



Project no.
518167
Project acronym
INNOCHEM

Project title
**Innovative Chemokine-based Therapeutic Strategies for Autoimmunity and
Chronic Inflammation**

Instrument: **Integrated Project**

Thematic Priority: **LSH-2004-1.2.4-2**

Title of report

Final report

Period covered: **November 1st 2005- October 31st 2010**

Date of preparation: **15th December 2010**

Start date of project: **November 1st 2005**

Duration: 60 months

Project coordinator name: **Alberto Mantovani**

Project coordinator organisation name: **Humànitás Mirasole SpA**

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1. Project execution

1.1 Summary of project objectives

The general objective of INNOCHEM was to develop innovative chemokine-based therapeutic strategies for autoimmunity and chronic inflammation. The programme was based on the scientific excellence of the applicants, which have made major recognized contributions to the field since the very beginning of chemokine discovery, and on the construction of shared technological platforms. This included: **i)** proteomics and **ii)** transcriptional profiling for the outline of the "chemokinome" in pathophysiological conditions and identification of new antagonists; **iii)** molecular modelling of agonist/antagonist receptor or agonist/inhibitor interaction, for pharmacology and drug design; **iv)** gene modified mice for target validation in autoimmune disorders. Genetic, structural, biological, and immunopathological studies provide a framework for the development of innovative chemokine-based therapeutic strategies. The therapeutic approaches investigated were innovative and not limited to conventional antagonists. These included decoy receptors, agonist binders, and non-competitive allosteric inhibitors. In addition to academic groups, therapy-oriented research included 3 biotech SMEs, 1 medium and 1 big Pharma companies. The companies involved developed complementary non-overlapping approaches to target the chemokine system with recombinant and low molecular weight molecules. This programme has re-established the European leadership in basic and applied chemokine research by integrating academic and industrial cutting edge groups to develop innovative therapeutic strategies against autoimmunity and chronic inflammatory disorders.

1.2 Contractors involved

Participant Role	Participant Number	Participant name	Participant short name	Country	Date enter project	Date exit project
CO	1	HUMÀNITAS MIRASOLE SPA, <i>Milano</i>	HUMANITAS	<i>Italy</i>	Month 1	Month 60
CR	2	Istituto di Ricerca in Biomedicina, <i>Bellinzona</i>	IRB	<i>Switzerland</i>	Month 1	Month 60
CR	3	Université Pierre et Marie Curie-Paris VI, INSERM U543, <i>Paris</i>	UPMC	<i>France</i>	Month 1	Month 60
CR	4	INSERM U131: Cytokines et Immunorégulation, <i>Paris</i>	INSERM U131	<i>France</i>	Month 1	Month 60
CR	5	Uniwersytet Medyczny w Łodzi, Department of Neurology, <i>Lodz</i>	MUL	<i>Poland</i>	Month 1	Month 60
CR	6	Max-Delbrueck- Centrum für Molekulare Medizin, <i>Berlin</i>	MDC	<i>Germany</i>	Month 1	Month 60
CR	7	Centro Nacional de Biotechnologia, CSIC, <i>Madrid</i>	CSIC	<i>Spain</i>	Month 1	Month 60
CR	8	Universität Bern, Institute of Cell Biology, <i>Bern</i>	UBERN	<i>Switzerland</i>	Month 1	Month 14
CR	9	Ludwig-Maximilians- University München, <i>München</i>	LMU	<i>Germany</i>	Month 1	Month 60
CR	10	Université Libre de Bruxelles, IRIBHM,	ULB	<i>Belgium</i>	Month 1	Month 60

		<i>Brussels</i>				
CR	11	King's College London, <i>London</i>	KCL	<i>UK</i>	Month 1	Month 17
CR	12	Università degli Studi di Firenze, "MCIDNENT", <i>Firenze</i>	UNIFI	<i>Italy</i>	Month 1	Month 60
CR	13	University of Copenhagen, The Panum Institute, Dpt. of Pharmacology, <i>Copenhagen</i>	MOLPHARM	<i>Denmark</i>	Month 1	Month 60
CR	14	Rega Institute for Medical Research, <i>Leuven</i>	KUL	<i>Belgium</i>	Month 1	Month 60
CR	15	Imperial College of Science, Technology and Medicine, <i>London</i>	ICS	<i>UK</i>	Month 1	Month 60
CR	16	BioKine Therapeutics Ltd., <i>Rehovot</i>	BKT	<i>Israel</i>	Month 1	Month 60
CR	17	BioXell SpA., <i>Milano</i>	BXL	<i>Italy</i>	Month 1	Month 46
CR	18	Dompe' R&D – Dompe' SpA, <i>L'Aquila</i>	Dompe'	<i>Italy</i>	Month 1	Month 2
CR	19	Polyphor Ltd.- PEMB Unit, <i>Zürich</i>	Polyphor	<i>Switzerland</i>	Month 1	Month 60
CR	20	Novartis Institutes for Biomedical Research, <i>Wien</i>	NIBR	<i>Austria</i>	Month 1	Month 24
CR	21	Merck Serono, <i>Genève</i>	MSSA	<i>Switzerland</i>	Month 1	Month 60
CR	22	ALTA S.r.l., <i>Siena</i>	ALTA	<i>Italy</i>	Month 1	Month 60
CR	23	Dompe pha.r.ma Spa, <i>L'Aquila</i>	Dompe'	<i>Italy</i>	Month 3	Month 47
CR	24	Universiade Federal de Minas Gerais	UFMG	<i>Brazil</i>	Month 15	Month 60
CR	25	Cardiff University	CU	<i>UK</i>	Month 15	Month 60
CR	26	University of Glasgow	UG	<i>UK</i>	Month 15	Month 60
CR	27	Queen Mary & Westfield College, University of London	QMW	<i>UK</i>	Month 18	Month 60
CR	28	Aziende chimiche riunite Agelini Francesco ACRAF SpA	ANGELINI	<i>Italy</i>	Month 39	Month 60
CR	29	NovImmune S.A.	NovImmune	<i>Switzerland</i>	Month 39	Month 60
CR	30	Dompé SpA	Dompé	<i>Italy</i>	Month 48	Month 60

1.3 Work performed and end results (elaborating on the degree to which the objectives were reached; describing the methodologies and approaches employed and relating the achievements of the project to the state-of-the-art)

The INNOCHEM consortium has coordinated most of the research activities on chemokines performed in Europe in the last 5 years, a pivotal role recognized internationally. INNOCHEM has significantly strengthened integration and collaboration among partners of the Consortium and their visibility and recognition outside the Consortium, as certified by the many collaborations established and by the many INNOCHEM fellowships dedicated to exchanges of young

scientists among the Consortium laboratories and with laboratories working on chemokines outside the Consortium, both in the EU and in the USA. The results obtained have been published in high impact peer-reviewed journals, and have significantly contributed in the improvement of our understanding of the chemokine system, as recognised by the scientific community. In particular, the Consortium has strengthened the European leadership in several fields of fundamental research on chemokines, including structure/function activities of chemokines and chemokine-binding proteins, chemokine decoy receptors, pharmacology of chemokines and chemokine receptor antagonists. The Consortium has also performed remarkably well in translating fundamental knowledge, through a number of studies in several preclinical models. New and original strategies to interfere with the chemokine system have been developed, including in particular the identification and structural characterization of natural compounds and the identification and development of the new class of synthetic compounds represented by non-competitive allosteric inhibitors. Finally, the Consortium has also played a major role in translating in the clinical setting, with the definition of pharmacodynamic profiles on two anti-chemokine antibodies, a phase I clinical trial started in 2009, and a phase II placebo-controlled clinical trial concluded in 2010.

1.4 Potential applications

The INNOCHEM goal was to develop innovative chemokine inhibitors as a novel therapeutic approach for the treatment of autoimmune and chronic inflammatory diseases. Development of innovative therapeutic strategies requires definition of pathophysiological significance and target validation, and for this reason INNOCHEM has strongly supported studies of several fundamental aspects of the chemokine system, which have indeed opened new avenues for the development of innovative approaches beyond conventional receptor antagonists. INNOCHEM has identified endogenous mechanisms controlling the chemokine system, including most of the evidence of biological relevance of post-translational modifications, agonist cooperation, receptor oligomerization, ligand scavenging by decoy receptors, ligand transcytosis. All these regulatory mechanisms represent new potential aspects to be exploited for an innovative approach aimed at controlling chemokines to interfere with the natural history of a wide range of human diseases. INNOCHEM has also identified and characterized exogenous tools able to interfere with the chemokine system. These include on the ligand side anti-chemokine antibodies and synthetic agents able to interfere with chemokine production, on the receptor side natural compounds and the new class of allosteric receptor inhibitors. Finally, for several of these agents INNOCHEM has provided the needed support for transfer in the clinical setting. A phase I clinical study has been designed and started with meraxin, an new allosteric dual CXCR1/CXCR2 inhibitor developed on the basis of previous knowledge acquired by extensive investigation of the first chemokine receptor allosteric inhibitor reparixin. In addition, a phase II placebo-controlled clinical trial of the chemokine synthesis inhibitor bindarit in diabetic nephropathy patients has been completed. Results obtained in this project have opened new perspectives in the therapeutic intervention against autoimmunity and chronic inflammation, with social impacts measurable as improved health, and reduction of health societal costs, including costs for patient assistance as well as loss of manpower.

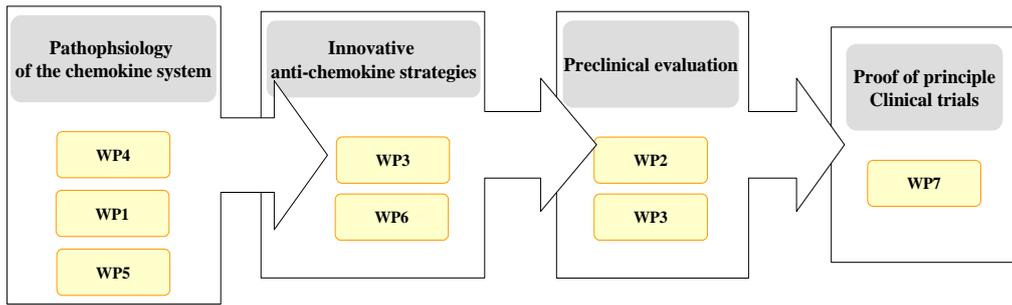
1.5 Impact of the project (on its industry or research sector)

Autoimmune/chronic inflammation disorders usually entail therapy with immunosuppressive medications that slow or suppress the immune system response in an attempt to stop the inflammation involved in the disease. Unfortunately, these medications also suppress the ability of the immune system to fight infection and have other potentially serious side effects. Therefore, a great effort of medical science is directed to find new therapies for the treatment of autoimmune and inflammatory diseases and that also improve the safety of human population. The goal of INNOCHEM project was the evaluation of the chemokine system as a new therapeutic target and the development of innovative approaches for its control. During its activity, INNOCHEM has generated a significant amount of preclinical data clearly showing that chemokines and their receptors are key players in a number of autoimmune/chronic inflammation disorders and indicating which specific molecules play central roles in driving different diseases. INNOCHEM also has identified innovative approaches to control this complex molecular system, each representing a new avenue of potential industrial interest. In addition, because of the tight interaction among the partners participating to the INNOCHEM project and of the novelty of some technological approaches, the proposed studies has also created new opportunities for education and training of young investigators. The proposed study has offered the opportunity to import technical skill and scientific knowledge in the fields of chemokine research in the different partner countries. This has been an input for the formation of young researchers and for the development of analogous projects with application to different targets. It is assumed that all this can result in new opportunities of employment in Europe.

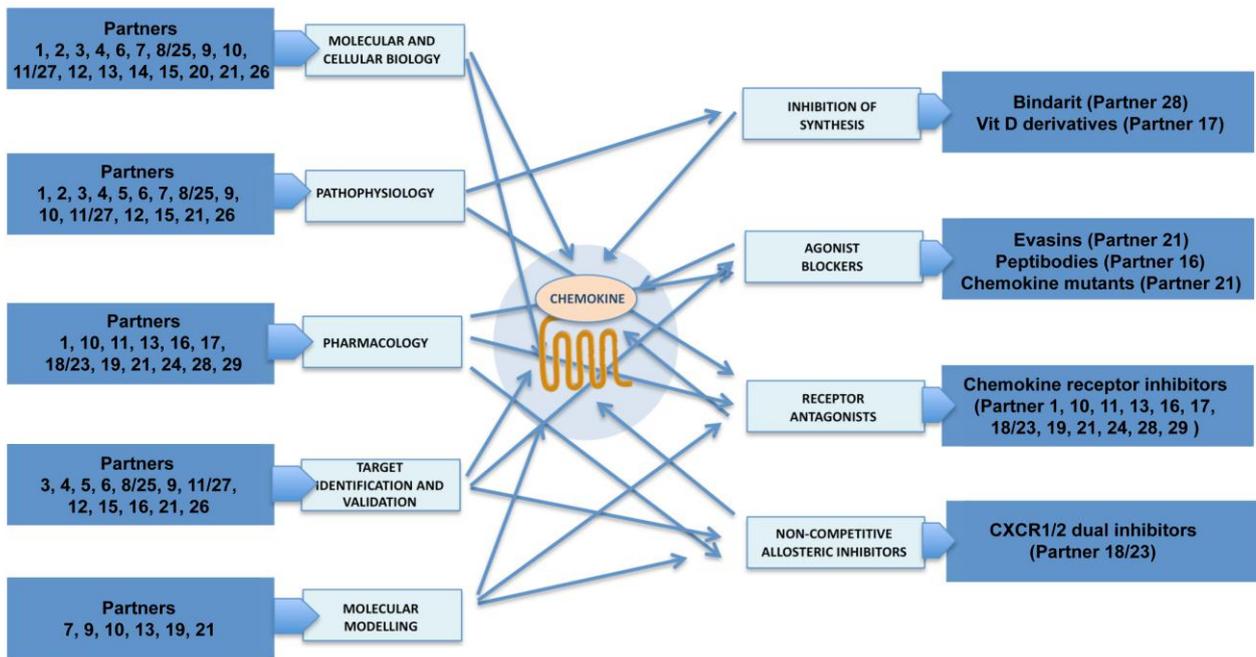
1.6 Project website

<http://www.innochem.org>

1.7 Diagrams/photos (illustrating the work of the project)



INNOCHEM pipeline



INNOCHEM output



INNOCHEM final meeting, Berlin, October 11-13, 2010

2 Dissemination and use

Annex 1 – Plan for using and disseminating the knowledge

Section 1 - Exploitable knowledge and its Use

Exploitable Knowledge (description)	Exploitable product(s) or measure(s)	Sector(s) of application	Timetable for commercial use	Patents or other IPR protection	Owner & Other Partner(s) involved
Chemokine mutants acting as chemokine antagonists		Inflammation	10 years	0511	Partner 21
Novel antagonists of cxcr3- binding cxc chemokines		Inflammation	10 years	0513	Partner 21
CC-chemokine mutants against liver diseases		Inflammation	10 years	0801	Partner 21
Novel CC-chemokine-binding tick proteins		Inflammation	10 years	0956	Partner 21
Novel CC-chemokine antagonists		Inflammation	10 years	1015	Partner 21
Chemokine-Mucin-GPI Anchored Proteins as Tumor Adjuvants and in Wound Repair		Cancer therapy and wound repair	10 years	Patent Ludwig-Maximilians-University-University, Munich	Partner 9
Use of Filamin A inhibitors to elaborate pharmaceutical compositions, inhibitory compounds of such activity and their therapeutic applications and procedures to identify those inhibitory compounds		Inflammation	10 years	200602494	Partner 7
Novel chemokine-binding peptibodies capable of inhibiting the course of autoimmunity, inflammation and cancer		Inflammation	10 years		Partner 16

Section 2 – Dissemination of knowledge

First Year

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
Milan, November 20-22 2005	Kick-off meeting	Scientists	EU	All consortium and EU Commission	1, 2 and 22
Overall period	Direct e-mailing	Scientists		All consortium	All participants
Bellinzona, October 2-4 th , 2006	Annual meeting	Scientists	EU	All consortium and EU Commission	1 and 2
Overall period	Publications	Scientists	Worldwide		All partners
Overall period	Seminars and Conferences	Scientists	Worldwide		All partners

Second Year

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
Milan, November 20-22, 2005	Kick-off meeting	Scientists	EU	All consortium and EU Commission	1, 2 and 22
Overall period	Direct e-mailing	Scientists		All consortium	All participants
Bellinzona, October 2-4, 2006	Annual meeting	Scientists	EU	All consortium, Scientific Advisory Board, and coordinator of MUGEN	1 and 2
2006	Press releases on Radio, Press, Television	Non specialistic Public	Switzerland and Italy		1 and 2
Madrid September 24-26, 2007	Annual course	Young scientists and students	EU, Brasil	40	1,2,7
San Lorenzo de El Escorial, Madrid September 27-29, 2007	Annual meeting	Scientists	EU, Brasil, USA	All Consortium members, EU Commission, Scientific Advisory Board, and coordinator of MAIN	7, 1, 2
Overall period	Publications	Scientists	Worldwide		All partners
Overall period	Seminars and Conferences	Scientists	Worldwide		All partners

Third year

Event Date and Location	Type	Audience	Countries addressed	Partner(s) involved
“Chemokines and Chemokine Receptors”, Keystone symposium, January 8-13, 2008, Keystone, CO - USA	Conference	Scientists	International	#1 (organizer) #3 (poster) # 2 (organizer joined symposium on “Leukocyte trafficking”) # 25 (session chair) #15 (oral presentation) #7 (poster) #21 (keynote lecture) #14 (session chair and speaker)
“Chemotactic cytokines”, September 21-26, 2008, Aussois, France	Conference	Scientists	International	#21 (organizer) #26 (vice organizer) #4 (poster) #2 (speaker) #10 (oral presentation) #7 (poster) #14 (speaker)
“Pharmacology of 7TM domain receptors”, September 11-13, 2008, Copenhagen, Denmark	Workshop	PhD students and post-docs	International	#1 (organizer) #2 (organizer) #13 (organizer)
18th National Congress of Immunology, April 20-24, 2008, Huatulco, Oaxaca, Mexico	Conference	Scientists	International	#3 (oral presentation)
Symposium on Cellular Interactions in Inflammation and Cancer, December 2007. Madrid, Spain	Conference	Scientists	International	#7 (lecture)
International symposium: Immunoregulation and translational research, immunology at the crossroad, April 2008. Pamplona, Spain	Conference	Scientists	International	#7 (lecture)
Cantoblanco workshops on Biology on Initiation of Antigen Receptor Signaling, October 2008. Madrid, Spain	Workshop	Scientists and PhD students	International	#7 (lecture)
MetaBre/BRESCOM, Breast Cancer and Metastasis conference, December 2007. Rome, Italy	Conference	Scientists	International	#7 (poster and oral presentation)
Keystone Symposium on Cell Biology of virus Entry, Replication and Pathogenesis, April 2008. Victoria, Canada	Conference	Scientists	International	#7 (poster and oral presentation)
Heidelberg Virology Seminars, May 2008. Heidelberg, Germany	Seminar	Scientists and students	International	#7 (seminar)
II International Workshop on Lipid Mediators, June 2008. Valladolid, Spain	Workshop	Scientists	International	#7 (lecture)
IV International meeting on Biotechnology, September 2008. Granada, Spain	Conference	Scientists	International	#7 (lecture)
International Symposium on Advanced Microscopy Techniques for Immunofluorescence, October 2008. Barcelona, Spain	Conference	Scientists	International	#7 (lecture)

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Master in Molecular Oncology (2007-2009). Madrid, Spain	Master	Physicians and PhD students	International	#7 (lecture)
“Inflammation, microenvironment and Cancer”. Keystone symposium, March 30 – April 4, 2008, Snowbird, UT – USA.	Conference	Scientists	International	#10 (poster)
“G Protein-Coupled Receptors: New Insights in Functional Regulation and Clinical Application”. Keystone Symposium, May 18-23, 2008. Killarney, Ireland.	Conference	Scientists	International	#10 (poster)
First International Conference: Advances in Clinical Neuroimmunology. December 7-8, 2008. Poznan, Poland	Conference	Scientists	International	#5 (poster)
American Society of Nephrology, October 30-November 5, 2007. San Francisco, CA - USA	Conference	Scientists	International	#9 (oral presentation)
Scandinavian Artherosclerosis Congress, March 28-31, 2008. Copenhagen, Denmark	Conference	Scientists	International	#9 (oral presentation)
Chemokines and chemokine receptors in the nervous system, October 27-28, 2008. Rome, Italy	Conference	Scientists	International	#2 (oral presentation)
XXII Annual Meeting EMDS “Diversity and Plasticity of the Innate Immune Response”, September 18-20, 2008. Brescia, Italy	Conference	Scientists	Europe	#14 (speaker)
“FPRs and their ligands in inflammation”. June 13, 2008, London, UK	Workshop	Scientists	Europe	#10 (oral presentation)
Chemokine expression in SIV infection, December 11, 2007. Innsbruck, Austria	Seminar	Scientists	National	#2 (seminar)
VI National Conference Italian Society for Immunology, Clinical Immunology and Allergology (SIICA), June 11-14, 2008. Rome, Italy	Conference	Scientists	National	#2 (lecture)
PhD programme lectures, Universidad de Alcala, January 2008. Alcala de Henares-Madrid, Spain	PhD programme	PhD students	National	#7 (lecture)
PhD programme lectures, Univesidad Autonoma de Madrid, March 2008. Madrid, Spain	PhD programme	PhD students	National	#7 (lecture)
Annual Joint Meeting of the Swiss Societies for Pneumology, Pediatric Pneumology, Allergology and Immunology, Thoracic Surgery, April 17-18, 2008. Fribourg, Switzerland	Conference	Scientists	National	#2 (lecture, oral presentation)
RDC1/CXCR7 a novel potential chemokine receptor, December 4, 2007. Brescia, Italy	Seminar	PhD students, scientists	National	#2 (lecture)
RDC1/CXCR7 a novel potential	Seminar	PhD	National	#2 (lecture)

chemokine receptor, September 4, 2008. Hamburg, Germany		students, scientists		
MRC Centre for Inflammation Research, March 14, 2008, Edinburgh, UK	Seminar	Scientists	National	#25 (seminar)
I3th IRG Gregynog Annual Meeting, September 4-5, 2008, Gregynog, Wales, UK	Conference	Scientists	National	#25 (meeting chair)
Seminars of the Chaire de Médecine Expérimentale “New data on G protein-coupled receptors”, Collège de France, March 3, 2008. Paris, France	Seminar	Scientists, students, general public	National	#10 (oral presentation)
Mini-symposium on “Infections and inflammation” May 9, 2008, Brussels, Belgium	Conference	Scientists, students	National	#10 (oral presentation)
Seminar at Institute Cochin, February 2008. Paris, France	Seminar	Scientists and students	Local	#7 (seminar)
Seminar, February 18, 2008 UCL, London, UK	Seminar	Scientists	Local	#25 (seminar)
Sheffield Regional Immunology Meeting, June 3, 2008. UK	Conference	Scientists	Local	#15 (oral presentation)
Imperial College, June 27, 2008. London, UK	Open day	Pupils aged 16-17 from local schools	Local	#15 (oral presentation and laboratory demonstrations)

Fourth year

Event Date and Location	Type	Audience	Countries addressed	Partner(s) involved
Quimioquinas: la complejidad del control del movimiento celular. Dec 19, 2008. Granada, ES	Junior Scientific Workshop. Instituto de Parasitología y Biomedicina “López-Neyra”	Master and PhD students	Worldwide	Partner 7
Communications on the role of chemokines in progenitor/stem cells mobilisation from the bone marrow Jan 2009, March 2009	Further coverage of this research in articles published by the New Scientist in Nature Reports Stem cells and in Nature Biotechnology	Scientists	Worldwide	Partner 15
GTCbio’s 7th annual meeting. Jan 2009. San Diego, California, US	Conference	Scientists	Worldwide	Partner 16
Role of chemokines in lymphoid neogenesis and effector/memory T cell differentiation Medical University of Vienna, General Hospital. Feb 11-12, 2009, Vienna, AT	2nd International Workshop Cell Communication In Health and Disease	Scientists	Worldwide	Partner 6
Role of chemokines in the mobilisation from the bone marrow of progenitors and stem cells. February 2009 Medical University of Vienna, General Hospital Vienna, AT	SMi conference – Stem cells: Drug discovery and Therapeutics	Scientists	Worldwide	Partner 15
Communications on the role of	An article about this	General public	Worldwide	Partner 15

chemokines in progenitor/stem cells mobilisation from the bone marrow	research and INNOCHEM was also published in "The Parliament Magazine: Research; European Research and Innovation Review", Issue 8 March 2009. http://www.e-pages.dk/dods/113/14	and scientists		
Role of chemokines in the mobilisation from the bone marrow of progenitors and stem cells March 2009 Asheville, NC	Keystone Conference "Cardiac development and regeneration"	Scientists	Worldwide	Partner 15
CXCR5-dependent lymphoid neogenesis in chronic inflammation CAESAR - Center of Advanced European Studies And Research. Bonn, Mar 6 -7, 2009, DE	International Symposium Immune Regulation Collaborative Research Center, SFB 704	Scientists	Worldwide	Partner 6
Modelling chronic inflammatory diseases in animals, Apr 20-22, 2009. Orleans, FR	INNOCHEM course	PhD students and postdocs	Worldwide	
Chemerin and ChemR23: Dendritic cell recruitment and anti-inflammatory actions 26-30.04.2009, Lille, FR	SBS 15 th annual Conference	Scientists	Worldwide	Partner 10
Molecular Pharmacology. May 2009, IT	Gordon Research Conference	Scientists	Worldwide	Partner 13
Chemokine/Chemokine receptors: perspectives for identifying new therapeutic targets. Jun 15, 2009. Athens, GR	I Meeting of Masterswitch consortium	Scientists	Worldwide	Partner 7
4 nd Chemokine meeting Conference. Jun 2009. IL		Scientists	Worldwide	Partner 16
Functional imaging of chemotaxis mediating receptors in migrating cells. Jul 2-3, 2009. University of Nottinnham, UK	IOBIOS Inaugural conference on Functional Optical Imaging	Scientists	Worldwide	Partner 2
Role of chemokines in the mobilisation from the bone marrow of progenitors and stem cells Sept 2009, Edimburgh, UK	2nd annual Stem Cells & Regenerative Medicine Europe conference	Scientists	Worldwide	Partner 15
Antitumoral effect of cannabinoids in a genetic model of breast cancer. Nov 27, 2009, Cordoba, ES	IX Congress of the Spanish Society for Research in Cannabinoids	Scientists	Worldwide	Partner 7
Communications on the role of chemokines in progenitor/stem cells mobilisation from the bone marrow	Press coverage included articles in the Guardian, the Telegraph and the Daily Express, while there was extensive coverage on the	General public	Worldwide	Partner 15

	internet, including Reuters, CNN and MSNBC			
Update on ChemR23 and FPRL2 characterization. Nov 14, 2008. Gosselies, BE	Euroscreen s.a. Scientific advisory board meeting	Scientists	National	Partner 10
Autoantigen-driven lymphoid neogenesis in chronic autoimmune diseases Singapore Immunology Network (SIgN) BIOPOLIS. Dec 12, 2008, SG	Seminar	Scientists	National	Partner 6
Autoantigen-driven lymphoid neogenesis in chronic autoimmune diseases Institute of Genome Research Tokushima University. Dec 8, 2008, JP	Seminar	Scientists	National	Partner 6
Hot topics in immunology: chemokine processing Jan, Feb 2009, Leuven, BE	Lesson	Master and PhD students, national	National	Partner 14
Advanced Course in Immunology: Cytokines and Chemokines Nov, Dec 2008, K.U.Leuven, BE	Lesson	Master and PhD students, national	National	Partner 14
Chemokine receptor signalling and scavenging. Dec 16, 2008 Leibniz-Institut für Molekulare Pharmakologie (FMP) Campus Berlin-Buch, Berlin, DE	Seminar	Scientists	National	Partner 2
Visit to King Saudi University Feb 2009, Ryadh, SA	Collaboration/exchange visit	Scientists	National	Partner 14
$\gamma\delta$ T-APCs induce antigen-specific CD8+ $\alpha\beta$ T cell responses. Feb 12, 2009. University of Glasgow, UK	BSI Scotland lecture	Scientists	National	Partner 25
Chemokines: role during normal and pathological processes Feb, Mar 2009, Leuven, BE	Lesson	MD students, national	National	Partner 14
Recent advances in antigen-presenting human $\gamma\delta$ T cells. March 9, 2009, The Royal Society of Medicine, UK	The other T cell in cancer and immunotherapy	Scientists	National	Partner 25
Human $\gamma\delta$ T cells: alternative antigen-presenting cells. March 25, 2009, Institute for Research in Biomedicine, Bellinzona, CH	Lesson	PhD students	National	Partner 25
Chemokine receptor signalling and scavenging for leukocyte migration. Apr 22, 2009. Institute Pasteur Paris, FR	Seminar	Scientists	National	Partner 2
Señalización de quimioquinas en inflamación. May 5, 2009. Murcia, ES	XXXV Congress of the Spanish Society of Rheumatology	Scientists	National	Partner 7
Lesson at the University of Italian Switzerland, May 2009,	Lesson	Master students,	National	Partner 2

Bellinzona, CH		national		
Antigen-presentation by human $\gamma\delta$ T cells. May 22, 2009, University of Birmingham, UK	John Squire Club Seminar	Scientists	National	Partner 25
Chemokine receptor signalling and scavenging for leukocyte migration. May 26, 2009. Pepsan Lelystad, NL	Seminar	Scientists	National	Partner 2
The yin yang of chemokine receptor functions. Jun 15, 2009. University of Birmingham, UK	John Squire Club Seminar	Scientists	National	Partner 2
The yin yang of chemokine receptor functions Department of Immunology. Jun 25, 2009. Univ. of Cardiff, UK	Seminar	Scientists	National	Partner 2
Functional chemokine receptor responses. Jun 30, 2009. Babraham Institute Babraham, Cambridge, UK	Seminar	Scientists	National	Partner 2
Presentation 2008. New Orleans, US	American Chemical Society Annual Meeting	Scientists	Worldwide	Partner 13
Communication of the INNOCHEM program and achievements. Septemebr 2009	French National Association of Patients with Lupus ("Lupus France") : contribution to the september issue of the association letter	Scientists and Genral Public	National	Partner 4
Communication of the INNOCHEM program and achievements. October 2009	French "Arthritis Foundation" : contribution to the october issue of the association letter	Scientists and Genral Public	National	Partner 4
Communications on the role of chemokines in progenitor/stem cells mobilisation from the bone marrow	Interviews for Radio 4's Today programme, UK the World service lunchtime news and TV interviews for Channel 4 lunch time news	General public	National	Partner 15
Communications on the role of chemokines in progenitor/stem cells mobilisation from the bone marrow. Jan 9, 2009	Interviews for Central Chinese TV	General public	National	Partner 15
Chemokines and macular degeneration. May, 28 th 2009. Bordeaux, FR	Colloque de la société de Neurosciences	Scientists	National	Partner 3
Chemokines and macular degeneration. Toulouse University. Nov 2008. Toulouse, FR	Seminar	Scientists	National	Partner 3
Anti-inflammatory and immunosuppressive function of GILZ in macrophages and dendritic cells. July 2009. Baylor Institute, Dallas, TX, US	Seminar	Scientists	National	Partner 4
Autoantigen-driven lymphoid	Seminar	Scientists	National	Partner 6

neogenesis in chronic autoimmune diseases December 12th, 2008 Singapore Immunology Network (SIgN) BIOPOLIS Singapore				
Autoantigen-driven lymphoid neogenesis in chronic autoimmune diseases December 8th, 2008 Institute of Genome Research Tokushima University, JP	Seminar	Scientists	National	Partner 6
Role of chemokines in lymphoid neogenesis and effector/memory T cell differentiation. February 11th-12th, 2009 Medical University of Vienna, General Hospital Vienna, AT	2nd International Workshop Cell Communication In Health and Disease	Scientists	Worldwide	Partner 6
Role of chemokines in the mobilisation from the bone marrow of progenitors and stem cells May 2009 Oxford Stem Cell Institute, UK	Seminar	Scientists	National	Partner 15
Role of chemokines in the mobilisation from the bone marrow of progenitors and stem cells June 2009. Royal Veterinary College. London, UK	Seminar	Scientists	National	Partner 15
Chemokine meeting - Genzyme, May 2009 Copenhagen, DK	Scientific meeting	Scientists	Worldwide	Partner 13
Role of chemokines in the mobilisation from the bone marrow of progenitors and stem cells July 2009, JP	17 th international Symposium on the Molecular Cell Biology of Macrophages	Scientists	Worldwide	Partner 15
Stem-cell meeting. Nov 2009, Uppsala, SE	Scientific meeting	Scientists	Worldwide	Partner 13
Press Release Tokio July 6-9, 2009, JP	Thomson Reuters (Scientific) Ltd.	Scientists and General Public	Worldwide	Partner 28
Press Release DailyDrugNews.com July 28, 2009	on--line	Scientists and General Public	Worldwide	Partner 28
Press Release NovImmune SA July 13, 2009	Media release Plan-Les-Ouates/Geneva	Scientists and General Public	Worldwide	Partner 29
Bindarit inhibits neointimal hyperplasia, an effect associated with inhibition of monocyte chemoattractant protein-1 synthesis Washington April 29-May 1, 2009, USA	ATVB Annual Conference	Scientists	Worldwide	Partner 28
Bindarit decreases monocyte chemoattractant protein-1 urinary excretion in humans. A pilot study in active lupus	9 th World Congress on Inflammation	Scientists	Worldwide	Partner 28

nephritis patients Tokio, July 6-10, 2009, JP				
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Fifth year

Event Date and Location	Type	Audience	Countries addressed	Partner(s) involved
Generation and preclinical development of a fully human anti-CXCL10 monoclonal antibody Hermenonville, France, April 2009	INNOCHEM 2009	Scientists	Worldwide	Partner 29
Engineering Antibodies For Targeting Redundant Signaling Pathways in Autoimmunity Beijing, China May 2009	International Cooperative alliance	Scientists	Worldwide	Partner 29
Chemokines and their role in inflammatory pathologies Bristol, UK July 2009	British Society of Immunology Meeting	Scientists	National	Partner 26
The D6 chemokine decoy receptor coordinates innate and adaptive immune responses Birmingham, UK August 2009	Microanatomy of the Immune Response Meeting	Scientists	Worldwide	Partner 26
Chemokines and in vivo trafficking of progenitor cells Istituto Clinico Humanitas, Milan, Italy October 2009	Invited seminar	Scientists	National	Partner 15
Chemokines and in vivo trafficking of progenitor cells Institute for Research in Biomedicine, Bellinzona, Switzerland October 2009	Invited seminar	Scientists	National	Partner 15
Chemokines and in vivo trafficking of progenitor cells Stem cell workshop Imperial College, London, UK October, 2009	Workshop	Scientists	National	Partner 15
Inflammatory chemokines in monocyte mobilisation Vina del mar, Chili November 2009	ImmunoChile 2009	Scientists	National	Partner 3
Inflammatory chemokines in monocyte mobilisation Academia Nacional de Medicina, Buenos Aires, Argentina November 2009	Scientific meeting	Scientists	National	Partner 3
Human gd T cells: novel tools for cellular immunotherapy Bristol, UK November 20, 2009	1 st SARTRE Meeting, Bristol	Scientists	National	Partner 25

Master lectures Alcalá University November 2009	Lecture	Master/PhD students	National	Partner 7
Master lectures ETSI telecomunicacion November 2009	Lecture	Master/PhD students	National	Partner 7
Increasing complexity of GPCR complexes and signaling networks Paris, France November 24, 2009	ESF Exploratory Workshop on "GPCR signalling systems: A new avenue for drug discovery ?"	Scientists	Worldwide	Partner 10
Chemokines and in vivo trafficking of progenitor cells Vascular Biology Meeting, Imperial College, London December 2009	Meeting	Scientists	National	Partner 15
Lecture to high school pupils Glasgow December 2009	lecture	High school pupils	National	Partner 26
Master lectures Centro Nacional de Biotecnologia December 2009	Lecture	Master/PhD students	National	Partner 7
Lecture to medical students Cardiff University December 04, 2009	Lecture	Medical students	National	Partner 25
Chemokines and in vivo trafficking of progenitor cells The Association for Science Education annual meeting, Nottingham, UK January 2010	Lecture "Stem cells the future of medicine"	Scientists	National	Partner 15
Chemokines and chemokine receptors in health and disease Amsterdam, The Netherlands January 2010	Amsterdam Doctoral Training Programme	Masters/ PhD students	National	Partner 26
Master lectures Autonomous University January 2010	Lecture	Master/PhD students	National	Partner 7
Synergy-inducing chemokines Institute of Oncology of Southern Switzerland, Bellinzona, CH, January 13, 2010	Seminar	Scientists	National	Partner 2
Lecture to medical students Cardiff University January 19, 2010	Lecture	Medical students	National	Partner 25
Master lectures National Center for Oncology Research February 2010	Lecture	Master/PhD students	National	Partner 7
Chemokines and in vivo	Seminar	Scientists	National	Partner 15

trafficking of progenitor cells SMi conference – Stem cells: Achieving success in science and commercialisation, London February 2010				
Master lectures Alcalá University February 2010	Lecture	Master/PhD students	National	Partner 7
Lecture to medical students Cardiff University February 22, 2010	Lecture	Medical students	National	Partner 25
Chemokines and in vivo trafficking of progenitor cells Stem Cell Club, Birmingham, UK February 2010	Seminar	Scientists	National	Partner 15
Expression of angiostatic CXCL4L1 counterbalances angiogenic impulses of VEGF, CXCL8 and CXCL12 Brussels, Belgium, February 5, 2010	Inter-Universitary Attract Pole (IAP/PAI) meeting	Scientists	Worldwide	Partner 14
Expression and function of GILZ in dendritic cells and macrophages Department for Molecular Biomedical Research, Flanders Institute for Biotechnology (VIB), Ghent, Belgium February 5, 2010	Seminar	Scientists	National	Partner 4
Chemokines and in vivo trafficking of progenitor cells Genes, Development and Disease Theme Seminar at UCL-ICH, London February 2010	Invited seminar	Scientists	National	Partner 15
Human antigen-presenting gd T cells Birmingham University, February 05, 2010	Cancer Immunotherapy Group	Scientists	Worldwide	Partner 25
Statins as immunomodulatory drugs in murine models of inflammation National Center for Cardiovascular Research. CNIC. Madrid. Spain March 01, 2010	MEICA Workshop	Scientists	National	Partner 7
Functional chemokine receptor responses EPFL Lausanne, Switzerland March 02, 2010	Seminar	Scientists	Worldwide	Partner 2
Chemokines and in vivo trafficking of progenitor cells Keynote address -Heart Lung Fest, Vancouver March 2010	Seminar	Scientists	Worldwide	Partner 15
Chemokines and in vivo trafficking of progenitor cells Tissue Engineering Institute, Porto, Portugal	Invited Seminar	Scientists	National	Partner 15

March 2010				
Synergy-inducing chemokines Bellinzona, CH, March 18, 2010	IRB – INGM joint meeting	Scientists	Worldwide	Partner 2
Citrullination affects the biological activity of chemokines St. Sorlin d’Arves – France, March 22-24, 2010	International workshop on “Cytokines and Chemokines”	Scientists	Worldwide	Partner 14
Generation and preclinical development of a fully human anti-CXCL10 monoclonal antibody St. Sorlin d’Arves – France, March 22-24, 2010	Cytokines and Chemokines-Post-transcriptional regulation.	Scientists	Worldwide	Partner 29
CXCR7 functions as a scavenger for CXCL12 St. Sorlin d’Arves – France, March 22-24, 2010	International workshop on “Cytokines and Chemokines”	Scientists	Worldwide	Partner 2
The COOH-terminal peptide of platelet factor-4 variant (CXCL4L1/PF-4var ⁴⁷⁻⁷⁰) strongly inhibits angiogenesis St. Sorlin d’Arves – France, March 22-24, 2010	International workshop on “Cytokines and Chemokines”	Scientists	Worldwide	Partner 14
The D6 chemokine decoy receptor coordinates innate and adaptive immune responses St. Sorlin d’Arves – France, March 22-24, 2010	International workshop on “Cytokines and Chemokines”	Scientists	Worldwide	Partner 26
HMGB1 synergises with CXCL12, St. Sorlin d’Arves – France, March 22, 2010	International workshop on “Cytokines and Chemokines”	Scientists	Worldwide	Partner2
Function and Transcriptional Regulation of Differentiation of Follicular T Helper (T _{FH}) Cells Würzburg, Germany, March 2010	Seminar	Scientists	National	Partner 6
Mouse ChemR23 is expressed in dendritic cell subsets and macrophages, and mediates an anti-inflammatory activity of chemerin in a lung disease model Davos, Switzerland March 29- April 01, 2010	World Immune Regulation Meeting	Scientists	Worldwide	Partner 10
Regulation of SOD3 by statins Centro de Investigaciones Biológicas. Madrid. Spain April 19, 2010	2nd Scientific Journey of the Spanish Network for Rheumatic Diseases	Scientists	National	Partner 7
The role of conserved regions in chemokine receptors for ligand-binding and receptor activation Breckenridge, USA April 2010	G protein-coupled receptors, a Keystone meeting	Scientists	Worldwide	Partner 13
A chimeric approach to study chemokine receptor activation Breckenridge, USA	G protein-coupled receptors, a Keystone meeting	Scientists	Worldwide	Partner 13

April 2010				
Inflammatory chemokines in monocyte mobilisation Il Ciocco, Italy May 2010	The Gordon Resarch Conference	Scientists	Worldwide	Partner 3
Artritis reumatoide: Una enfermedad autoinmune Madrid, Spain, May 2010	Curso de formación de Monitores Clínicos Quintiles	Scientists	National	Partner 7
Human gd T-APCs: an update Kiel, Germany, May 19-21, 2010	Int. gd T Cell Conference	Scientists	Worldwide	Partner 25
Function of chemokine decoy receptors in tuning the immune response Sylt, Germany, May 06-09, 2010	Forefronts Symposium (Int. Society of Nephrology)	Scientists	Worldwide	Partner 2
Effect of bindarit in a porcine coronary artery model of vascular restenosis Il Ciocco, Italy May 30 – June 4, 2010	The Gordon Resarch Conference	Scientists	Worldwide	Partner 28
Inflammatory chemokines in monocyte mobilisation Il Ciocco, Italy May 30 – June 4, 2010	The Gordon Resarch Conference	Scientists	Worldwide	Partner 9
Generation and early clinical development of a fully human anti-CXCL10 monoclonal antibody Il Ciocco, Italy May 30 – June 4, 2010	The Gordon Resarch Conference	Scientists	Worldwide	Partner 29
The Yin Yang of CXCR7 functions Il Ciocco, Italy May 30 – June 4, 2010	The Gordon Resarch Conference	Scientists	Worldwide	Partner 2
The carboxy-terminal peptide of platelet factor-4 variant (CXCL4L1/PF-4var ⁴⁷⁻⁷⁰) Leuven, Belgium, May 27, 2010	Oncoforum	Scientists	Worldwide	Partner 14
Citrullination of chemokines as a regulatory mechanism for biological activity Il Ciocco, Italy, May 30 – June 4, 2010	Gordon Research Conference “Chemotactic Cytokines”	Scientists	Worldwide	Partner 14
Chemokines and in vivo trafficking of progenitor cells Il Ciocco, Italy, May 30 – June 4, 2010	Gordon Research Conference “Chemotactic Cytokines”	Scientists	Worldwide	Partner 15
Chair’s introductory remarks Il Ciocco, Italy, May 30 – June 4, 2010	Gordon Research Conference “Chemotactic Cytokines”	Scientists	Worldwide	Partner 26
Chemerin and ChemR23 in inflammatory and viral diseases Il Ciocco, Italy, May 30 – June 4, 2010	Gordon Research Conference “Chemotactic Cytokines”	Scientists	Worldwide	Partner 10
PhD-course- Pharmacology now and in the future	course	Scientists	National	Partner 13

Copenhagen University, Denmark, May 2010				
“Pharmacologically characterization of functionally selective CXCR inhibitors” Camerino, Italy, May 16-20, 2010	28 th Camerino- Cyprus- Noordwijkerhout Symposium “Trekking through Receptor Chemistry”	Scientists	Worldwide	Partner 23
Papel de SOCS1 como supresor tumoral Universidad de Alcalá May 2010	Seminarios externos Departamento de Fisiología.	Scientists	National	Partner 7
Bindarit an inhibitor of MCPs synthesis: history & perspectives Siena, Italy, June 04-06, 2010	INNOCHEM course 2010	Scientists	Worldwide	Partner 28
Chemokines and in vivo trafficking of progenitor cells BHF Centre for Excellence Symposium, Imperial, London June 2010	Seminar	Scientists	National	Partner 15
Master lectures Quintiles SL June 2010	Lecture	Master/PhD students	National	Partner 7
Inflammatory chemokines in monocyte mobilisation French Society of Biology France June 2010	Seminar	Scientists	National	Partner 3
The D6 chemokine decoy receptor coordinates innate and adaptive immune responses June 2010	Immunology Meeting	Scientists	Worldwide	Partner 26
The Yin Yang of Chemokine Receptor Functions University of Bern, Switzerland July 07, 2010	Seminar	Scientists	Worldwide	Partner 2
Activation and inactivation of chemokine receptors Copenhagen, Denmark July 2010	WorldPharma2010	Scientists	Worldwide	Partner 13
A chimeric approach to study chemokine receptor activation Copenhagen, denmark July 2010	WorldPharma2010	Scientists	Worldwide	Partner 13
The Yin Yang of Chemokine Receptor Functions Novartis, Basel, Switzerland July 08, 2010	Seminar	Scientists	Worldwide	Partner 2
Human gd T-APCs: an overview London, UK July 13, 2010	UCL Child Health Science Seminar series	Scientists	Worldwide	Partner 25
The Yin Yang of Chemokine Receptor Functions University of Geneva, Switzerland July 21, 2010	Seminar	Scientists	Worldwide	Partner 2

Exhibit "Tra l'ombra e la luce" – "Between shadow and light" Bellinzona, CH, July 14 – August 22, 2010	Photographic (poverty-related diseases) and didactic ("The Birth of the Immunology") exhibition	General Public	Bellinzona and Bellinzona visitors	Partner 2
Chemokines and in vivo trafficking of progenitor cells Stem cell workshop Imperial College, London, UK July and August 2010	Workshop	Scientists	National	Partner 15
PhD-course in grant-application and research reports Copenhagen University, Denmark, August 2010	course	Scientists	National	Partner 13
CXCR5-directed Immunotherapy of B cell Non- Hodgkin lymphoma and autoimmune disease Kobe, Japan, August 2010	14 th International Congress of Immunology	Scientists	Worldwide	Partner 6
Bindarit, an inhibitor of monocyte chemotactic proteins (MCPs) production, reduces restenosis in a porcine coronary stent model Stoccolm, Sweden August 30, 2010	ESC 2010	Scientists	World wide	Partner 29
CCL2 synthesis inhibitors modulate inflammatory and neuropathic pain behaviour in rats Montreal, Canada September 02, 2010	13 th World Conference on pain	Scientists	Worldwide	Partner 28
EBI2-an orphan 7TM receptors involved in EBV pathogenesis Birmingham, UK, September 2010	Epstein-Barr virus conference	Scientists	Worldwide	Partner 13
Chemokines and in vivo trafficking of progenitor cells European Respiratory Society, Barcelona, Spain September 2010	Invited seminar	Scientists	National	Partner 15
Chemokine Receptor Functions University of Münster, Germany, September 08, 2010	Seminar	Scientists	Worldwide	Partner 2
Cytokines/ Chemokines Leuven, Belgium, September 17, 2010	Symposium on Chronic Inflammatory Bowel Diseases	Scientists	Worldwide	Partner 14
CXCR5 as Therapeutic Target in B cell Non-Hodgkin lymphoma and autoimmune diseases Leipzig, Germany, September 2010	40 th Annual Meeting German Society for Immunology	Scientists	Worldwide	Partner 6
Chemokines in pathology Berlin, Germany, October 11-13, 2010	V INNOCHEM annual meeting	Scientists	Worldwide	Partner 2

WP5 Progress Report Berlin, Germany October 11-13, 2010	Final INNOCHEM meeting	Scientists	Worldwide	Partner 25
Signalling pathways in stem cell biology, Ulm, Germany October 2010	Seminar	Scientists	Worldwide	Partner 15
Chemokines and in vivo trafficking of progenitor cells SFB 497 Symposium, Ulm Germany October 2010	Invited seminar	Scientists	National	Partner 15
Generation and preclinical development of a fully human anti-CCL5 monoclonal antibody. Chicago, USA October 2010	8th joint Meeting of the International Cytokine Society (ICS) and the International Society for Interferon and Cytokine Research (ISICR)	Scientists	Worldwide	Partner 29

Section 3 - Publishable results

During the course of the project the following publications were made:

1. Abu El-Asrar, A.M., S.Struyf, D.Kangave, K.Geboes, and J.Van Damme. 2006. Chemokines in proliferative diabetic retinopathy and proliferative vitreoretinopathy. *Eur. Cytokine Netw.* 17:155-165.
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3. Bottazzi, B., C.Garlanda, G.Salvatori, P.Jeannin, A.Manfredi, and A.Mantovani. 2006. Pentraxins as a key component of innate immunity. *Curr. Opin. Immunol.* 18:10-15.
4. Bottazzi, B., A.Bastone, A.Doni, C.Garlanda, S.Valentino, L.Deban, V.Maina, A.Cotena, F.Moalli, L.Vago, A.Salustri, L.Romani, and A.Mantovani. 2006. The long pentraxin PTX3 as a link among innate immunity, inflammation, and female fertility. *J. Leukoc. Biol.* 79:909-912.
5. Doni, A., M.Michela, B.Bottazzi, G.Peri, S.Valentino, N.Polentarutti, C.Garlanda, and A.Mantovani. 2006. Regulation of PTX3, a key component of humoral innate immunity in human dendritic cells: stimulation by IL-10 and inhibition by IFN-gamma. *J. Leukoc. Biol.* 79:797-802.
6. Loos, T., L.Dekeyser, S.Struyf, E.Schutyser, K.Gijsbers, M.Gouwy, A.Fraeyman, W.Put, I.Ronsse, B.Grillet, G.Opdenakker, J.V.Damme, and P.Proost. 2006. TLR ligands and cytokines induce CXCR3 ligands in endothelial cells: enhanced CXCL9 in autoimmune arthritis. *Lab Invest* 86:902-916.
7. Mantovani, A. and F.Balkwill. 2006. RalB signaling: a bridge between inflammation and cancer. *Cell* 127:42-44.
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9. Pawar, R.D., P.S.Patole, D.Zeicher, S.Segerer, M.Kretzler, D.Schlondorff, and H.J.Anders. 2006. Toll-like receptor-7 modulates immune complex glomerulonephritis. *J. Am. Soc. Nephrol.* 17:141-149.
10. Pello, O.M., B.Duthey, D.Garcia-Bernal, J.M.Rodriguez-Frade, J.V.Stein, J.Teixido, C.Martinez, and M.Mellado. 2006. Opioids trigger alpha 5 beta 1 integrin-mediated monocyte adhesion. *J. Immunol.* 176:1675-1685.
11. **Proost, P., S.Struyf, T.Loos, M.Gouwy, E.Schutyser, R.Conings, I.Ronsse, M.Parmentier, B.Grillet, G.Opdenakker, J.Balzarini, and J.Van Damme.** 2006. Coexpression and interaction of CXCL10 and CD26 in mesenchymal cells by synergising inflammatory cytokines: CXCL8 and CXCL10 are discriminative markers for autoimmune arthropathies. *Arthritis Res. Ther.* 8:R107.
12. Rosenkilde, M.M., R.David, I.Oerlecke, T.ned-Jensen, U.Geumann, A.G.Beck-Sickinger, and T.W.Schwartz. 2006. Conformational constraining of inactive and active states of a seven transmembrane receptor by metal ion site engineering in the extracellular end of transmembrane segment V. *Mol. Pharmacol.* 70:1892-1901.
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- Differential regulation of chemokine production by Fcγ receptor engagement in human monocytes: association of CCL1 with a distinct form of M2 monocyte activation (M2b, Type 2). *J. Leukoc. Biol.* 80:342-349.
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 16. Migeotte, I., D. Communi, and M. Parmentier. 2006. Formyl peptide receptors: a promiscuous subfamily of G protein-coupled receptors controlling immune responses. *Cytokine Growth Factor Rev.* 17:501-519.
 17. Patole, P.S., R.D. Pawar, M. Lech, D. Zecher, H. Schmidt, S. Segerer, A. Ellwart, A. Henger, M. Kretzler, and H.J. Anders. 2006. Expression and regulation of Toll-like receptors in lupus-like immune complex glomerulonephritis of MRL-Fas(lpr) mice. *Nephrol. Dial. Transplant.* 21:3062-3073.
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