

## Bio Sketch

**NAME:** Françoise BRIGNOLE-BAUDOUIN, MD, PhD

**POSITION TITLE :** Associate professor in Toxicology

### Academic positions and research team membership

- **1987**            **Medical Degree Thesis** December 16, 1987, Nice – Highest level of distinction and recommended for a thesis prize.
- **1991-92**        **Master in Biological and Medical Sciences in Haematology and Pathology**
- **1993**            **Master of « Biomechanics and Biomaterials»**, Aix-Marseille University.
- **1995**    **Assistant Professor in Immunology** (1995-1999) Paris 5 University.
- **1999**    **Associate-Assistant Professor in Immunology** (1999 à 2001) Paris 5 University.
- **2001**    **University Doctorate Thesis**, Immunology, Paris 12 University (06/20/2001), Highest level of distinction.
- **2001**    **Teaching and Research Temporary Assistant**, Department of Toxicology, Faculty of Pharmaceutical and Biological Sciences, Paris 5 University (11/1/2001-09/31/2003).
- **2004**    **Associate Professor**, section 40, Department of Toxicology (9/1/2003-)
- **2009**    **Qualification to professorship**

**Member of** “Equipe de Recherche Clinique Associée” à l’INSERM (Clinical Research Team associated with INSERM), 1997-1999.

**Member of** “Equipe d’Accueil 3123”, University Paris VI, UFR St Antoine: “Cell therapy and pharmacology of anterior segment of the eye” (2001-2004)

**Member of** INSERM U-598, team #3, Institut Médical des Cordeliers – Paris Descartes University (2004-2007)

**Member of** INSERM UMR-S968, team #8, « Département Thérapeutique », Pierre & Marie Curie University (2008-2013)

**Member of** INSERM UMR\_S968, CNRS 7210, team #12, « Département Thérapeutique », Pierre & Marie Curie University (2013-)

### Hospital appointments

- Staff physician, Central Laboratory of Hematology, University Hospital Nice (1988-1995).
- University hospital assistant - Immunohematology Laboratory, Ambroise Paré Hospital, Boulogne-Billancourt (1995-2001).
- Staff physician, Laboratory of Quinze-Vingts National Ophthalmology Hospital (2003-).

### Scientific and Administration board and committees

- Pedagogy referee at the Faculty of Pharmacy of Paris
- Pedagogical council member of the Faculty of Pharmacy of Paris
- Scientific manager of the Flow Cytometry platform at the Vision Institute

### Scientific committees

Member of AFC (Association Française de Cytométrie, 1992-)

Member of ARVO (Association for Research in Vision and Ophthalmology, 1989-)

Member of ASSIM (Association des enseignants d’Immunologie des Universités, 1996-)

Member of GEIL (Groupe d’Etude Immunologique des Leucémies, 1992-)

Member of GERBAP (Groupe d’Evaluation et de Recherche en Biologie de l’Assistance Publique, (1996-2001).

Member of ISAC (International Society of Analytical Cytometry, 2002-).  
Member of SFH (Société Française d'Hématologie, 1996-)  
Member of SFI (Société Française d'Immunologie, 1996-)  
Member of SPTC (Société de Pharmaco-Toxicologie Cellulaire, 2002-)  
Member of GATOX (groupe des enseignants en Toxicologie, 2003-)  
Member of SFT (Société Française de Toxicologie, 2005-).  
Member of TFOS (Tear Film and Ocular Surface, 2006-).

### **More than 50 publications in peer-reviewed journals:**

Main topics in developing new techniques and experimental models for exploring pathological processes occurring in the ocular surface as allergy, dry eye, glaucoma, toxic effects of eye drops and environmental pollutants through new technologies like flow cytometry, confocal microscopy and mass spectrometry. The flow cytometry method I developed to analyze the conjunctival cells collected by impression cytology was used in several phase II and III clinical studies and reported in international publications.

### **B. Publications in peer-reviewed journals (2004-2014)**

#### **2014**

Labbé A, Gabison E, **Brignole-Baudouin F**, Riancho L, Menashi S, Baudouin C. Increased Extracellular Matrix Metalloproteinase Inducer (EMMPRIN) Expression in the Conjunctival Epithelium Exposed to Antiglaucoma Treatments. *Curr Eye Res.* 2015;40(1):40-7.

Trinh L, Saubamv@a B, Auclin F, Denoyer A, Lai-Kuen R, El Hamdaoui M, Labbé A, Despiauc MC, **Brignole-Baudouin F**, Baudouin C. Femtosecond and excimer laser-assisted endothelial keratoplasty (FELEK): a new technique of endothelial transplantation. *J Fr Ophtalmol.* 2014; 37(3):211-9.

Mortemousque B, Bourcier T, Khairallah M, Messaoud R, **Brignole-Baudouin F**, Renault D, Rebika H, Brv@mond-Gignac D; Ketotifen Study Group. Comparison of preservative-free ketotifen fumarate and preserved olopatadine hydrochloride eye drops in the treatment of moderate to severe seasonal allergic conjunctivitis. *J Fr Ophtalmol.* 2014;37(1):1-8.

Muselier-Mathieu A, Bron AM, Mathieu B, Souchier M, **Brignole-Baudouin F**, Acar N, Brétilon L, Creuzot-Garcher C. Ocular surface assessment in soft contact lens wearers; the contribution of tear osmolarity among other tests. *Acta Ophthalmol.* 2014; 92(4): 364-9. 23506409.

#### **2013**

Michée S, **Brignole-Baudouin F**, Riancho L, Rostene W, Baudouin C, Labbé A. Effects of benzalkonium chloride on THP-1 differentiated macrophages in vitro. *PLoS One.* 2013; 8(8): e72459.

**Brignole-Baudouin F**, Warnet JM, Barritault D, Baudouin C. RGTA-based matrix therapy in severe experimental corneal lesions: safety and efficacy studies. *J Fr Ophtalmol.* 2013;36(9):740-7.

Trinh L, Saubaméa B, Auclin F, Denoyer A, Lai-Kuen R, El Hamdaoui M, Labbé A, Despiauc MC, **Brignole-Baudouin F**, Baudouin C. A new technique of endothelial graft: the femtosecond and excimer lasers-assisted endothelial keratoplasty (FELEK). *Acta Ophthalmol.* 2013; 91:e497-9.

Desbenoit N, Schmitz-Afonso I, Baudouin C, Laprévotte O, Touboul D, **Brignole-Baudouin F**, Brunelle A. Localisation and quantification of benzalkonium chloride in eye tissue by TOF-SIMS imaging and liquid chromatography mass spectrometry. *Anal Bioanal Chem.* 2013;405(12):4039-49.

**Brignole-Baudouin F**, Desbenoit N, Hamm G, Liang H, Both JP, Brunelle A, Fournier I, Guerineau V, Legouffe R, Stauber J, Touboul D, Wisztorski M, Salzet M, Laprevote O, Baudouin C. A new safety concern for glaucoma treatment demonstrated by mass spectrometry imaging of

benzalkonium chloride distribution in the eye, an experimental study in rabbits. *PLoS One*. 2012;7(11):e50180. Erratum in: *PLoS One*. 2013;8(1).

## 2012

Pauly A, Roubéix C, Liang H, **Brignole-Baudouin F**, Baudouin C. In vitro and in vivo comparative toxicological study of a new preservative-free latanoprost formulation. *Invest Ophthalmol Vis Sci*. 2012; 53(13):8172-80.

Liang H, Baudouin C, Daull P, Garrigue JS, Buggage R, **Brignole-Baudouin F**. In vitro and in vivo evaluation of a preservative-free cationic emulsion of latanoprost in corneal wound healing models. *Cornea*. 2012;31(11):1319-29.

Liang H, Baudouin C, Daull P, Garrigue JS, **Brignole-Baudouin F**. Ocular safety of cationic emulsion of cyclosporine in an in vitro corneal wound-healing model and an acute in vivo rabbit model. *Mol Vis*. 2012;18:2195-204.

Denoyer A, Godefroy D, CV©IV©rier I, Frugier J, Riancho L, **Baudouin F**, Rostène W, Baudouin C. CX3CL1 expression in the conjunctiva is involved in immune cell trafficking during toxic ocular surface inflammation. *Mucosal Immunol*. 2012;5(6):702-11.

Denoyer A, Godefroy D, CV©IV©rier I, Frugier J, Degardin J, Harrison JK, **Brignole-Baudouin F**, Picaud S, Baleux F, Sahel JA, Rostène W, Baudouin C. CXCR3 antagonism of SDF-1(5-67) restores trabecular function and prevents retinal neurodegeneration in a rat model of ocular hypertension. *PLoS One*. 2012;7(6):e37873.

Clouzeau C, Godefroy D, Riancho L, RostV®ne W, Baudouin C, **Brignole-Baudouin F**. Hyperosmolarity potentiates toxic effects of benzalkonium chloride on conjunctival epithelial cells in vitro. *Mol Vis*. 2012;18:851-63.

Liang H, **Brignole-Baudouin F**, Riancho L, Baudouin C. Reduced in vivo ocular surface toxicity with polyquad-preserved travoprost versus benzalkonium-preserved travoprost or latanoprost ophthalmic solutions. *Ophthalmic Res*. 2012;48(2):89-101.

Liang H, Baudouin C, Labbe A, Riancho L, **Brignole-Baudouin F**. Conjunctiva-associated lymphoid tissue (CALT) reactions to antiglaucoma prostaglandins with or without BAK-preservative in rabbit acute toxicity study. *PLoS One*. 2012;7(3):e33913.

Chassignol A, Brasnu E, Baudouin C, Riancho L, Warnet JM, **Brignole-Baudouin F**. In vitro interactions between peripheral blood lymphocytes and the Wong-Kilbourne derivative of Chang conjunctival cells. *Invest Ophthalmol Vis Sci*. 2012;53(3):1492-8.

## 2011

**Brignole-Baudouin F**, Riancho L, Liang H, Baudouin C. Comparative in vitro toxicology study of travoprost polyquad-preserved, travoprost BAK-preserved, and latanoprost BAK-preserved ophthalmic solutions on human conjunctival epithelial cells. *Curr Eye Res*. 2011;36(11):979-88.

**Brignole-Baudouin F**, Baudouin C, Aragona P, Rolando M, Labetoulle M, Pisella PJ, Barabino S, Siou-Mermet R, Creuzot-Garcher C. A multicentre, double-masked, randomized, controlled trial assessing the effect of oral supplementation of omega-3 and omega-6 fatty acids on a conjunctival inflammatory marker in dry eye patients. *Acta Ophthalmol*. 2011;89(7):e591-7.

Creuzot-Garcher C, Baudouin C, Labetoulle M, Pisella PJ, Mouriaux F, Meddeb-Ouertani A, El Matri L, Khairallah M, **Brignole-Baudouin F**. [Efficacy assessment of Nutrilarm-Æ, a per os omega-3 and omega-6 polyunsaturated essential fatty acid dietary formulation versus placebo in patients with bilateral treated moderate dry eye syndrome]. *J Fr Ophtalmol*. 2011;34(7):448-55.

Pauly A, Brasnu E, Riancho L, **Brignole-Baudouin F**, Baudouin C. Multiple endpoint analysis of BAC-preserved and unpreserved antiallergic eye drops on a 3D-reconstituted corneal epithelial model. *Mol Vis*. 2011;17:745-55.

Liang H, Pauly A, Riancho L, Baudouin C, Brignole-Baudouin F. Toxicological evaluation of preservative-containing and preservative-free topical prostaglandin analogues on a three-dimensional-reconstituted corneal epithelium system. *Br J Ophthalmol*. 2011;95(6):869-75.

Liang H, Brignole-Baudouin F, Pauly A, Riancho L, Baudouin C. Polyquad-preserved travoprost/timolol, benzalkonium chloride (BAK)-preserved travoprost/timolol, and

latanoprost/timolol in fixed combinations: a rabbit ocular surface study. *Adv Ther.* 2011;28(4):311-25.

Mehanna C, Baudouin C, Brignole-Baudouin F. Spectrofluorometry assays for oxidative stress and apoptosis, with cell viability on the same microplates: a multiparametric analysis and quality control. *Toxicol In Vitro.* 2011;25(5):1089-96.

Brignole-Baudouin F, Riancho L, Liang H, Nakib Z, Baudouin C. In vitro comparative toxicology of polyquad-preserved and benzalkonium chloride-preserved travoprost/timolol fixed combination and latanoprost/timolol fixed combination. *J Ocul Pharmacol Ther.* 2011;27(3):273-80.

## 2010

Vaede D, Baudouin C, Warnet JM, Brignole-Baudouin F. [Preservatives in eye drops: toward awareness of their toxicity]. *J Fr Ophtalmol.* 2010;33(7):505-24.

Uusitalo H, Chen E, Pfeiffer N, Brignole-Baudouin F, Kaarniranta K, Leino M, Puska P, Palmgren E, Hamacher T, Hofmann G, Petzold G, Richter U, Riedel T, Winter M, Ropo A. Switching from a preserved to a preservative-free prostaglandin preparation in topical glaucoma medication. *Acta Ophthalmol.* 2010;88(3):329-36.

Gabison EE, Labbé A, Brignole-Baudouin F, Nourry H, Putterman M, Malecaze F, Hoang-Xuan T, Baudouin C. Confocal biomicroscopy of corneal intraepithelial neoplasia regression following interferon alpha 2b treatment. *Br J Ophthalmol.* 2010;94(1):134-5.

Baudouin C, Labbé A, Liang H, Pauly A, Brignole-Baudouin F. Preservatives in eyedrops: the good, the bad and the ugly. *Prog Retin Eye Res.* 2010;29(4):312-34.

Labbé A, Gheck L, Iordanidou V, Mehanna C, Brignole-Baudouin F, Baudouin C. An in vivo confocal microscopy and impression cytology evaluation of pterygium activity. *Cornea.* 2010;29(4):392-9.

M'Bika JP, Baudouin F, Courty J, Achour A. Host factor pleiotrophin induces human immunodeficiency virus type 1 replication associated with inflammatory cytokine expression. *J Gen Virol.* 2010;91(Pt 5):1346-53.

Liang H, Baudouin C, Dupas B, Brignole-Baudouin F. Live conjunctiva-associated lymphoid tissue analysis in rabbit under inflammatory stimuli using in vivo confocal microscopy. *Invest Ophthalmol Vis Sci.* 2010;51(2):1008-15.

## 2009

Liang H, Baudouin C, Faure MO, Lambert G, **Brignole-Baudouin F.** Comparison of the ocular tolerability of a latanoprost cationic emulsion versus conventional formulations of prostaglandins: an in vivo toxicity assay. *Mol Vis.* 2009;15:1690-9.

Pauly A, Meloni M, **Brignole-Baudouin F,** Warnet Jm, Baudouin C. Multiple endpoint analysis of the 3D-reconstituted corneal epithelium after treatment with benzalkonium chloride: early detection of toxic damage. *Invest Ophthalmol Vis Sci,* 2009; 50:1644:1652.

## 2008

Pauly A, Labbe A, Baudouin C, Liang H, Warnet JM, **Brignole-Baudouin F.** In vivo confocal microscopic grading system for standardized corneal evaluation: application to toxic-induced damage in rat. *Curr Eye Res.* 2008; 33:826-38.

Liang H, Baudouin C, Pauly A, **Brignole-Baudouin F.** Conjunctival and corneal reactions in rabbits following short- and repeated exposure to preservative-free tafluprost, commercially available latanoprost and 0.02% benzalkonium chloride. *Br J Ophthalmol.* 2008; 92:1275-82.

Trinh L, **Brignole-Baudouin F,** Labbé A, Raphaël M, Bourges JL, Baudouin C. The corneal endothelium in an endotoxin-induced uveitis model: correlation between in vivo confocal microscopy and immunohistochemistry. *Mol Vis.* 2008; 14:1149-56.

Dutot M, Liang H, Pauloin T, **Brignole-Baudouin F,** Baudouin C, Warnet JM, Rat P. Effects of toxic cellular stresses and divalent cations on the human P2X7 cell death receptor. *Mol Vis.* 2008; 14:889-97.

Achour A, M'bika JP, **Baudouin F**, Caruelle D, Courty J. Pleiotrophin induces expression of inflammatory cytokines in peripheral blood mononuclear cells. *Biochimie*. 2008; 90:1791-5.

Brasnu E, **Brignole-Baudouin F**, Riancho L, Guenoun JM, Warnet JM, Baudouin C. In vitro effects of preservative-free tafluprost and preserved latanoprost, travoprost, and bimatoprost in a conjunctival epithelial cell line. *Curr Eye Res*. 2008; 33:303-12.

Liang H, **Brignole-Baudouin F**, Rabinovich-Guilatt L, Mao Z, Riancho L, Faure MO, Warnet JM, Lambert G, Baudouin C. Reduction of quaternary ammonium-induced ocular surface toxicity by emulsions: an in vivo study in rabbits. *Mol Vis*. 2008; 14:204-16.

Brasnu E, **Brignole-Baudouin F**, Riancho L, Warnet JM, Baudouin C. Comparative study on the cytotoxic effects of benzalkonium chloride on the Wong-Kilbourne derivative of Chang conjunctival and IOBA-NHC cell lines. *Mol Vis*. 2008; 14:394-402.

Baudouin C, Liang H, Hamard P, Riancho L, Creuzot-Garcher C, Warnet JM, **Brignole-Baudouin F**. The ocular surface of glaucoma patients treated over the long term expresses inflammatory markers related to both T helper 1 and T helper 2 pathways. *Ophthalmology* 2008; 115:109-115.

Trinh L, **Brignole-Baudouin F**, Pauly A, Liang H, Houssier M, Baudouin C. Th1- and Th2-related chemokine and chemokine receptor expression on the ocular surface in endotoxin-induced uveitis. *Mol Vis*. 2008; 14:2428-34.

## 2007

Baudouin C, Riancho L, Warnet JM, **BRIGNOLE-BAUDOIN F**. In vitro studies of anti-glaucomatous prostaglandin analogues: travoprost with and without benzalkonium chloride and preserved latanoprost. *Invest Ophthalmol Vis Sci* 2007, 48:4123-8.

47. Trinh L, Brignole-Baudouin F, Raphaël M, Dupont-Monod S, Cassoux N, Lehoang P, Baudouin C. Th1 and Th2 responses on the ocular surface in uveitis identified by CCR4 and CCR5 conjunctival expression. *Am J Ophthalmol* 2007, 144:580-5.

Liang H, Brignole-Baudouin F, Labbé A, Pauly A, Warnet JM, Baudouin C. LPS-stimulated inflammation and apoptosis in corneal injury models. *Mol Vis* 2007; 13:1169-80.

Pauly A, Brignole-Baudouin F, Labbé A, Liang H, Warnet JM, Baudouin C. New tools for the evaluation of toxic ocular surface changes in the rat. *Invest Ophthalmol Vis Sci* 2007, 48:5473-83.

Baudouin C, Liang H, Hamard P, Riancho L, Creuzot-Garcher C, Warnet JM, Brignole-Baudouin F. The Ocular Surface of Glaucoma Patients Treated over the Long Term Expresses Inflammatory Markers Related to Both T-Helper 1 and T-Helper 2 Pathways. *Ophthalmology* 2008, 115:109-115.

Pauly A, Brignole-Baudouin F, Guenoun JM, Riancho L, Rat P, Warnet JM, Baudouin C. Comparative in vitro study of topical ocular anti-allergic eye-drops on human conjunctiva-derived cells: responses to cytokines and toxic effects. *Graefe's Arch Clin Exp Ophthalmol* 2007; 245:534-46.

## 2006

Guenoun JM, Baudouin C, Rat P, Pauly A, Warnet JM, **Brignole-Baudouin F**. In vitro comparison of cytoprotective and antioxidative effects of latanoprost, travoprost, and bimatoprost on conjunctiva-derived epithelial cells. *Invest Ophthalmol Vis Sci* 2005, 46:4594-4599.

LABBE A, LIANG H, MARTIN C, **BRIGNOLE-BAUDOIN F**, WARNET J-M, BAUDOIN C. Comparative anatomy of laboratory animal corneas with a new-generation high-resolution in vivo confocal microscope. *Curr Eye Res*. 2006, 31:501-509.

Labbé A, Pauly A, Liang H, **Brignole-Baudouin F**, Martin C, Warnet JM, Baudouin C. Comparison of toxicological profiles of benzalkonium chloride and polyquaternium-1: an experimental study. *J Ocul Pharmacol Ther* 2006, 22:267-78.

Liang H, Baudouin C, Labbé A, Pauly A, Martin C, Warnet JM, **Brignole-Baudouin F**. In vivo confocal microscopy and ex vivo flow cytometry: new tools for assessing ocular inflammation applied to rabbit lipopolysaccharide-induced conjunctivitis. *Mol Vis* 2006, 12:1392-402.

Trabado S, Nguyen Van Binh P, Martin C, Lafarge-Frayssinet C, Thevenin M, **Baudouin F**, Warnet JM, Duc HT. Modulated expression of cell surface molecules and in vivo outgrowth of modified melanoma cells. *Biomed Pharmacother* 2006, 60:693-7.

Dutot M, Pouzaud F, Larosche I, **Brignole-Baudouin F**, Warnet J-M, Rat P. Fluoroquinolone eye drop-induced cytotoxicity: role of p2x7 cell death receptor in preserved fluoroquinolone eye drop-mediated apoptosis. *Invest Ophthalmol Vis Sci* 2006, 47:2812-9.

## 2005

**Brignole-Baudouin F**, Pisella Pj, Dupas B, Baeyens V, Baudouin C. Efficacy and safety of 0.18% sodium hyaluronate in patients with moderate dry eye syndrome and superficial keratitis. *Graefe's Arch Clin Exp Ophthalmol* 2005, 243:531-8.

Guenoun Jm, Baudouin Ch, Rat P, Pauly A, Warnet Jm, **Brignole-Baudouin F**. *In vitro* comparison of inflammatory potential and toxicological profiles between latanoprost, travoprost and bimatoprost on conjunctiva-derived epithelial cells. *Invest Ophthalmol Vis Sci* 2005, 46:2444-5

Baudouin Ch, Liang H, Bremond-Gignac D, Hamard P, Hreiche R, Creuzot-Garcher C, Warnet Warnet Jm, **Brignole-Baudouin F**. CCR4 and CCR5 expression in conjunctival specimens as differential markers of T<sub>H</sub>1/ T<sub>H</sub>2 in ocular surface disorders. *J Allergy Clin Immunol* 2005, 116:614-619.

## 2004

Baudouin C, Hamard P, Liang H, Creuzot-Garcher C, Bensoussan L, **Brignole-Baudouin F**. Conjunctival epithelial cell expression of interleukins and inflammatory markers in glaucoma patients treated over the long term. *Ophthalmology* 2004, 111:2186-92.

Nguyen Van Binh P, Zhou D, **Brignole-Baudouin F**, Martin C, Radionoff M, Dutertre H, Marchand V, Thevenin M, Warnet Jm, Duc Ht. In vitro and in vivo immunotoxic and immunomodulatory effects of nonsupplemented and selenium-supplemented cigarette smoke condensate. *Biomed Pharmacother* 2004, 58:90-4.

Nguyen Van Binh P, Zhou D, **Brignole-Baudouin F**, Martin C, Radionoff M, Dutertre H, Marchand V, Thevenin M, Warnet Jm, Thien Duc H. Modulation of the primary and the secondary antibody response by tobacco smoke condensates. *Biomed Pharmacother* 2004, 58:527-30.

Pisella Pj, Debbasch C, Hamard P, Creuzot-Garcher C, Rat P, **Brignole-Baudouin F**, Baudouin C. Conjunctival proinflammatory and proapoptotic effects of latanoprost and preserved and unpreserved timolol: an ex vivo and in vitro study. *Invest Ophthalmol Vis Sci* 2004, 45:1360-8.

**Brignole-Baudouin F**, Ott Ac, Warnet Jm, Baudouin C. Flow cytometry in conjunctival impression cytology: a new tool for exploring ocular surface pathologies. *Exp Eye Res* 2004, 78:473-81.

Brossas Jy, Tanguy R, **Brignole-Baudouin F**, Courtois Y, Torriglia A, Treton J. L-DNase II associated with active process during ethanol induced cell death in ARPE-19. *Mol Vis* 2004, 27:65-73.

De Saint Jean M, Baudouin C, Di Nolfo M, Roman S, Lozato P, Warnet Jm, **Brignole-Baudouin F**. Comparison of morphological and functional characteristics of primary-cultured human conjunctival epithelium and of Wong-Kilbourne derivative of Chang conjunctival cell line. *Experimental Eye Research* 2004, 78:257-74.

