						Accueil					
Label Unité	City	Name, First Name of the Head of the	Brief description of the research performed by the team (3 lines)	6 main publications related to the proposed thematic scope	proposed thematic scope(s)	Number of	profil, expertise,	Number of	profil, expertise,	Domain	mail
UMR_S 924	Valbonne	Glaichenhaus, Nicolas	Our team has a broad interest in immunology, and more specifically on T cell differentiation, antigen presentation and immune tolerance. Our studies focus on the molecular and cellular mechanisms that are responsible for the development of allergic airway inflammation. Major questions tackled are what initiates inflammation, how is its progression regulated, what are the final effector mechanisms, and how do genetic and environmental factors impact on disease unfolding. Our current specific aims are (1) to identify the molecular signals that regulate T cell accumulation in the inflamed lungs, (2) to elucidate how airway epithelial cells interact with aerosolized allergens, and (3) to elucidate the role of chemokine and chemokine receptors in airway inflammation.	Muraille, E., P. Gounon, J. Cazareth, J. Hoebeke, C. Lippuner, A.-C. Davalos Misslitz, T. Aebischer, S. Muller, N. Glaichenhaus, and E. Mougneau. 2010. Direct visualization of peptide/MHC complexes at the surface and in the intracellular compartments of cells infected in vivo by Leishmania major. PLoS Pathog. 6:e1001154. Mionnet, C., V. Buatois, A. Kanda, V. Milcent, S. Fleury, D. Lair, M. Langelot, Y. Lacoeuille, E. Hessel, R. Coffman, A. Magnan, D. Dombrowicz, N. Glaichenhaus, and V. Julia. 2010. CX3CR1 is required for airway inflammation by promoting T helper cell survival and maintenance in inflamed lung. Nat. Med. 16: 1305-1312. Ortiz-Stern, A., Kanda, A., Mionnet, C., Cazareth, J., Lazzari, A., Fleury, S., Dombrowicz, D. Glaichenhaus, N. and Julia, V. (2010). Langerin-positive dendritic cells are responsible for LPS-induced reactivation of allergen-specific Th2 responses in postasthmatic mice. Mucosal Immunol. Published on line on November 5, 2010 Navarro, S., G. Cossalter, C. Chiavaroli, A. Kanda, S. Fleury, J. Cazareth, T. Sparwasser, D. Dombrowicz, N. Glaichenhaus, and V. Julia. 2010. The oral administration of bacterial extracts prevents asthma via the recruitment of regulatory T cells to the airways. Mucosal Immunol. 4: 53-65. Muraille, E., P. Gounon, J. Cazareth, J. Hoebeke, C. Lippuner, A.-C. Davalos Misslitz, T. Aebischer, S. Muller, N. Glaichenhaus, and E. Mougneau. 2010. Direct visualization of peptide/MHC complexes at the surface and in the intracellular compartments of cells infected in vivo by Leishmania major. PLoS Pathog. 6:e1001154. Verhasselt, V., V. Milcent, J. Cazareth, A. Kanda, S. Fleury, D. Dombrowicz, N. Glaichenhaus, and V. Julia. 2008. Breast milk-mediated transfer of an antigen induces tolerance and protection from allergic asthma. Nat Med 14:170-175.	Molecular and cellular mecanisms in allergic airway inflammation	1 per year	Immunology	1 per year	immunology	immunology, pneumology	glaichenhaus@ipmc.cnrs.fr
UMR 999	Le Plessis Robinson	Humbert, Marc	Pulmonary hypertension: pathophysiology and innovative therapies with a focus on immunology, growth factors, endothelial and smooth muscle cell dysfonction and clinical trials	Montani D, Perros F, Gambaryan N, Girerd B, Dorfmuller P, Price LC, Huertas A, Hammad H, Lambrecht B, Simonneau G, Launay JM, Cohen-Kaminsky S, Humbert M. C-kit positive cells accumulate in remodeled vessels of idiopathic pulmonary arterial hypertension. **Am J Respir Crit Care Med** 2011 Feb 4 [Epub ahead of print]; Tu L, Dewachter L, Gore B, Fadel E, Dartevelle P, Simonneau G, Humbert M, Eddahibi S, Guignabert C. Autocrine FGF2 Signaling Contributes to Altered Endothelial Phenotype in Pulmonary Hypertension. Am J Respir Cell Mol Biol 2010 Oct 29 [Epub ahead of print]; Humbert M, Sitbon O, Chaouat A, Bertocchi M, Habib G, Gressin V, Yaïci A, Weitzenblum E, Cordier JF, Chabot F, Dromer C, Pison C, Reynaud-Gaubert M, Haloun A, Laurent M, Hachulla E, Cottin V, Degano B, Jaïs X, Montani D, Souza R, Simonneau G. Survival in patients with idiopathic, familial, and anorexigen-associated pulmonary arterial hypertension in the modern management era. Circulation 2010; 122:156-63; Guignabert C, Tu L, Izikki M, Dewachter L, Zadigue P, Humbert M, Adnot S, Fadel E, Eddahibi S. Dichloroacetate treatment partially regresses established pulmonary hypertension in mice with SM22{alpha}-targeted overexpression of the serotonin transporter. FASEB J 2009; 23:4135-47; Izikki M, Guignabert C, Fadel E, Humbert M, Tu L, Zadigue P, Dartevelle P, Simonneau G, Adnot S, Maitre B, Raffestin B, Eddahibi S. Endothelial-derived FGF2 contributes to the progression of pulmonary hypertension in humans and rodents. J Clin Invest 2009; 119:512-23; Perros F, Montani D, Dorfmuller P, Durand-Gasselin I, Tcherakian C, Le Pavec J, Mazmanian M, Fadel E, Mussot S, Mercier O, Herve P, Emilie D, Eddahibi S, Simonneau G, Souza R, Humbert M. Platelet Derived Growth Factor expression and function in idiopathic pulmonary arterial hypertension. Am J Respir Crit Care Med 2008; 178:81-8.	Pulmonary hypertension; animal models; endothelial cells; smooth muscle cells; genetics; autoimmunity; growth factors; right-heart failure; experimental surgery; pulmonary vascular remodelingimmunology; innovative therapies	We currently have 6 PhD students and can host 2 more	The 2 topics are autoimmunity/immunology and remodeling/growth factors	We can host 2	Topics would be innovative therapies and translational medicine	pneumology, vascular	marc.humbert@abc.aphp.fr
768	Paris	de Saint Basile, geneviève	The goal of our research project is to further characterize the pathways regulating lymphocyte homeostasis and to identify new effectors involved in the cytotoxic machinery of lymphocytes. Three major objectives will be developed : 1-The search for new components of the cytotoxic machinery through the identification of proteins interacting with the effectors recently characterized. 2- The search for new components of the cytotoxic machinery and/or lymphocyte homeostasis through the identification of the causes leading to inherited forms of HLH, that are yet molecularly uncharacterized. 3-The use of murine models of these conditions, already available or in the process of generation, to better analyze the precise mechanisms leading of HLH onset and to test a new therapeutic approach based on IFNY neutralisation.	**1.** de Saint Basile G, Menasche G, Fischer A. Molecular mechanisms of biogenesis and exocytosis of cytotoxic granules. Nat Rev Immunol 2010;10:568-79. **2.** Cote M, Menager MM, Burgess A, Mahlaoui N, Picard C, Schaffner C, Al-Manjomi F, Al-Harbi M, Alangari A, Le Deist F, Gennery AR, Prince N, Cariou A, Nitschke P, Blank U, El-Ghazali G, Menasche G, Latour S, Fischer A, de Saint Basile G. Munc18-2 deficiency causes familial hemophagocytic lymphohistiocytosis type 5 and impairs cytotoxic granule exocytosis in patient NK cells. J Clin Invest 2009;119:3765-73. **3.** Menasche G, Menager MM, Lefebvre JM, Deutsch E, Athman R, Lambert N, Mahlaoui N, Court M, Garin J, Fischer A, de Saint Basile G. A newly identified isoform of Slp2a associates with Rab27a in cytotoxic T cells and participates to cytotoxic granule secretion. Blood 2008;112:5052-62. **4.** Menager MM, Menasche G, Romao M, Knapnougel P, Ho CH, Garfa M, Raposo G, Feldmann J, Fischer A, de Saint Basile G. Secretory cytotoxic granule maturation and exocytosis require the effector protein hMunc13-4. Nat Immunol 2007;8:257-67. **5.** Feldmann J, Menasche G, Callebaut I, Minard-Colin V, Bader-Meunier B, Le Clainche L, Fischer A, Le Deist F, Tardieu M, de Saint Basile G. Severe and progressive encephalitis as a presenting manifestation of a novel missense perforin mutation and impaired cytolytic activity. Blood 2005;105:2658-63. **6.** Feldmann J, Callebaut I, Raposo G, Certain S, Bacq D, Dumont C, Lambert N, Ouachee-Chardin M, Chedeville G, Tamary H, Minard-Colin V, Vilmer E, Blanche S, Le Deist F, Fischer A, de Saint Basile G. Munc13-4 is essential for cytolytic granules fusion and is mutated in a form of familial hemophagocytic lymphohistiocytosis (FHL3). Cell 2003;115:461-73.	Either one of the three objectives developped in the research project of the team	1	cell biologist, immunologist, molecular biology/genetic	1	cell biologist, immunologist, molecular biology/genetic	immunology	genevieve.de-saint-basile@inserm.fr

UMR643	Nantes	Vanhove, Bernard	autoimmunity		In vitro and in vivo identification and blockade of costimulatory molecules regulating Teff and Treg functions			1	Cell and molecular biology	immunology	Bernard.Vanhove@univ-nantes.fr
U631	Marseille	Ewbank, Jonathan	Dissecting innate immunity in the simple animal model, C. elegans	1. Couillault C, Pujol N, Reboul J, Sabatier L, Guichou JF, et al. (2004) TLR-independent control of innate immunity in Caenorhabditis elegans by the TIR domain adaptor protein TIR-1, an ortholog of human SARM. Nat Immunol 5: 488-494. 2. Pujol N, Cypowyj S, Ziegler K, Millet A, Astrain A, et al. (2008) Distinct Innate Immune Responses to Infection and Wounding in the C. elegans Epidermis. Curr Biol 18: 481-489. 3. Pujol N, Zugasti O, Wong D, Couillault C, Kurz CL, et al. (2008) Anti-fungal innate immunity in C. elegans is enhanced by evolutionary diversification of antimicrobial peptides. PLoS Pathog 4: e1000105. 4. Ziegler K, Kurz CL, Cypowyj S, Couillault C, Pophillat M, et al. (2009) Antifungal innate immunity in C. elegans: PKCdelta links G protein signaling and a conserved p38 MAPK cascade. Cell Host Microbe 5: 341-352. 5. Zugasti O, Ewbank JJ (2009) Neuroimmune regulation of antimicrobial peptide expression by a noncanonical TGF-beta signaling pathway in Caenorhabditis elegans epidermis. Nat Immunol 10: 249-256. 6. Dierking K, Polanowska J, Omi S, Engelmann I, Gut M, et al. (2011) Unusual Regulation of a STAT Protein by an SLC6 Family Transporter in C. elegans Epidermal Innate Immunity. Cell host & microbe 9: 425-435.	Investigation of molecular subversion of host innate immune pathways by pathogenic fungi.	1	Any	1	Molecular biology and/or fungal genetics	innate immunity	ewbank@ciml.univ-mrs.fr
U631	Marseille	PIERRE Philippe	Cell biology of Dendritic cells. Biochemical mechanisms of innate response to microbes.Antigen processing and presentation	PMID: 21642595, PMID: 21413007, PMID: 20962078, PMID: 19328667, PMID: 19305406, PMID: 19193853	Role of the unfolded protein response during microbial detection by Dendritic cells	1	Cell biology/immunology	1	Cell biology/immunology	anti- infectious immunology	pierre@ciml.univ-mrs.fr
U985-INSERM	Villejuif	BERNARD, Olivier	The overall aim of the team is to identify genetic abnormalities in human hematopoietic tumors and understand their participation to both normal and malignant hematopoiesis.	1. Quivoron, C., Couronne, L., Della Valle, V., Lopez, C. K., Plo, I., Wagner-Ballon, O., Do Cruzeiro, M., Delhommeau, F., Arnulf, B., Stern, M. H., Godley, L., Opolon, P., Tilly, H., Solary, E., Duffourd, Y., Dessen, P., Merle-Beral, H., Nguyen-Khac, F., Fontenay, M., Vainchenker, W., Bastard, C., Mercher, T., and Bernard, O. A. (2011). TET2 inactivation results in pleiotropic hematopoietic abnormalities in mouse and is a recurrent event during human lymphomagenesis. Cancer Cell 20, 25-38.7. 2. Cornejo MG, Mabialah V, Sykes SM, Khandan T, Lo Celso C, Lopez CK, Rivera-Muñoz P, Rameau P, Tothova Z, Aster JC, DePinho RA, Scadden DT, Gilliland DG, Mercher T. (2011). Crosstalk between NOTCH and AKT signaling during murine megakaryocyte lineage specification. Blood 118(5):1264-73. 3. Ragu, C., Elain, G., Mylonas, E., Ottolenghi, C., Cagnard, N., Daegelen, D., Passegue, E., Vainchenker, W., Bernard, O. A., and Penard-Lacronique, V. (2010). The transcription factor Srf regulates hematopoietic stem cell adhesion. Blood 116, 4464-4473. 4. Couronne, L., Lippert, E., Andrieux, J., Kosmider, O., Radford-Weiss, I., Penther, D., Dastugue, N., Mugneret, F., Lafage, M., Gachard, N., Nadal, N., Bernard, O. A., and Nguyen-Khac, F. (2010). Analyses of TET2 mutations in post-myeloproliferative neoplasm acute myeloid leukemias. Leukemia 24, 201-203. 5. Mercher, T., Raffel, G. D., Moore, S. A., Cornejo, M. G., Baudry-Bluteau, D., Cagnard, N., Jesneck, J. L., Pikman, Y., Cullen, D., Williams, I. R., Akashi, K., Shigematsu, H., Bourquin, J. P., Giovannini, M., Vainchenker, W., Levine, R. L., Lee, B. H., Bernard, O. A., and Gilliland, D. G. (2009). The OTT-MAL fusion oncogene activates RBPJ-mediated transcription and induces acute megakaryoblastic leukemia in a knockin mouse model. J Clin Invest 119, 852-864. 6. Delhommeau, F., Dupont, S., Della Valle, V., James, C., Trannoy, S., Masse, A., Kosmider, O., Le Couedic, J. P., Robert, F., Alberdi, A., Lecluse, Y., Plo, I., Dreyfus, F. J., Marzac, C., Casadevall, N., Lacombe, C., Romana, S. P., Dessen, P., Soulier, J., Viguie, F., Fontenay, M., Vainchenker, W., and Bernard, O. A. (2009). Mutation in TET2 in myeloid cancers. N Engl J Med 360, 2289-2301.	Test and analyze the cooperation between TET2 inactivation and other oncogenes. We are interested in the associations observed in humans or identified in our mouse models. Follow-up the molecular analyses of malignant megakaryoblasts to identify oncogenic and cooperating hits.	3	Genomic, mouse analyses, bioinformatic, etc	3	Genomic, mouse analyses, bioinformatic, etc	hematology, cancer	olivier.bernard@inserm.fr
CIML UMR 631	Marseille	Hai-Tao HE & Didier MARGUET	We study the immune (particularly T) cell signal transduction using state-of-the-art biophysical and imaging technologies. The two major focuses in the group are (i) the molecular basis of T cell antigen receptor (TCR) triggering upon engagement with pMHC and (ii) how the Ras signalosome converts analog input into digital molecular response.	(1) Lenne PF*, Wawrezinieck L*, Conchonaud F, Wurtz O, Boned A, Guo XJ, Rigneault H, He HT, Marguet D. Dynamic molecular confinement in the plasma membrane by microdomains and the cytoskeleton meshwork. **EMBO J** 2006 *25* :3245-56 (2) Chakrabandhu K, Hérincs Z, Huault S, Dost B, Peng L, Conchonaud F, Marguet D, He HT, Hueber AO. Palmitoylation is required for efficient Fas cell death signaling. **EMBO J** 2007 *26* :209-20 (3) Lasserre R, Guo XJ, Conchonaud F, Hamon Y, Hawchar O, Bernard AM, M'Homa Soudja S, Lenne PF, Rigneault H, Olive D, Bismuth G, Nunes JA, Payrastre B, Marguet D, He HT. Raft nanodomains contribute to Akt/PKB plasma membrane recruitment and activation. **Nat Chem Biol** 2008 *4* :538-47 (4) Sergé A, Bertaux N, Rigneault H, Marguet D. Dynamic multiple-target tracing probes spatiotemporal cartography of cell membranes. **Nat Methods** 2008 *5* :687-94 Epub 2008 Jul 6. (5) He HT, Marguet D Detecting nanodomains in living cell membrane by fluorescence correlation spectroscopy **Ann Rev Phys Chem** 2011 *62* :417-36 (6) Guia S, Jaeger BN, Piatek S, Mailfert S, Trombik T, Fenis A, Chevrier N, Kerdiles YM, Walzer T, Marguet D, Vivier E, Ugolini S Activating receptor confinement at the plasma membrane controls Natural Killer cell tolerance **Science Signaling** 2011 *4* :ra21	(1) Organization and conformation dynamics of the TCR/CD3 complex responsible for activation of the antigen receptor upon ligand binding. (2) Molecular dynamics of protein-protein interactions by superresolution microscopy and Fluorescence Correlation Spectroscopy related methods on Ras signalosome	1	cell biologist	1 1	immunologist biophysist	immunology	marguet@ciml.univ-mrs.fr, he@ciml.univ-mrs.fr

INSERM UMR 643 "Center for Research in Transplantation and Immunology" **équipe 1**	Nantes	Ignacio ANEGON	a) CD8+ Tregs in rodents and humans. b) Tolerogenic DCs by treatment with heme oxygenase-1 or carbon monoxide. c) Genenetic engineering of cells (gene therapy) and rats (transgenic and KO) using ZFNs.	1) Guillot, C., C. Guillonneau, P. Mathieu, C. Gerdes, S. Ménoret, C. Braudeau, L. Tesson, K. Renaudin, M. C. Castro, P. Lowenstein, I. Anegon. Prolonged blockade of CD40-CD40L interactions by gene transfer of CD40Ig results in long-term heart allograft survival and donor-specific hyporesponsiveness but does not prevent chronic rejection. 2002. J. Immunol. 168:1600-1699. 2) Carole Guillonneau 1, Cédric Louvet 1, Karine Renaudin, Jean-Marie Heslan, Michèle Heslan, Caroline Vignes, Cécile Guillot, Yongwon Choi, Larry Turka, Maria-Cristina Cuturi, Ignacio Anegon 2 and Régis Josien 2. The role of TNF-related activation-induced cytokine (TRANCE) – receptor activating NF- B (RANK) interaction in acute allograft rejection and CD40L-independent chronic allograft rejection. 2004. J. Immunol. 172:1619-1629. 3) Carole Guillonneau, Venceslas Aubry, Karine Renaudin, Céline Séveno, Claire Usal, Katsunari Tezuka, Ignacio Anegon. Inhibition of chronic rejection and development of tolerogenic T cells after ICOS-ICOSL and CD40-CD40L costimulation blockade. 2005. Transplantation. 80:255-63. 4) C. Guillonneau, M. Hill, F-X. Hubert, E. Chiffoleau, C. Hervé, X-L Li, M. Heslan, C. Usal, L. Tesson, S. Ménoret, A. Saoudi, B. Le Mauff, R. Josien, M. C. Cuturi and I. Anegon. CD40lg treatment results in allograft acceptance mediated by CD8+CD45RClow T cells, IFN and indoleamine 2,3 dioxygenase. 2007. J. Clin. Invest. 117 :1096-1106. 5) C. Guillonneau1, C. Séveno1, A-S. Dugast, X-L. Li, K. Renaudin, F. Haspot, C. Usal, J. Véziers, I. Anegon2 and B. Vanhove2. Anti-CD28 antibodies modify regulatory mechanisms and reinforce tolerance in CD40lg-treated heart allograft recipients. 2007. J. Immunol. 179: 8164-8171. 6) X-L. Li, S. Ménoret, S. Bezie, L. Caron, D. Chabannes, M. Hill, F. Halary, M. Angin, M. Heslan, C. Usal, L. Liang, C. Guillonneau, B. Le Mauff, M-C. Cuturi, R. Josien, I. Anegon. Mechanism and localization of CD8 regulatory T cells in a heart transplant model of tolerance. 2010. J. Immunol. 185:823-33.	a) phenotype and function of CD8+ Tregs in transplanted and autoimmune patients. b) optimization of homologous recombination in rats using ZFNs or TALENs	a) 1. b)1.	a) immunologist. b) molecular biologist.	a) 1. b)1.	a) immunologist. b) molecular biologist.	immunology	Ignacio.Anegon@univ-nantes.fr
U1013	Paris	VAN ENDERT, Peter	antigen processing		Team focusing on antigen processing including cell biology of cross-presentation and processing proteases as well as on type 1 diabetes	2	cell biologist and/or immunologist	2	cell biologist and/or immunologist	immunology	peter.van-endert@inserm.fr
Macrophages and Development of Immunity' Unit, Institut Pasteur	Paris	Herbomel Philippe	Type 1 diabetes	Murayama E., Kissa K., Zapata A., Mordelet E., Briolat V., Lin HF., Handin R.I., Herbomel P. (Déc. 2006). Tracing hematopoietic precursor migration to successive hematopoietic organs during zebrafish development. *Immunity* 25, 963-75	In vivo emergence and fate of hematopoietic stem cells	1	any	1	cell biologist or physicist	hematology, development	herbomel@pasteur.fr
CRCL INSERM U1052 CNRS 5286	Lyon	CAUX Christophe, BLAY Jean-Yves	Blood DC in cancer	1- Labidi-Galy SI., et al. Systemic and local dysfunctions of plasmacytoid dendritic cells in ovarian carcinoma could contribute to immune tolerance. Cancer Research, 171:5423-34, 2011. 2-Sisirak V, et al. CCR6/CCR10-mediated plasmacytoid dendritic cells recruitment to inflamed epithelia following instruction in lymphoid organs. Blood, in Press, 2011. 3-Faget J., et al. Early detection of tumor cells by innate immune cells leads to Treg recruitment through CCL22 production by tumor cells. Cancer Res.171:6143-52, 2011. 4- Hirsch I, et al. Impaired TLR7 and TLR9 signaling: from chronic viral infections to cancer. Trends Imumnol, 31(10):391-7, 2010. 5-Perrot I, et al. TLR3 on mDC and RIG-I on NK cells engagement by dsRNA are required for optimal innate immune cell activation. J Immunol 185(4):2080-8, 2010. 6-Gobert M, et al. Regulatory T cells recruited through CCL22/CCR4 are selectively activated in lymphoid infiltrates surrounding primary breast tumors and lead to an adverse clinical outcome, Cancer Res., 69: 2000-9, 2009	- phenotypic profile of blood DCs in cancer patients (mainly costimulatory/inhibitory molecules / B7 family)- functional assays of blood DCs in cancer patients (phagocytic skills, lymphocyte stimulation/proliferation, cytokine production, etc)	1	immunologist	**0**		immunology cancer	
U745	Paris	N Cartier	Gene therapy for CNS diseaese based on : 1) lentiviral gene transfer in hematopoietic stem cells; 2) direct AAV gene transfer to the brain; 3) optimization of brain delivery (blood brain barrier targeting, aav serotype selection, intraveinous or intrathecal gene delivery. From preclinical proof of concept in rodents and primates to clinical application.	Asheuer M, Pflumio F, Benhamida S, Dubart-Kupperschmitt A, IMAI I, Aubourg P, Cartier N. Human CD34+ cells differentiate into brain microglia and express recombinant therapeutic protein : an approach to gene delivery into the central nervous system Proc Natl Acad Sci USA, 2004 , 101 : 3557-3562Sevin C, Benraiss A, DeDeyn P, Bonnin D, Vannier MT, Moullier P, Gieselmann V, Aubourg P., Cartier N. AAV5-mediated delivery of human aryl sulfatase A (ARSA) prevents sufatide storage and neuropathological phenotype in metachromatic leukodystrophy (MLD) mice Hum Mol Genet, 2006 :15 :53-64 Cartier N, Hacein-Bey-Abina S, Bartholomä C, Veres G, Schmidt M, Kutschera I, Vidaud M, Dal-Cortivo L, Caccavelli L, Malhaoui N, Kiermer V, Mittelstaedt D, Bellesme C, Audat F, Blanche S, Audit M, l'Homme B, Bougnères P, Fischer A, Von Kalle C, Cavazzana-Calvo M, Aubourg P. Hematopoietic Stem Cell Gene Therapy With Lentiviral Vector in Xadrenoleukodystrophy Science, 2009 : 326(5954):818-23. Marie-Anne Colle*, Françoise Piguet*, Lise Bertrand, Sylvie Raoul, Ivan Bieche, Laurence Dubreuil, Didi Sloothaak, Philippe Moullier, Patrick Aubourg, Yan Cherel, Nathalie Cartier*, Caroline Sevin*. Intracerebral delivery of AAV2-5 vector encoding human ARSA in non-human primates : transgene expression and bioactivity Hum Mol Genet. 19(1):147-58. 2010. Eloise Hudry,Debby Van Dam, Wim Kulik, Peter Paul De Deyn, Femke S. Stet, Ornella Ahouansou, Abdellatif Benraiss, André Delacourte, Pierre Bougnères, Patrick Aubourg, Nathalie Cartier. Adeno associated vector gene therapy with cholesterol 24-hydroxylase reduces the amyloid pathology before or after the onset of amyloid plaques in mouse models of Alzheimer disease. Mol Ther. 2010 : 18 : 44-59. Cavazzana-Calvo M, Payen E, Negre O, Wang G, Hehir K, Fusil F, Down J, Denaro M, Brady T, Westerman K, Cavallesco R, Gillet-Legrand B, Caccavelli L, Sgarra R, Maouche-Chrétien L, Bernaudin F, Girot R, Dorazio R, Mulder GJ, Polack A, Bank A, Soulier J, Larghero J, Kabbara N, Dalle B, Gourmel B, Socie G, Chrétien S, Cartier N, Aubourg P, Fischer A, Cornetta K, Galacteros F, Beuzard Y, Gluckman E, Bushman F, Hacein-Bey-Abina S, Leboulch P. Transfusion independence and HMGA2 activation after gene therapy of human β-thalassaemia. Nature. 2010 : 467 : 318-22	preclinical proof of concept of efficacy of a gene therapy approach for neurodegenerative diseases	2	cell and molecular biology	3	biochemistry, molecular biology, neuropathology, animal behavior analysis		nathalie.cartier@inserm.fr

UMR 892 (Inserm, CNRS, Université) team 6	Nantes	JACQUES, Yannick	The IL-15 system: structure, function, regulation and immunointervention in inflammation and cancer.	(1) Mortier, E, Bernard, J, Plet, A, Jacques, Y. (2004) natural, proteolytic release of a soluble form of human IL-15ra that behaves as a specific, high affinity Interleukin-15 antagonist. J Immunol, 173 : 1681-1688. (2) Mortier E, Quemener A, Vusio P, Boublik I, Grotzinger J, Plet A, Jacques Y.(2006) The soluble IL-15Ra sushi domain acts as a selective and potent agonist of IL-15 action through the IL-15Rb/g complex : conception of hyper-agonist IL-15-IL-15Ra fusion proteins. J Biol Chem, 281 : 1612-1619. (3) 180 Bouchaud G, Garrigue-Antar L, Solé V, Quemener A, Boublick Y, Mortier E, Perdreau H, Jacques Y*, Plet A* (2008) The exon-3 domain of IL-15Ra contributes to IL-15 high-affinity binding and is crucial for the IL-15 antagonistic effect of soluble IL-15Ra. J Mol Biol, 382, 1-12 (4) 184 Bessard A, Solé V, Bouchaud G, Quemener A*, Jacques Y* (2009) Antitumor activity of RLI, an IL-15 fusion protein, in metastatic melanoma and colorectal cancer. Mol Cancer Therap, 8 :2736-45 (5) 185 Bouchaud G, Mortier E, Flamant M, Plet A, Galmiche JP, Jacques Y*, Boureille A* (2010) Interleukin-15 and its soluble receptor sIL-15Ralpha are implicated in the response to infliximab in Crohn's disease. Gastroenterology, 138 (7): 2378-87 (6) 187 Perdreau H, Mortier E, Bouchaud G, Solé V, Boublik Y, Plet A, Jacques Y (2010) Different dynamics of IL-15R activation following IL-15 cis- or trans presentation. Eur Cyt Netw. 21(4):297-307.	Analysis of the dynamics of IL-15 receptor chains oligomerization at the cell surface.	1	biochemist, immunologist			immunology, cancer	Yannick.Jacques@univ-nantes.fr
UMR_S 940	Paris	Mooney, Nuala	We study the role of endothelial cells as targets for HLA alloantibodies and as antigen presenting cells in acute and chronic rejection of renal transplants	Taflin C, Favier B, Baudhuin J, Savenay A, Hemon P, Bensussan A, Charron D, Glotz D, Mooney N. Human endothelial cells generate Th17 and regulatory T cells under inflammatory conditions. Proc Natl Acad Sci USA 2011 Feb 15; 108 (7) 2891-6. Zilber, MT, Setterblad N, Vasselon T, Doliger C, Charron D, Mooney N & Gelin C (2005) MHC class II/CD38/CD9: a lipid raft-dependent signaling complex in human monocytes Blood 2005 Nov 1;106(9):3074-81Lefaucheur, C., C. Antoine, C. Suberbielle, and D. Glotz. 2011. Mastering the Risk of HLA Antibodies in Kidney Transplantation: An Algorithm Based on Pretransplant Single-Antigen Flow Bead Techniques. Am J Transplant 11:1592-1598. Bécart S., Setterblad N, Ostrand-Rosenberg S, Ono S.J., Charron D and Mooney N (2003) Intracytoplasmic domains of MHC class II molecules are essential for lipid raft-dependent signalling. J. Cell Science, 116:2565-75. Lefaucheur, C., A. Loupy, G.S. Hill, J. Andrade, D. Nochy, C. Antoine, C. Gautreau, D. Charron, D. Glotz, and C. Suberbielle-Boissel. 2010. Preexisting donor-specific HLA antibodies predict outcome in kidney transplantation. J Am Soc Nephrol 21:1398-1406	Immunological mechanisms of rejection of renal transplants	1	Immunology	1	Immunology	immunology	Nuala.Mooney@univ-paris-diderot.fr
U1019	Lille	Tsicopoulos Anne	The pulmonary Immunity team is interested in the regulation of the adaptive pulmonary immunity in particular in allergic diseases and asthma by NLR, IL-33, NK cells, and obesity	Chang Y, Sénéchal S, de Nadai P, Chenivesse C, Gilet J, Vorng H, Legendre B, Tonnel AB, Wallaert B, Lassalle P, Tsicopoulos A. Diesel exhaust exposure favors TH2 cell recruitment in nonatopic subjects by differentially regulating chemokine production. J Allergy Clin Immunol. 2006;118(2):354-60. de Nadaï P, Charbonnier AS, Chenivesse C, Sénéchal S, Fournier C, Gilet J, Vorng H, Chang Y, Gosset P, Wallaert B, Tonnel AB, Lassalle P, Tsicopoulos A. Involvement of CCL18 in allergic asthma. J Immunol. 2006 ;176(10):6286-93.Gilet J, Chang Ying, Chenivesse C, Legendre B, Vorng H, Duez C, Wallaert B, Porte H, Senechal S, Tsicopoulos A. Role of CCL17 in the generation of cutaneous inflammatory reactions in hu-PBMC-SCID mice grafted with human skin, J Invest Dermatol, 2009, 129 :879-890.Ple C, Barrier M, Amniai L, Marquillies P, Bertout J, Tsicopoulos A, Walzer T, Lassalle P, Duez C. Natural killer cells accumulate in lung-draining lymph nodes and regulate airway eosinophilia in a murine model of asthma. Scand J Immunol. 2010 Aug;72:118-27. Chang Y, de Nadai P, Azzaoui I, Morales O, Delhem N, Vorng H, Tomavo S, Ait Yahia S, Zhang G, Wallaert B, Chenivesse C, Tsicopoulos A. The chemokine CCL18 generates adaptive regulatory T cells from memory CD4+ T cells of healthy but not allergic subjects. FASEB J. 2010; 24:5063-72. Azzaoui I, Ait Yahia S, Chang Y, Vorng H, Morales O, Fan Y, Delhem N, Ple C, Tonnel AB, Wallaert B, Tsicopoulos A. CCL18 differentiates dendritic cells in tolerogenic cells able to prime regulatory T cells in healthy subjects. Blood. 2011 Jul 29.	Role of the endothelial IL-33 transcription factor form in asthma			1	Immunology and cell biology	pneumology, immunology	Anne.Tsicopoulos@pasteur-lille.fr
U700	Paris	Pretolani Marina	Studies of the mechanisms involved in airway remodeling in asthma and COPD.	1. Ferhani N, Letuve S, Kozhich A, Thibaudeau O, Grandsaigne M, Maret M, Dombret MC, Sims GP, Kolbeck R, Coyle AJ, Aubier M, Pretolani M. Expression of high-mobility group box 1 and of receptor for advanced glycation end products in chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2010 May 1;181(9):917-27. ` 2. Létuvé S, Kozhich A, Humbles A, Brewah Y, Dombret MC, Grandsaigne M, Adle H, Kolbeck R, Aubier M, Coyle AJ, Pretolani M. Lung chitinolytic activity and chitotriosidase are elevated in chronic obstructive pulmonary disease and contribute to lung inflammation. Am J Pathol. 2010 Feb;176(2):638-49. 3. Létuvé S, Kozhich A, Arouche N, Grandsaigne M, Reed J, Dombret MC, Kiener PA, Aubier M, Coyle AJ, Pretolani M. YKL-40 is elevated in patients with chronic obstructive pulmonary disease and activates alveolar macrophages. J Immunol. 2008 Oct 1;181(7):5167-73. 4. Druilhe A, Zahm JM, Benayoun L, El Mehdi D, Grandsaigne M, Dombret MC, Mosnier I, Feger B, Depondt J, Aubier M, Pretolani M. Epithelium expression and function of retinoid receptors in asthma. Am J Respir Cell Mol Biol. 2008 Mar;38(3):276-82 5. Chupp GL, Lee CG, Jarjour N, Shim YM, Holm CT, He S, Dziura JD, Reed J, Coyle AJ, Kiener P, Cullen M, Grandsaigne M, Dombret MC, Aubier M, Pretolani M,* Elias JA*. A chitinase-like protein in the lung and circulation of patients with severe asthma. N Engl J Med. 2007 Nov 15;357(20):2016-27. * co-senior authors 6. Pégorier S, Arouche N, Dombret MC, Aubier M, Pretolani M. Augmented epithelial endothelin-1 expression in refractory asthma. J Allergy Clin Immunol. 2007 Dec;120(6):1301-7.	To examine alterations in the phenotype, activation and differentiation of fibroblasts isolated from bronchial biopsies of asthmatics of variable severity and of patients with COPD. Stategies will include : primary cell cultures, tests of activation, migration and proliferation and DNA chips. A bio-bank of frozen cells from different patients is aready available on-site and it is regularly implemented.			1	cell biologist/ molecular biologist	pneumology	marina.pretolani@inserm.fr
U1016	Paris	PORTEU Françoise	Signaling pathways in hematopoietic. stem cells and their niche. Identification of new targets and pathways. Animals models	Frisan et al. Haematologica. 2010, 95 :1964-8. Pawlikowska et al., Cell Death and Diff. 2010, 17:1739. Guihard et al. , Blood. 2010 115:3686. Letourneux et al; Embo J. 2006, 25:737.Hamelin et al.; Blood.2006, 107:3106. Garcia et al., Embo J. 2002, 21:5151	Cytokine signaling and genomic stability in HSCs Role of ERKs in HSCs/niche interaction and HSC development	1	Cell biologist	1	Hematologist. Cell biologist Animal handling.	hematology, development	francoise.porteu@inserm.fr

U967	Paris	ROMEO Paul-Henri	This team is working on hematopoiesis. This team has recently shown that a transcription factor, TIF1γ, has a major role in hematopoietic stem cells (HSCs) and during inflammation. The research performed aims at the characterization of the molecular and cellular pathways regulated by TIF1γ in HSCs and during inflammation.	Kusy S, Gault N, Ferri F, Lewandowski D, Barroca V, Jaracz-Ros A, Losson R and Romeo PH Adult hematopoiesis is regulated by TIF1γ, a repressor of TAL1 and PU.1 transcriptional activity, Cell Stem Cell, 2011, 4: 412-425 Kusy S., Gerby B., Goardon N., Gault N., Ferri F., Gérard D., Armstrong F., Ballerini P., Cayuela JM., Baruchel A., Pflumio F. and Romeo PH. NKX3.1 is a direct TAL1 target gene that médiates prolifération of TAL1-expressing human T-ALL. J.Exp.Med., 2010, 207: 2141-56. Lewandowski D, Barroca V, Ducongé F, Bayer J, Van Nhieu JT, Pestourie C, Fouchet P, Tavitian B, Romeo PH. In vivo cellular imaging pinpoints the role of reactive oxygen species in the early steps of adult hematopoietic reconstitution. Blood, Plenary Paper. 2010, 115: 443-52. Kadri Z, Shimizu R, Ohneda O, Maouche-Chretien L, Gisselbrecht S, Yamamoto M, Romeo PH, Leboulch P, Chretien S. Direct binding of pRb/E2F-2 to GATA-1 regulates maturation and terminal cell division during erythropoiesis. PLoS Biol. 2009 Jun 9;7(6):e1000123. Goardon N., Lambert JA., Rodriguez P., Nissaire P., Herblot S., Thibault P., Dumenil D., Strouboulis J., Romeo PH and Hoang T. ETO2 coordinates cellular proliferation and differentiation during erythropoiesis. EMBO J., 2006, 25: 357-366 (last two authors co-corresponding authors) Bourbie-Vaudaine S., Blanchard N., Hivroz C. and Romeo PH. Dendritic cells can turn CD4 T-lymphocytes into VEGF carrying cells by intercellular Neuropilin-1 transfer. J.Immunology, 2006, 177 : 1460-1469	Control of inflammation by hematopoietic stem cells and myeloid cells	1	Cell biologist	2	Regulation of transcription (1) and myeloid differentiation (2)	hematology, stem cells	paul-henri.romeo@cea.fr
INSERM U851	LYON	DEFRANCE Thierry	Physiology of the antibacterial B cell responses with a focus on T cell-independent B cell memory and plasma cells	1. Defrance et al. Curr. Opin. Immunol. 2011.23: 330. 2. Taillardet et al. J. Infect. Dis. 2010. 202: 470. 3. Taillardet et al. Blood. 2009. 114: 4432. 4. Thaunat et al. Blood. 2010. 116: 515.5. Genestier et al. J. Immunol. 2007. 178: 7779. 6. Pelletier et al. J. Immunol. 2006. 176: 1340.	B cell derived cytokines produced in response to T cell-dependent and T cell-independent vaccines and during bacterial infections. Targeting of protein antigens to the T cell-independent arm of the humoral response	1	immunologist	1	immunologist	anti-infectious immunology	thierry.defrance@inserm.fr
INSERM U940, IUH, Hôpital Saint-Louis	Paris, France	TOUBERT Antoine	Immunobiology of Hematopietic Stem Cell Transplantation in Human, anti-leukemic immune responses, Physiopathology of NK immune responses, Autoimmunity	J. Immunol., 2006; 176:5662-5670. Gastroenterology, 2007; 132 : 2346-2358. Blood 2009; 114 : 5216-24. Blood 2009; 113 : 6477-6484. Blood 2011; 173 : 1021-9. Gastroenterology 2011 ; 141 : 217-226.	Immune responses after allogeneic HSCT, regulation of anti-leukemic immune responses, Autoimmunity (Crohn's disease), thymic function in the regulation of immune responses and vaccionation	1	Cellular and molecular Biology	1	Cellular and Molecular Biology	immunology	antoine.toubert@univ-paris-diderot.fr
	Genoble	Jean-Luc COLL	Mirian Hayashi (Sao Paulo) identification and characterization of natural molecules with potential pharmaceutical applications, scuh as crotamine, a potential theratogenic compound	• Pereira A, Kerkis A, Hayashi MA, Pereira AS, Silva FS, Oliveira EB, Prieto da Silva AR, Yamane T, Rádis-Baptista G, Kerkis I. Crotamine toxicity and efficacy in mouse models of melanoma. Expert Opin Investig Drugs. 2011 Sep;20(9):1189-200. • Morais KL, Hayashi MA, Bruni FM, Lopes-Ferreira M, Camargo AC, Ulrich H, Lameu C. Bj-PRO-5a, a natural angiotensin-converting enzyme inhibitor, promotes vasodilatation mediated by both bradykinin B $_2$and M1 muscarinic acetylcholine receptors. Biochem Pharmacol. 2011 Mar 15;81(6):736-42. Epub 2010 Dec 24. • Negraes PD, Lameu C, Hayashi MA, Melo RL, Camargo AC, Ulrich H. The snake venom peptide Bj-PRO-7a is a M1 muscarinic acetylcholine receptor agonist. Cytometry A. 2011 Jan;79(1):77-83. • Hayashi MA, Nascimento FD, Kerkis A, Oliveira V, Oliveira EB, Pereira A, Rádis-Baptista G, Nader HB, Yamane T, Kerkis I, Tersariol IL. Cytotoxic effects of crotamine are mediated through lysosomal membrane permeabilization. Toxicon. 2008 Sep 1;52(3):508-17. Epub 2008 Jul 10. • Nascimento FD, Hayashi MA, Kerkis A, Oliveira V, Oliveira EB, Rádis-Baptista G, Nader HB, Yamane T, Tersariol IL, Kerkis I. Crotamine mediates gene delivery into cells through the binding to heparan sulfate proteoglycans. J Biol Chem. 2007 Jul 20;282(29):21349-60. Epub 2007 May 9. • Murayama N, Hayashi MA, Ohi H, Ferreira LA, Hermann VV, Saito H, Fujita Y, Higuchi S, Fernandes BL, Yamane T, de Camargo AC. Cloning and sequence analysis of a Bothrops jararaca cDNA encoding a precursor of seven bradykinin-potentiating peptides and a C-type natriuretic peptide. Proc Natl Acad Sci U S A. 1997 Feb 18;94(4):1189-93.	The main objective of the present project is to exchange/share the knowledge of each participant Institution on the study of natural snake toxins, namely crotamine, with potential application for cancer therapy and/or diagnosis. The proponent has a wide experience in the toxin fields, even by using different tools/technologies, which will be complemented by the fundamental collaboration of Dr JL Coll, who will provide the access to advanced and unique optical imaging methods for functional and molecular imaging.	1	cell and molecular biologist with some knowledge in pharmacology	1	cell and molecular biologist with knowledge in pharmacology	immunology cancer	Jean-Luc.Coll@ujf-grenoble.fr
INSERM U1043	Toulouse	Jean-Charles Guéry	Our research projects focus on the two following themes: 1) the impact of estrogens on adaptive and innate immune responses and their implication in the pathogenesis of autoimmune diseases, and 2) the understanding of Ca-signaling in Th2 cells and its implication in the treatment of allergic asthma.	Seillet C, Laffont S, Trémollières F, Rouquié N, Ribot C, Arnal JF, Douin-Echinard V, Gourdy P and JC Guéry. The TLR-mediated response of plasmacytoid dendritic cells is positively regulated by estrogens in vivo through cell-intrinsic estrogen receptor alpha-signaling. Blood. 2011 (under revision) Lélu K, Laffont S, Delpy L, Paulet PE, Périnat T, Tschanz SA, Pelletier L, Engelhardt B, and Guéry JC. Estrogen receptor α-signaling in T lymphocytes is required for estradiol-mediated inhibition of Th1 and Th17 cell differentiation and protection against EAE. J. Immunol. 2011 Sep 1;187(5):2386-93. Lélu K, Delpy L, Robert V, Foulon E, Laffont S, Pelletier L, Engelhardt B, Guéry JC. Endogenous estrogens, through estrogen receptor α, constrain autoimmune inflammation in female mice by limiting CD4+ T-cell homing into the CNS. Eur J Immunol. 2010 Dec;40(12):3489-98. doi: 10.1002/eji.201040678. Laffont S, Seillet C, Ortaldo J, Coudert JD, Guéry JC. Natural killer cells recruited into lymph nodes inhibit alloreactive T cell activation through perforin-mediated killing of donor allogeneic dendritic cells. Blood. 2008 Aug 1;112(3):661-71. Douin-Echinard V, Laffont S, Seillet C, Delpy L, Krust A, Chambon P, Gourdy P, Arnal JF, Guéry JC. Estrogen Receptor {alpha}, but Not {beta}, Is Required for Optimal Dendritic Cell Differentiation and CD40-Induced Cytokine Production. J Immunol. 2008 Mar 15;180(6):3661-9. Laffont S, Coudert JD, Garidou L, Delpy L, Wiedemann A, Demur C, Coureau C, Guéry JC. CD8+ T-cell-mediated killing of donor dendritic cells prevents alloreactive T helper type-2 responses in vivo. Blood. 2006 Oct 1;108(7):2257-64.	Estrogens in immunity and autoimmune diseases (AID): Despite the obvious impact of estrogens on the pathophysiology of AID, the cellular targets and the molecular mechanisms are still unclear. Using in vivo experimental models, we provided evidence for anti-inflammatory or immuno-stimulatory effects of E2 on immune responses and autoimmunity. Although it is clear that these effects are mediated through ER alpha-signaling, the underlying mechanisms responsible for these paradoxical actions of estrogens on autoimmune diseases are still ill defined. The aims of our research project are now to determine the respective roles of two recognized cellular targets of E2 through the inactivation of endothelium and/or hematopoietic ER alpha in the protective effect of estrogens in CNS autoimmunity. Concerning the immuno-stimulatory effect of E2 on immune responses and autoimmunity, we are currently studying the role of ligand inducible ER alpha-activation in DC biology in both mouse and Human, with a particular focus on the effect of E2 on TLR-mediated responses in plasmacytoid DCs.	1	Immunologist	1	immunologist/cell biologist	immunology	Jean-Charles.Guery@inserm.fr
INSERM UMR 643 "Center for Research in Transplantation and Immunology" **équipe 4**	Nantes	Sophie BROUARD	The objectives is to explore B cells in patients with operational tolerance after a kidney transplantation; the objective is to look at the phenotype, the function and the immunosuppressive properties of these cells in blood of this cohorte of unique and rare patients	1. Comparison of transcriptional and blood cell phenotypic markers between operationally tolerant liver and kidney recipients. JJ. Lozano, A. Pallier, MM. Llordella, M. López, M. Giral, MC. Londoño, A. Rimola, JP. Soulillou, S. Brouard*, A. Sánchez-Fueyo*. (*equal contribution). Am J Transplant. 2011 Sep;11(9):1916-26. 2. Patients with drug-free long-term graft function display increased numbers of peripheral B cells with a memory and inhibitory phenotype A. Pallier, S. Hillion, R. Danger, M. Giral, M. Racapé, N. Degauque, E. Dugast, J. Ashton-Chess, S. Pettré, JJ. Lozano, R. Bataille, A. Devys, A. Cesbron-Gautier, C. Braudeau, C. Larrose, JP. Soulillou and S. Brouard. Kidney Int. 2010 Sep;78(5):503-13. 3. Indices of tolerance: development of cross-platform biomarkers to detect renal transplant tolerance in man. Pervinder Sagoo, Esperanza Perucha, Birgit Sawitzki, Stefan Tomiuk, David A. Stephens, Patrick Miqueu, Stephanie Chapman, Ligia Craciun, Ruhena Sergeant, Sophie Brouard, Flavia Rovis, Elvira Jimenez, Amany Ballow, Magali Giral, Irene Rebollo-Mesa, Alain Le Moine, Cecile Braudeau, Rachel Hilton, Bernhard Gerstmayer, Kasia Bourcier, Adnan Sharif, Magdalena Krajewska, Collaborating Physicians: www.transplant-tolerance.org.uk, Graham M. Lord, Ian Roberts, Michel Goldman, Kathryn J. Wood, Kenneth Newell, Vicki Seyfert-Margolis, Laurence Turka, Anthony N. Warrens, Uwe Janssen, Hans-Dieter Volk, Jean-Paul Soulillou, Maria P. Hernandez-Fuentes, Robert I. Lechler. J Clin Invest. 2010 Jun 1;120(6):1848-61. 4. Regulatory, effector, and cytotoxic T cell profiles in long-term kidney transplant patients. Ashton-Chess J, Dugast E, Colvin RB, Giral M, Foucher Y, Moreau A, Renaudin K, Braud C, Devys A, Brouard* S, Soulillou JP*. (*equal contribution). J Am Soc Nephrol. 2009 May;20(5):1113-22. 5. Identification of a peripheral blood transcriptional biomarker panel for diagnosis and prediction of operational renal allograft tolerance. Brouard S, Mansfield E, Li L, Hsieh S, Dupont A, Zhang M, Giral M, Hsieh F, Sherlock G, Braudeau C, Ashton-Chess J, Baeten D, Louis S, Pallier A, Salvatierra O, Soulillou JP and M Sarwal. Proc Natl Acad Sci U S A. 2007 Sep 25;104(39):15448-53. 6. Clinical operational tolerance after kidney transplantation. G Roussey-Kesler, M Giral, A Moreau, JF Subra, C Legendre, C Noël, E Pilleboult, S Brouard and JP Soulillou. Am J Transplant. 2006 Apr;6(4):736-46.	B cells, tolerance, kidney transplantation	3	Immunologist	1	Immunologist	immunology	Sophie.Brouard@univ-nantes.fr

UMR_S 608 "Physiopathologie de l'Endothélium"	Marseille, France	Françoise Dignat-George	To study the mechanisms of endothelial lesion and regeneration and to transfer these knowledge for a better understanding of vascular disorders, the development of novel endothelial-driven biomarkers and therapeutic strategies based on biotherapies	Simoncini S, Njock M.S, Robert S, Camoin-Jau L, Sampol J, Harle J.R, Nguyen C, Dignat-George F, Anfosso F. (2009) TRAIL/Apo2L mediates the release of procoagulant endothelial microparticles induced by thrombin in vitro: a potential mechanism linking inflammation and coagulation. Circ Res 104, 943-51. Al-Massarani G, Vacher-Coponat H, Paul P, Arnaud L, Loundou A, Robert S, Moal V, Berland Y, Dignat-George F, Camoin-Jau L. (2009) Kidney transplantation decreases the level and procoagulant activity of circulating microparticles. Am J Transplant 9, 550-7. Thomas G.M, Panicot-Dubois L, Lacroix R, Dignat-George F, Lombardo D, Dubois C, (2009) Cancer cell-derived microparticles bearing P-selectin glycoprotein ligand 1 accelerate thrombus formation in vivo. J Exp Med 206, 1913-27. Harhouri K, Kebir A, Guillet B, Foucault-Bertaud A, Bardin N, Dignat-George F, and M Blot-Chabaud. Soluble CD146 displays angiogenic properties and promotes therapeutic angiogenesis in experimental hind limb ischemia. Blood, 6, 2010, 115, 3843-51.Bardin N, Dignat-George F and Blot-Chabaud M. CD146 short isoform increases the pro-angiogenic potential of endothelial progenitor cells in vitro and in vivo. Circ Res, 2010, 107, 66-75. Ligi I, Simoncini S, Tellier E, Vassallo PF, Sabatier F, Guillet B, Lamy E, Sarlon G, Quemener C, Bikfalvi A, Marcelli M, Pascal A, Dizier B, Simeoni U, Dignat-George F,Anfosso F. (2011) Switch toward angiostatic gene expression impairs the angiogenic properties of endothelial progenitor cells in low birth weight preterm infants. Blood. 11, 1699-709. Berda-Haddad Y, Robert S, Salers P, Zekraoui L, Farnarier C, Dinarello C, Dignat-George F, Kaplanski G. The sterile inflammation of endothelial cell-derived apoptotic bodies is mediated by interleukin-1a. PNAS. 2011. In press	Endothelial microparticles : Role in the transfer of biological information and novel biomarkers Endothelial Progenitors cells: form mechanisms of endothelial repair to therapeutic angiogenesis	2	cell biologist, Haematologist , vascular biology , animal models	2	cell biologist, Haematologist , vascular biology, animal models	vascular	francoise.dignat-george@univmed.fr
U1035	Bordeaux	MAHON François-Xavier	The team is involved for more than 10 years in clinical research regarding the efficacy of tyrosine kinase inhibitors (TKI) used in the treatment of Chronic Myeloid Leukemia (CML). In a bed-to-benchtop approach, as well as by using cell lines as models, we participated to the description of the different aspects of TKI effects, at the molecular and cellular level. Our research now focus on the mechanisms of resistance to TKI which characterize the leukemia stem cells.	Quantitative phosphoproteomics revealed interplay between Syk and Lyn in the resistance to nilotinib in chronic myeloid leukemia cells. Gioia, Leroy C, Drullion C, Lagarde V, Etienne G, Dulucq S, Lippert E, Roche S, Mahon FX, Pasquet JM. **Blood.** 2011 Aug 25;118(8):2211-21 / Discontinuation of imatinib in patients with chronic myeloid leukaemia who have maintained complete molecular remission for at least 2 years: the prospective, multicentre Stop Imatinib (STIM) trial. Mahon FX, Réa D, Guilhot J, Guilhot F, Huguet F, Nicolini F, Legros L, Charbonnier A, Guerci A, Varet B, Etienne G, Reiffers J, Rousselot P; Intergroupe Français des Leucémies Myéloïdes Chroniques. **Lancet Oncol**. 2010 Nov;11(11):1029-35. / The stem cell factor-c-KIT pathway must be inhibited to enable apoptosis induced by BCR-ABL inhibitors in chronic myelogenous leukemia cells. Belloc F, Airiau K, Jeanneteau M, Garcia M, Guérin E, Lippert E, Moreau-Gaudry F, Mahon FX. **Leukemia**. 2009 Apr;23(4):679-85 / Control of vertebrate multiciliogenesis by miR-449 through direct repression of the Delta/Notch pathway. Marcet B, Chevalier B, Luxardi G, Coraux C, Zaragosi LE, Cibois M, Robbe-Sermesant K, Jolly T, Cardinaud B, Moreilhon C, Giovannini-Chami L, Nawrocki-Raby B, Birembaut P, Waldmann R, Kodjabachian L, Barbry P. **Nat Cell Biol**. 2011 Jun;13(6):693-9 / miR-34b/miR-34c: a regulator of TCL1 expression in 11q- chronic lymphocytic leukaemia? Cardinaud B, Moreilhon C, Marcet B, Robbe-Sermesant K, LeBrigand K, Mari B, Eclache V, Cymbalista F, Raynaud S, Barbry P. **Leukemia**. 2009 Nov;23(11):2174-7. / Evidence that resistance to nilotinib may be due to BCR-ABL, Pgp, or Src kinase overexpression. Mahon FX, Hayette S, Lagarde V, Belloc F, Turcq B, Nicolini F, Belanger C, Manley PW, Leroy C, Etienne G, Roche S, Pasquet JM. **Cancer Res**. 2008 Dec 1;68(23):9809-16.	We recently showed that BCR-ABL, the oncogene responsible for the development of CML, activates or repress the expression of numerous genes in the cell line K562 and in primary CD34+ cells. Among them, a certain number of microRNAs (miRNAs) which clearly differentiate TKI treated- and non-treated cells. The functional consequences of these dys-regulations are not know and will constitute a part of the working program of the PhD student. The other part will concern the study of the molecular mechanisms responsible for the observed up- and down-regulations.	1	Molecular biologist			cancer	francois-xavier.mahon@umr5540.u-bordeaux2.fr
Inserm U1043	Toulouse	Vergnolle Nathalie	Characterization of mediators of inflammation and pain	Vergnolle et al Nat Med 2000, Cenac et al J Clin Invest 2007, Motta et al Gastroenterology 2011, D'Aldebert et al Gastroenterology 2011	gastrointestinal pathologies, proteases and protease inhibitors, calcium channels	2	Pharmacologist, Immunologist	2	Pharmacologists, Physiologists, Immunologists	immunology neurology	nathalie.vergnolle@inserm.fr
Inserm U1048	Toulouse	Bernard PAYRASTRE	Molecular mechanisms of platelet production and functions, phosphoinositides in signal transduction, cytoskeleton organization and intracellular trafficking .	1- Séverin S., Gratacap M-P. et al. Src homology 2 domain-containing inositol 5-phosphatase 1 is required for efficient platelet activation and thrombus growth. J. Clin. Invest. 2007, 117, 944-952. 2- Martin V., Guillermet-Guibert et al. Deletion of p110 beta isoform of phosphoinositide 3-kinase in platelets reveals its central role in heterotrimeric G protein and ITAM-signaling. Blood 2010, 115, 2008-2013. 3- Hnia K, Tronchère H, et al. The Phosphoinositide Phosphatase Myotubularin Controls Desmin Intermediate Filament Architecture and Mitochondrial Dynamics in human and mouse skeletal muscle. J. Clin. Invest. 2011, 121, 70-85. 4- Dupuis-Coronas S, Lagarrigue F et al. The NPM-ALK oncogene interacts, activates and uses PIKfyve to increase cell invasive properties. J. Biol. Chem. 2011, in press. 5- Lhermusier T, Van Rottem J et al. The Syk-kinase inhibitor R406 impairs platelet activation and monocyte tissue factor expression triggered by heparin-PF4 complex directed antibodies. J. Thromb. Haemost. 2011, in press. 6 - Ramel D, Lagarrigue F et al. Shigella flexneri Infection Generates the Lipid PI5P to Alter Endocytosis and Prevent Termination of EGFR Signaling. **Science Signal** 2011, 4, in press.	Molecular mechanisms of platelet production and functions, phosphoinositides in signal transduction, cytoskeleton organization and intracellular trafficking .			1	cell Biologist or medical/pharmaceutical studies + master degree in molecular/cellular Biology.	hemostasis	bernard.payrastre@inserm.fr
INSERM U773	PARIS	EL BENNA Jamel	The team studies the activation and regulation of the phagocyte and non phagocyte NADPH oxidase, an enzyme responsible for the ROS production during innate immunity and inflammation.	Dang PM, Stensballe A, Boussetta T, Raad H, Dewas C, Kroviarski Y, Hayem G, Jensen ON, Gougerot-Pocidalo MA, El-Benna J. A specific p47phox -serine phosphorylated by convergent MAPKs mediates neutrophil NADPH oxidase priming at inflammatory sites. **J Clin Invest**. 2006 Jul;116(7):2033-43. Raad H, Paclet MH, Boussetta T, Kroviarski Y, Morel F, Quinn MT, Gougerot-Pocidalo MA, Dang PM, El-Benna J. Regulation of the phagocyte NADPH oxidase activity: phosphorylation of gp91phox/NOX2 by protein kinase C enhances its diaphorase activity and binding to Rac2, p67phox, and p47phox. **FASEB J.** 2009 Apr;23(4):1011-22. Boussetta T, Raad H, Lettéron P, Gougerot-Pocidalo MA, Marie JC, Driss F, El-Benna J. Punicic acid a conjugated linolenic acid inhibits TNFalpha-induced neutrophil hyperactivation and protects from experimental colon inflammation in rats. **PLoS One**. 2009 Jul 31;4(7):e6458 Boussetta T, Gougerot-Pocidalo MA, Hayem G, Ciappelloni S, Raad H, Arabi Derkawi R, Bournier O, Kroviarski Y, Zhou XZ, Malter JS, Lu PK, Bartegi A, Dang,PM, El-Benna J. The prolyl isomerase Pin1 acts as a novel molecular switch for TNF{alpha}-induced priming of the NADPH oxidase in human neutrophils. **Blood.** 2010 Dec 23;116(26):5795-802. Kroviarski Y, Debbabi M, Bachoual R, Périanin A, Gougerot-Pocidalo MA, El-Benna J, My-Chan Dang P. Phosphorylation of NADPH oxidase activator 1 (NOXA1) on serine 282 by MAP kinases and on serine 172 by protein kinase C and protein kinase A prevents NOX1 hyperactivation. **FASEB J**. 2010 Jun;24(6):2077-92. Patel S, Djerdjouri B, Raoul-Des-Essarts Y, Dang PM, El-Benna J, Périanin A. Protein kinase B (AKT) mediates phospholipase D activation via ERK1/2 and promotes respiratory burst parameters in formylpeptide-stimulated neutrophil-like HL-60 cells. **J Biol Chem.** 2010 Oct 15;285(42):32055-63	Phosphorylation of p47phox in phagocytes and role in NOX2 activation;- Phosphorylation of NOXO and NOXA in epithelial cells and role in NOX1 activation; - Role of PLD in NADPH oxidase activation	1	Biochemist, immunologist, cell biologist	1	Biochemist, immunologist, cell biologist	immunology	jamel.elbenna@inserm.fr

U823	Grenoble	Marche, Patrice	Sudy of the immune system of the liver in Viral Hepatitis infections and in the development of primary liver cancer: liver lymphocytes functions and in situ proteomics.	1 Sturm, N. et al. Characterization and role of intra-hepatic regulatory T cells in chronic hepatitis C pathogenesis. J Hepatol 53, 25-35 (2010). 2 Sene, D. et al. Hepatitis C virus (HCV) evades NKG2D-dependent NK cell responses through NS5A-mediated imbalance of inflammatory cytokines. PLoS Pathog 6, e1001184 (2010). 3 Thuderoz, F. et al. Numerical Modelling Of The V-J Combinations Of The T Cell Receptor TRA/TRD Locus. PLoS Comput Biol 6, e1000682 (2010). 4 Villiers, C. et al. From Secretome Analysis to Immunology: Chitosan induces major alterations in the activation of dendritic cells via a TLR4-dependent mechanism. Mol Cell Proteomics 8, 1252-64 (2009). 5 Bonorino, P. et al. Fine characterization of intrahepatic NK cells expressing natural killer receptors in chronic hepatitis B and C. J Hepatol 51, 458-67 (2009). 6 Bonorino, P. et al. Features and distribution of CD8 T cells with human leukocyte antigen class I-specific receptor expression in chronic hepatitis C. Hepatology 46, 1375-86 (2007).	Analysis of liver immune infiltrates from surgical and biospsies of cirrhotic patients to define cells and proteins regulation inflammation and development of liver diseases (fibrosis, cancer).	1	Immunologist, Infectious Diseeases	1	Immunologist, Proteomics	anti- infectious immunology	Patrice.Marche@uif-grenoble.fr
U633	Paris	Michel PUCÉAT/Daniel ABERDAM	Our projects are mainly focused on the mechanisms underlying early cardiac development and specification. We are studying the interplay between transcription factors during the specification of the two heart lineages. Among them, we identified p63, a member of the p53 family, as a new major player in that field.	Michel Pucéat/Daniel Aberdam (U633, Paris) 1: Rouleau M, Medawar A, Hamon L, Shivtiel S, Wolchinsky Z, Zhou H, De Rosa L, Candi E, de la Forest Divonne S, Mikkola ML, van Bokhoven H, Missero C, Melino G, Pucéat M, Aberdam D. Tap63 is Important for Cardiac Differentiation of Embryonic Stem Cells and Heart Development. Stem Cells. 2011 Sep 2. [Epub ahead of print] 2: Blin G, Nury D, Stefanovic S, Neri T, Guillevic O, Brinon B, Bellamy V, Rücker-Martin C, Barbry P, Bel A, Bruneval P, Cowan C, Pouly J, Mitalipov S, Gouadon E, Binder P, Hagège A, Desnos M, Renaud JF, Menasché P, Pucéat M. A purified population of multipotent cardiovascular progenitors derived from primate pluripotent stem cells engrafts in postmyocardial infarcted nonhuman primates. J Clin Invest. 2010 Apr 1;120(4):1125-39. 3: Stefanovic S, Abboud N, Désilets S, Nury D, Cowan C, Pucéat M. Interplay of Oct4 with Sox2 and Sox17: a molecular switch from stem cell pluripotency to specifying a cardiac fate. J Cell Biol. 2009 Sep 7;186(5):665-73. 4: Blin G, Lablack N, Louis-Tisserand M, Nicolas C, Picart C, Pucéat M. Nano-scale control of cellular environment to drive embryonic stem cells selfrenewal and fate. Biomaterials. 2010 Mar;31(7):1742-50. 5: Leschik J, Stefanovic S, Brinon B, Pucéat M. Cardiac commitment of primate embryonic stem cells. Nat Protoc. 2008;3(9):1381-7. 6: Tomescot A, Leschik J, Bellamy V, Dubois G, Messas E, Bruneval P, Desnos M, Hagège AA, Amit M, Itskovitz J, Menasché P, Pucéat M. Differentiation in vivo of cardiac committed human embryonic stem cells in postmyocardial infarcted rats. Stem Cells. 2007 Sep;25(9):2200-5. 7: Zeineddine D, Papadimou E, Chebli K, Gineste M, Liu J, Grey C, Thurig S, Behfar A, Wallace VA, Skerjanc IS, Pucéat M. Oct-3/4 dose dependently regulates specification of embryonic stem cells toward a cardiac lineage and early heart development. Dev Cell. 2006 Oct;11(4):535-46. 8: Ménard C, Hagège AA, Agbulut O, Barro M, Morichetti MC, Brasselet C, Bel A, Messas E, Bissery A, Bruneval P, Desnos M, Pucéat M, Menasché P. Transplantation of cardiac-committed mouse embryonic stem cells to infarcted sheep myocardium: a preclinical study. Lancet. 2005 Sep 17-23;366(9490):1005-12. 9: Papadimou E, Ménard C, Grey C, Pucéat M. Interplay between the retinoblastoma protein and LEK1 specifies stem cells toward the cardiac lineage. EMBO J. 2005 May 4;24(9):1750-61. Michel Pucéat/Daniel Aberdam (U633, Paris) 1: Rouleau M, Medawar A, Hamon L, Shivtiel S, Wolchinsky Z, Zhou H, De Rosa L, Candi E, de la Forest Divonne S, Mikkola ML, van Bokhoven H, Missero C, Melino G, Pucéat M, Aberdam D. Tap63 is Important for Cardiac Differentiation of Embryonic Stem Cells and Heart Development. Stem Cells. 2011 Sep 2. [Epub ahead of print] 2: Blin G, Nury D, Stefanovic S, Neri T, Guillevic O, Brinon B, Bellamy V, Rücker-Martin C, Barbry P, Bel A, Bruneval P, Cowan C, Pouly J, Mitalipov S, Gouadon E, Binder P, Hagège A, Desnos M, Renaud JF, Menasché P, Pucéat M. A purified population of multipotent cardiovascular progenitors derived from primate pluripotent stem cells engrafts in postmyocardial infarcted nonhuman primates. J Clin Invest. 2010 Apr 1;120(4):1125-39. 3: Stefanovic S, Abboud N, Désilets S, Nury D, Cowan C, Pucéat M. Interplay of Oct4 with Sox2 and Sox17: a molecular switch from stem cell pluripotency to specifying a cardiac fate. J Cell Biol. 2009 Sep 7;186(5):665-73. 4: Blin G, Lablack N, Louis-Tisserand M, Nicolas C, Picart C, Pucéat M. Nano-scale control of cellular environment to drive embryonic stem cells selfrenewal and fate. Biomaterials. 2010 Mar;31(7):1742-50. 5: Leschik J, Stefanovic S, Brinon B, Pucéat M. Cardiac commitment of primate embryonic stem cells. Nat Protoc. 2008;3(9):1381-7. 6: Tomescot A, Leschik J, Bellamy V, Dubois G, Messas E, Bruneval P, Desnos M, Hagège AA, Amit M, Itskovitz J, Menasché P, Pucéat M. Differentiation in vivo of cardiac committed human embryonic stem cells in postmyocardial infarcted rats. Stem Cells. 2007 Sep;25(9):2200-5. 7: Zeineddine D, Papadimou E, Chebli K, Gineste M, Liu J, Grey C, Thurig S, Behfar A, Wallace VA, Skerjanc IS, Pucéat M. Oct-3/4 dose dependently regulates specification of embryonic stem cells toward a cardiac lineage and early heart development. Dev Cell. 2006 Oct;11(4):535-46. 8: Ménard C, Hagège AA, Agbulut O, Barro M, Morichetti MC, Brasselet C, Bel A, Messas E, Bissery A, Bruneval P, Desnos M, Pucéat M, Menasché P. Transplantation of cardiac-committed mouse embryonic stem cells to infarcted sheep myocardium: a preclinical study. Lancet. 2005 Sep 17-23;366(9490):1005-12. 9: Papadimou E, Ménard C, Grey C, Pucéat M. Interplay between the retinoblastoma protein and LEK1 specifies stem cells toward the cardiac lineage. EMBO J. 2005 May 4;24(9):1750-61.	Study of the function and regulation of p63 during cardiac fate in vivo by the use of transgenic mice and in vitro with embryonic stem cell model.			2	Cell biology and developmental biology (animal manipulation)		michel.puceat@inserm.fr
U.892 INSERM	NANTES	BARBET Jacques	Our team is dedicated to research in nuclear oncology and integrates therefore chemist, radiochemist, biologist, MDs.	(1) M. Shokeen, C. J. Anderson; Acc. Chem. Res. 2008, 42, 832-841.(2) T. K. Nayak, M. W. Brechbiel; Bioconjugate Chem. 2008, 20, 825-841.(3) P. D. Bonnitcha, S. R. Bayly, M. B. M. Theobald, H. M. Betts, J. S.Lewis, J. R. Dilworth; J. Inorg. Biochem. 2010, 104, 126-135.(4) J. P. Holland, J. S. Lewis, F. Dehdashti; Q. J. Nucl. Med. Mol.Imaging 2009, 53, 193-200. (5) A. J. Arduengo, III, R. L. Harlow, M. Kline; J. Am. Chem. Soc. 1991, 113, 361.(6) W. A. Herrmann; Angew. Chem., Int. Ed. 2002, 41, 1290.	N-heterocyclic carben synthesize for Hypoxia detectionusing 64Cu and radiolabelling o f divalent haptens with 211At and 64Cu for imaging and therapeutical application in Oncology	1	chemist, radiochemist	1	chemist, radiochemist	cancer	Jacques.Barbet@univ-nantes.fr

UMR 1037	Toulouse	Bardies Manuel	Radiopharmaceutical dosimetry: quantitative scintigraphic imaging, detector modelling, absorbed dose calculation, Monte-Carlo Modelling, Radiation transport, Absorbed dose effect relationship, molecular radiotherapy, small animal and cellular dosimetry	**1.** Bardiès M, Buvat I (2011). What are the specifics in image quantification for dosimetry ? Q J Nucl Med Mol Imaging 55, 5-20 **2.** Lassmann M, Chiesa C, Flux, G and Bardiès M (2011). "EANM Dosimetry Committee Guidance Document: Good Practice of Clinical Dosimetry Reporting". Eur J Nucl Med Mol Im 38(1): 192-200. **3.** Ferrer L, Kraeber-Bodéré, F, Bodet-Milin C, Rousseau C, Le Gouill S, Wegener WA, Goldenberg DM, Bardiès M (2010). "Three methods assessing red marrow dosimetry in lymphoma patients treated with radioimmunotherapy". Cancer 116, 1093-1100. **4.** Stabin MG and Bardiès M (2010) "Radiation Dose Assesment in Nuclear Medicine", in Handbook of Anatomical Models for Radiation Dosimetry, G Xu and KF Eckerman, Editors. 2009, Taylor and Francis Group, LCC. **5.** Divoli A, Chiavassa S, Ferrer L, Barbet J, Flux GD, Bardiès M (2009). "Effect of patient morphology on dosimetric calculations for internal irradiation as assessed by comparisons of Monte-Carlo versus conventional methodology". J Nucl Med 50(2): 316-323. **6.** Boutaleb S, Pouget JP, Pèlegrin A, Hindorf C, Barbet J, Kotzki PO, Bardiès M (2009). "Impact of mouse model on pre-clinical dosimetry in Targeted Radionuclide Therapy". Proceedings of the IEEE 97(12), 2076-2085.	Radiopharmaceutical dosimetry, for clinical and preclinical experiments. Assesment of uncertainties in radiopharmaceutical dosimetry Optimization of molecular radiotherapy Monte-Carlo-based quantitative SPECT/PET imaging and radiation transport modelling	1	Medical physicist	1	Medical physicist/ Computing Scientist	Radiation biology	manuel.bardies@inserm.fr