

VIEILLARD Vincent, PhD

Directeur de Recherche CNRS

Chef d'Equipe / Team Leader **NK et maladies pathologiques / NK and Pathologies**

Bio

Contact

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Formation / Education

1992	Master, Pasteur Institute, Paris, France
1995	Ph.D, University Paris XI, France
2010	Research Habilitation in Immunology (HDR), University Pierre et Marie Curie, France

Expérience professionnelle antérieure / Past Professional experience

2012-Present	Research Director (DR-2) at the CNRS, INSERM Unit, Pitié-Salpêtrière Hospital, Paris, France
2000-2011	Senior Researcher (CR-1) at the CNRS, INSERM Unit, Pitié-Salpêtrière Hospital, Paris, France
1998-2001	Postdoctoral Fellow, Harvard University, Molecular & Cellular Biology Department, Strominger's Lab. Cambridge, MA, USA
1996-1999	Junior Researcher (CR-2) at the CNRS, Curie Institute, Orsay, France

Distinctions - Titres honorifiques / Honors and Awards

1995	Thesis Award – French Society of Biology
2011	CNRS Award for career excellence
2011-Present	Hospital contract of translational research (CHRT)

Recherche / Research

Mots-clés / Keywords : Nouveaux vaccins, nouvelles stratégies thérapeutiques / *New vaccines, new therapeutic strategies*

Programmes en cours / Current Research

L'activité de l'Equipe est centrée autour des cellules NK; elle va de la recherche fondamentale aux applications cliniques. Elle est organisée autour de l'identification et de la caractérisation de nouveaux marqueurs impliqués dans le contrôle et/ou l'activité des cellules NK en physiologie et physiopathologie. Ceci inclus l'exploration des effets bénéfiques et délétères des cellules NK :

- dans les pathologies virales. Les modèles étudiés sont principalement le VIH et les infections émergentes (Chikungunya, Dengue et fièvres hémorragiques)
- dans les pathologies tumorales et inflammatoires

Our team is interested in the biology of human natural killer (NK) cells and how they contribute to disease processes. NK cells are critical participants in innate immunity and have the ability to recognize and kill virally infected cells and tumor cells. The integration of signals that they received

through various inhibitory and activating cell surface receptors controls their activation and ability to kill target cells and produce cytokines/chemokines. The key focus of our research is to understand through different pathology models, the beneficial/deleterious relationship between an NK cell and its cellular target. Improved understanding how NK cells behave is critical to advancing our ability to harness their innate capacity for stress recognition. Therefore, an important component of the laboratory focuses on the basic biology of the NK cells, identifying new molecules involved in the control of NK function, and determining the laboratory and clinical conditions under which NK actions can be modified.

From the works that we led these last 10-years, we were able to identify various specific markers of the NK cells, which can allow to elaborate new therapeutic and vaccine strategies. Since 2007, we have already performed several pre-clinical studies in a macaque model and constituted a patent family, which brought to us to the creation of a start-up of biotechnologies, InnaVirVax SA, with Patrice DEBRE and Vincent VIEILLARD, as co-founders, for the valorization of our researches. The company has developed a therapeutic vaccine candidate, which is actually tested in a phase-I clinical trial in HIV infected individuals. In parallel of this vaccine approach, we have begun the first National study of infusion of mature NK cells in patients with malignant hematologic disorders.

Locally, our team is already linked with number of clinical departments, and also strongly implicated in the training of students (academic and medical) providing from the local University (UPMC, and also member of the new cancer Institute of the UPMC (IUC).

Réalisations représentatives / Major achievements

- Identification and characterization of NKp44L, the cellular ligand of an activating NK receptor, only expressed in stress situations
- Application of a highly conserved motif in HIV vaccine
- Basic description of « clonal » NK cells expansion after virus infections
- Role of NK cells after allogeneic hematopoietic transplantation

Domaines d'applications / Fields of application

HIV vaccine, Immuno-therapy, cellular-therapy

Contrats de recherche récents / External peer-reviewed funding

- *Académique*
 - PHRC-regional : Role of NK cells in the reactivation of viral infection in post-transplanted patients with hematological disorders
 - ANR Immuno-Lassa (2014-2017) Role of NK cells in Lassa virus infection
 - HIVera (2014-2015) Viral neutralization by gp41 HIV peptides
- *Industriel*
 - InnaVirVax SA (France), 2014
 - Metabiota Inc (USA)

Valorisation des résultats / Exploitation of results

Création de Startup 2009 InnaVirVax SA

Essais cliniques / *Clinical trials*

- Phase I : HIV-1 3S-based therapeutic vaccination (ongoing)
- Phase II : HIV-1 3S-based therapeutic vaccination (ongoing)
- Phase I : infusion of activated NK cells in consolidation of hematopoietic stem cell transplantation in patients with hematological disorders

Evaluateur de projets et membre de comités d'évaluation / Grant reviewer and member of grant review committees (récent)

- Frontiers Immunol

- Am J Clin Exp Immunol

Membre de comités scientifiques / Member of scientific committee

- 2013 - UPMC Member of Doctoral School (ED394)
- 2013 - UPMC Member of scientific council of IUC (Institut of Cancer)

Brevets et Demandes de brevet / Patents and patent applications

- Deposit Number: PCT/EP2004/01106 (06 Février 2003). European patent – International extensions. Inventors: **Vieillard Vincent** & Debré Patrice « A method for the in vitro assessment of the progression status of an individual ». INSERM & AP-HP, France. Publication date: 05/07/2009 - Patent application number: 20090117110
- Deposit Number: PCT/EP2005/001395, (07 Février 2005), European patent - International extensions. Inventors: **Vieillard Vincent** & Debré Patrice «A polypeptide derived from gp41, a vaccine composition comprising said polypeptide, and uses for treating an infection by an HIV virus in an individual ». INSERM & AP-HP, France. Publication date: 05/28/2009 Patent application number: 20090136533
- Deposit Number: PCT/EP2009/063244 (12 Octobre 2009). N° Publication WO/2010/040853. European patent. Inventors: **Vieillard Vincent** & Debré Patrice « A method for the screening of candidate substances active against the infection of a subject by a hiv virus and kits for performing the said method. « INSERM, France.
- Deposit Number: EP11305187.4 - 1223 (22 Février 2011). European patent. Inventors: **Vieillard Vincent**, Debré Patrice, Laurence Meyer, Joël Crouzet "A method for the prognostic of progression of an HIV disease." INSERM, AP-HP & InnaVirVax SA, France
- Deposit Number: EP113055451.4 (15 Avril 2011). European patent International extensions.. Inventors: **Vieillard Vincent** & Debré Patrice "Composition for preventing and/or treating an infection by an HIV-1 virus". INSERM & InnaVirVax SA, France.

Enseignement / Teaching

Encadrement / Supervision

▪ **Master and PhD programs**

En cours / Current	<u>PhDs</u>	Caroline Petitdemange Baptiste Hervier (PH)
	<u>Master</u>	Cecile Bergua, Olivier Lucar

Antérieurs / Completed

-	Stephanie Nguyen	PhD	Now	MCU-PH
-	Magali Le Garff-Tavernier	PhD		PH
-	Hugue Fausther-Bovendo	PhD		Post-Doc Canada
-	Nadia Wauquier	PhD		Post-Doc Sierra Leone
-	Vivien Beziat	PhD		Post-Doc Sweden

▪ **Postgraduate education medical doctors and postdocs**

En cours / Current	Isabelle Nel , Pharma-D		
Antérieurs / Completed	Florence Baychelier	Now	Post Doc Pasteur Institute Paris

Publications

Publications les plus représentatives / Selected publications

- Achour A, Baychelier F, Besson C, Arnoux A, Marty M, Hannoun L, Sammuël D, Debré P, **Vieillard V** (2014). Expansion of CMV-mediated NKG2C+ NK cells associates with the development of de novo malignancies in liver-transplanted patients. *J Immunol.* 192: 503-511.

- Le Garff-Tavernier M, Herbi L, de Romeuf C, Nguyen-Khac F, Davi F, Brissard M, Maloum K, Choquet S, Urbain R, **Vieillard V**, Merle-Béral H (2014). Antibody-dependent cellular cytotoxicity efficiency of the optimized anti-CD20 monoclonal antibody Ublituximab on chronic lymphocytic leukemia cells with 17p deletion. *Leukemia* 28: 230-233.
- Petitdemange C, Achour A, Dispinseri S, Malet I, Sennepin A, Ho Tsong Fang R, Crouzet J, Marcelin AG, Calvez V, Scarlatti G, Debré P, **Vieillard V** (2013). A single amino-acid Cchange in a highly conserved motif of gp41 elicits virus neutralization and protects against CD4 depletion. *Clin. Inf. Dis.* 57: 745-755.
- Baychelier F, Sennepin A, Ermonval M, Dorgham K, Debré P, **Vieillard V** (2013). Identification of a cellular ligand for the natural killer receptor NKp44. *Blood* 122: 2935-2942.
- Le Garff-Tavernier M, Decocq J, de Romeuf C, Parizot C, Dutertre CA, Chapiro E, Davi F, Debré P, Prost JF, Teillaud JL, Merle-Beral H, **Vieillard V** (2011). Analysis of CD16⁺CD56^{dim} NK cells from CLL patients: evidence supporting a therapeutic strategy with optimized anti-CD20 monoclonal antibodies. *Leukemia* 25: 101-109.
- Hervier B, Béziat V, Haroche J, Mathian A, Lebon P, Guillani-Dalbin P, Debré P, Amoura Z, **Vieillard V** (2011). Phenotype and function of natural killer cells in systemic lupus erythematosus : effect of over IFN- γ production in active patients *Arthritis & Rheumatism* 63: 1698-1706.
- Béziat V, Hervier B, Achour A, Boutolleau D, Marfaing-Koka, **Vieillard V** (2011). Human NKG2A overrides NKG2C effector functions to prevent autoreactivity of NK cells. *Blood* 117: 4394-4396.
- Béziat V, Duffy D, Nguyen Quoc S, Le Garff-Tavernier M, Decocq J, Combadière B, Debré P, **Vieillard V** (2011). CD56^{bright}CD16⁺ NK cells: a functional intermediate stage of NK cell differentiation. *J. Immunol.* 186: 6753-6761.
- Petitdemange C, Becquart P, Wauquier N, Béziat V, Debré P, Leroy EM, **Vieillard V** (2011). Unconventional repertoire profile is imprinted during acute chikungunya infection for natural killer cells polarization toward cytotoxicity. *PLoS Pathogens* 7: e1002268.
- Fausther-Bovendo H, **Vieillard V**, Sagan S, Bismuth G, Debré P (2010). HIV gp41 engages gC1qR on CD4⁺ T cells to induce the expression of an NK ligand through the PIP3/H2O2 pathway. *PLoS Pathogens* 6: e1000975.

Publications 5 dernières années / Last 5 years

2014

- Achour A, Baychelier F, Besson C, Arnoux A, Marty M, Hannoun L, Sammuël D, Debré P, **Vieillard V** (2014). Expansion of CMV-mediated NKG2C⁺ NK cells associates with the development of de novo malignancies in liver-transplanted patients. *J Immunol.* 192: 503-511.
- Le Garff-Tavernier M, Herbi L, de Romeuf C, Nguyen-Khac F, Davi F, Brissard M, Maloum K, Choquet S, Urbain R, **Vieillard V**, Merle-Béral H (2014). Antibody-dependent cellular cytotoxicity efficiency of the optimized anti-CD20 monoclonal antibody Ublituximab on chronic lymphocytic leukemia cells with 17p deletion. *Leukemia* 28: 230-233.

2013

- Petitdemange C, Achour A, Dispinseri S, Malet I, Sennepin A, Ho Tsong Fang R, Crouzet J, Marcelin AG, Calvez V, Scarlatti G, Debré P, **Vieillard V** (2013). A single amino-acid Cchange in a highly conserved motif of gp41 elicits virus neutralization and protects against CD4 depletion. *Clin. Inf. Dis.* 57: 745-755.
- Baychelier F, Sennepin A, Ermonval M, Dorgham K, Debré P, **Vieillard V** (2013). Identification of a cellular ligand for the natural killer receptor NKp44. *Blood* 122: 2935-2942.
- Sennepin A, Baychelier F, Guihot A, Nel I, Fang RH, Calin R, Katlama C, Simon A, Crouzet J, Debré P, Vieillard V. NKp44L expression on CD4⁺ T cells is associated with impaired immunological recovery in HIV-infected patients under highly active antiretroviral therapy. *AIDS.* 2013 Jul 31;27(12):1857-66.
- Baychelier F, Vieillard V. The Modulation of the Cell-Cycle: A Sentinel to Alert the NK Cells of Dangers. *Front Immunol.* 2013 Oct 7;4:325

- Białoszewska A, Baychelier F, Niderla-Bielińska J, Czop A, Debré P, Vieillard V, Kieda C, Malejczyk J. Constitutive expression of ligand for natural killer cell NKp44 receptor (NKp44L) by normal human articular chondrocytes. *Cell Immunol.* 2013 Sep-Oct;285(1-2):6-9.
- Potard V, Ait-Arkoub Z, Agut H; ALT ANRS CO15 Study Group. Polymorphism of gp41 glycoprotein might influence the progression to disease in HIV-1 infection. *AIDS.* 2013 Apr 24;27(7):1189-91.

2012

- **Vieillard V**, Dereuddre-Bosquet N, Mangeot-Méderlé I, Le Grand R, Debré P. An HIVgp41 vaccine protects CD4 central memory T cells in SHIV-infected macaques. *Vaccine.* 2012 Nov 6;30(48):6883-91.
- **Vieillard V**, Crouzet J, Boufassa F, Sennepin A, Ho Tsong Fang R, Debré P, Meyer L. Specific anti-gp41 antibodies predict HIV-1 disease progression. *J Acquir Immune Defic Syndr.* 2012 Nov 1;61(3):403-5.
- Curriu M, Fausther-Bovendo H, Pernas M, Massanella M, Carrillo J, Cabrera C, López-Galíndez C, Clotet B, Debré P, **Vieillard V**, Blanco J. Viremic HIV infected individuals with high CD4 T cells and functional envelope proteins show anti-gp41 antibodies with unique specificity and function. *PLoS One.* 2012;7(2):e30330.
- Béziat V, Dalgard O, Asselah T, Halfon P, Bedossa P, Boudifa A, Hervier B, Theodorou I, Martinot M, Debré P, Björkström NK, Malmberg KJ, Marcellin P, **Vieillard V**. CMV drives clonal expansion of NKG2C+ NK cells expressing self-specific KIRs in chronic hepatitis patients. *Eur J Immunol.* 2012 Feb;42(2):447-57.

2011

- Le Garff-Tavernier M, Decocq J, de Romeuf C, Parizot C, Dutertre CA, Chapiro E, Davi F, Debré P, Prost JF, Teillaud JL, Merle-Beral H, **Vieillard V** (2011). Analysis of CD16⁺CD56^{dim} NK cells from CLL patients: evidence supporting a therapeutic strategy with optimized anti-CD20 monoclonal antibodies. *Leukemia* 25: 101-109.
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- Béziat V, Hervier B, Achour A, Boutolleau D, Marfaing-Koka, **Vieillard V** (2011). Human NKG2A overrides NKG2C effector functions to prevent autoreactivity of NK cells. *Blood* 117: 4394-4396.
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- Petitdemange C, Becquart P, Wauquier N, Béziat V, Debré P, Leroy EM, **Vieillard V** (2011). Unconventional repertoire profile is imprinted during acute chikungunya infection for natural killer cells polarization toward cytotoxicity. *PLoS Pathogens* 7: e1002268.

2010

- Le Garff Tavernier M, Béziat V, Decocq J, Siguret V, Gandjbakhch F, Pautas E, Debré P, Merle-Béral H, **Vieillard V** (2010). Human NK cells display major phenotypic and functional changes over the life span. *Aging Cell* 9: 527-535.
- Fausther-Bovendo H, **Vieillard V**, Sagan S, Bismuth G, Debré P (2010). HIV gp41 engages gC1qR on CD4+ T cells to induce the expression of an NK ligand through the PIP3/H2O2 pathway. *PLoS Pathogens* 6: e1000975.

2009

- Béziat V, Nguyen S, Lapusan S, Hervier B, Dhédin N, Bories D, Uzunov M, Boudifa A, Trebeden-Negre H, Norol F, Marjanovic Z, Marie JP, Vernant JP, Debré P, Rio B, **Vieillard V** (2009). Fully functional NK cells after unrelated cord blood transplantation. *Leukemia* 23: 721-728.

2008

- Nguyen S, Kuentz M, Vernant JP, Dhédin N, Debré P, **Vieillard V** (2008). NK cell reconstitution after haploidentical hematopoietic stem cell transplantation: effect of mature T cells in the graft. *Leukemia* 22: 344-352.
- **Vieillard V**, Le Grand R, Dausset J, Debré P (2008). A new vaccine strategy against AIDS: HIV gp41 peptide immunization prevents NKp44L expression and CD4+ T cell depletion in SHIV-infected macaques. *Proc. Natl. Acad. Sci. USA*. 105: 2100-2104.

Nombre total de publications : 60

Total IF :

Original Article n = 55

IF =

H-Index : 20