates were 35 RBC units, three PLT doses, and 6 plasma units per 1000 population-year. Demographic changes anticipate a 30% increase in RBC transfusion by year 2030. CONCLUSIONS: These results allow for identification of blood uses that are susceptible to improvement, help appraise the expected yield of blood safety measures, and will assist in planning the future blood supply.

Reesink HW, Panzer S, McQuilten ZK, Wood EM, Marks DC, Wendel S, Trigo F, Biagini S, Olyntho S, Devine DV, Mumford I, Cazenave JP, Rasonglès P, Garraud O, Richard P, Schooneman F, Vezon G, Al Radwan R, Brand A, Hervig T, Castro E, Lozano M, Navarro L, Puig L, Almazán C, MacLennan S, Cardigan R, Franklin IM, Prowse C. Pathogen inactivation of platelet concentrates VOX SANG 99; 86-95, 2010. QUARTILE 2, DECILE 5, IMPACT FACTOR 2.75

Pérez A, Sancho JM, Grífols JR, Ribera JM. Response to rituximab in two patients with plasma exchange-refractory thrombotic thrombocytopenic purpura. MED CLIN BARC Nov 10, 2010. QUARTILE 3, DECILE 6, IMPACT FACTOR 1.26

Bosch A. A critical analysis of who and when we trasfuse REV MEX MED TRAN 3 (1); 22-29, 2010

The knowledge of where and when the transfusion goes (Transfusion epidemiology) is necessary to identify the key factors involved in the demand and predicting the future trends of use of blood components. In Catalonia, a 7 million inhabitant North-East Region of Spain, the use of blood transfusion will probably increase in the next years because of the population aging and the increment tendency in the blood components use ratio for inhabitant/year. Blood Transfusion Centres and Hospital Transfusion Services must work together in order to achieve an optimal and sustainable use of blood.

Massuet L. Supportive treatment. II transfusion of blood cell elements. Practical manual of Pediatric Hematology and Oncology. Ed. Ergon, Sanchez de Toledo, j. Ortega JJ. 2010