

Resume

Jean-François BRUGERE, Ph.D, HDR

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Date of Birth: 24th December, 1970 (50 y.)

Address (*Research lab*) : LMGE UMR CNRS UCA 6023 – Université Clermont Auvergne UCA - Impasse Amélie Murat – Campus des Cézeaux - F-63177 Aubière, France

Current Position Associate Professor in Molecular Biology, Biochemistry and Biotechnology
University Institute of Technology (IUT), Université Clermont Auvergne, France

Previous positions

- 2000-2001 (18 months) as Project Manager, NUCLEICA
Head of technological developments (biopôle Clermont-Limagne)
- 2001-2014 Full-position as Associate Professor at Faculty of Pharmacy
Grenoble University (Joseph Fourier University)

Leadership Positions skills

Internationally recognized expert in **human gut methanogens**

Internationally recognized expert in the **7th order of methanogens**

Pharmabiotics conceptualization with the domain ARCHAEA (**Archaebiotics**)

Research Summary

Initially, genetics, genomics and gene expression regulation in eucaryotes (mammals and unicellular organisms encompassing parasites): molecular biology, cellular biology and bioanalysis. Development of SNPs and mutation detection assays for human (based on solid-phase PCR and enzymatic reactions)

Since last position: Research interests in

- diet-gut microbiota-health interactions with emphasis on the archaeal component of the gut microbiome (microbial ecology, biochemistry, anaerobic microbiology) in the context of cardiovascular disease (CVD) / CVD prevention / ageing.
- Development of technological tools for *in vitro* (continuous) simulation systems mimicking the environment of gut microbes, for maintaining gut microbes and allowing their differentiation (ECSIM systems).
- Methanogenesis and C1-compound metabolism by gut methanogens – Pyrrolysine-encoding and genome evolution of free vs host-associated gut inhabitants, using Methanomassiliicoccales as a biological model

Academic responsibilities

Grenoble 1 University (Joseph Fourier University - UJF)

2002-2004 Establishment and then educational manager of Professional MSC degree "In vitro Diagnostic Industry", Grenoble1 University (*still existing as an option of Master Grade*)

Auvergne University Uda (Clermont-Auvergne University – UCA since 01/2017)

2003-2004 Elected alternate member, 41th scientific commission for associate professor positions
2007-2008 Elected alternate member of the Health and Safety Committee
2007-2011 Elected member "department council" of the **Diploma of Higher Education: Applied Biology (Biological & Biochemical Analyses)**
2008-2011 Elected member of Board of Directors of the University
2009-2011 Elected member of joint technical committee of the University
2011-2015 Elected member of Board of Directors of the University
2012-2015 Member of « Disciplinary Board » of the University, for teachers and associate professors
2013-2015 Elected member "department council" of the **Diploma of Higher Education: Applied Biology (Biological & Biochemical Analyses)**
2013-2016 Chairmanships for recruitments of teachers (PRCE/PRAG)
Member of the Standing Committee for the Empowerment of Externals, Life Sciences
Since 2015 Member of the "Technical Committee" of the University

Other

2008-2011 Member of "scientific animation committee" of CRNH-Auvergne
Human Nutrition Research Centre, one of the 4th national nutrition-dedicated research centre
2010-2011 Member of working package "Characterization" of the *Pharmabiotic Research Institute IRP-PRI*
2015 Member of the Organizing Committee for the « 3rd International Congress of Translational Research in Human Nutrition » (3rd ICTRHN), « Intestinal Microbiota & Chronic Diseases », Clermont-Fd, June 26-27.
Since 2016 Member of working package "Case of strict anaerobes and their specificity", *Pharmabiotic Research Institute IRP-PRI*
Since 2017 Referent individual from CRNH Auvergne for "Institut Carnot QUALIMENT" working package "Gut microbiota, probiotics, ferments of food and health interests"

Academic Qualifications (French names)

1988 **High School Degree**, major Mathematics *Baccalauréat série C*
1990 **Diploma of Higher Education: Applied Biology (Biological & Biochemical Analyses)**
DUT, Diplôme Universitaire Technologique, Université d'Auvergne, Clermont-Ferrand
1992-93 **BSC Degree in Cellular Biology** with honors
Master's Degree in Molecular & Cellular Physiology (Animal Physiology), with honors
Licence & Maîtrise, Université Blaise Pascal, Clermont-Ferrand
1994 **Certificate in Medical Molecular Genetics** with honors (during military service)
Certificat Universitaire de Génétique Moléculaire Médicale, University Rennes I
1995 **MSC in Molecular & Cellular Biology** with honors
DEA, Ecole Doctorale des Sciences de la Vie et de la Santé, Clermont-Ferrand
1996-2000 **PhD in Biology** with honors
"Physical map of the microsporidian genome of *Encephalitozoon cuniculi*"
Panel chaired by C. Vivarès ; external examiners: Mr Katinka (INSERM), Mr Pagès (CNRS)
2004 Diploma entitled "**Habilitation à Diriger des Recherches –HDR**", Université Grenoble I
French diploma mandatory for supervision of thesis
Panel composition: Prof R Grillot (chair), M.Alric, E. Drouet, B.Mandrand, P.Peyret, R Robert

Funding

French governmental funding, to which is added (since 2012):

- various industrial research contracts: the main one was with Lesaffre Int. (total contribution, 2012-2017, about 420 k€.).
- Lab equipments acquired through Auvergne Council-Europe co-funding (CPER/FEDER calls) 120 k€,
- Principal Investigator on a European project (JPI -Joint Program Initiative) "Healthy Diet for a Healthy Life (HDHL)": DINAMIC project coordinated by Thomas Clavel, Aachen et Dirk Haller, TUM, Munich

Patents:

- **Brugère J.-F., Borrel G., Alric M., Malpuech-Brugère C., O'Toole P.W. (2013)** Utilisation de microorganismes pour diminuer le taux de triméthylamine dans une cavité du corps humain, notamment pour le traitement de la triméthylaminurie ou d'une vaginose bactérienne et la prévention des maladies cardiovasculaires. Brevet WO2014082773 A1 → *Use of microorganisms for reducing the level of trimethylamine in a human body cavity, in particular for the treatment of trimethylaminuria or of bacterial vaginosis and the prevention of cardiovascular diseases. US Patent App. 14/648,186-2016*
- **Ben Hania W., Brugère J.-F., Fardeau M.-L., Ollivier B. (2017)** Procédé d'isolement de *Methanomassiliicoccales* – (French demand, 1st December 2017, # 1761536)

Guest speaker at conferences:

- Archaeobiotics: a new approach in preventing human cardiovascular diseases. Pharmabiotics Conference 2014, PRI-IRP, The Meridien Etoile Hotel, Paris, October 2014.
- Diversités phylogénétique et métabolique de la composante méthanogène du microbiote intestinal humain : vers des probiotiques de nouvelle génération ? GDR CNRS 3635 Archaea, Museum d'Histoire Naturelle, Toulouse, France, Mars 2015.
- Diversité et Fonctions : exemple de l'étude des archées méthanogènes du microbiote intestinal humain. Réseau INRA NEM Nutrition et Ecologie Microbienne, Toulouse, France, Mai 2015.
- Biomarqueurs prédictifs et microbiote intestinal, un biomarqueur en lui-même. Université d'été de la nutrition, Clermont-Ferrand, France, Septembre 2016.
- Contribution of the gut microbiota to cardiovascular disease: the beneficial role of Archaea? *Theodor Escherich Symposium 2016*, Graz, Austria, 3-4 November 2016.
- Archaea: great expectations from a forgotten island in next generation probiotics. *9th Probiotics, Prebiotics & Newfoods, Nutraceuticals and Botanicals*, Roma (Italia), 10-12 September 2017
- *programmed*
 - EMBO International workshop on "Molecular Biology of Archaea: from mechanisms to ecology". 6th European MBoA conference series (MBoA6). Vienna (Austria), 5-7 September 2018
 - French National Pharmacy Academy (Feb. 2018)

PhD and post-doctoral mentorship

Post-doc :

- David Feria-Gervasio (24 months), Regional Council-European co-funding
- Guillaume Borrel (12 months), Industrial funding
- Prem Prashant Chaudhary (18 months, university funding)
- Wajdi Ben Hania (24 months, industrial funding)
- Bérénice Battut (18 months, Regional Council-European co-funding)
- Marie-Edith Arnal (12 months, university funding)

PhD:

- Agnès Mihajlovski (2006-2009), governmental funding
- William Tottey (2010-2013), Regional Council-European co-funding
- Nadia Gaci (2012-2015), governmental funding

Peer reviewing for various journals, encompassing:

Alimentary Pharmacology & Therapeutics, Anaerobe, Applied & Environmental Microbiology, Biochimie, BMC Microbiology, British Journal of Nutrition, Emerging Topics in Life Sciences, Expert Review in Gastroenterology and Hepatology, FEMS Microbiology Letters, ISME Journal, Journal of Food Engineering, Life, PlosOne, Scientific Reports,...

Expertise for governmental agencies

- 2014, CSO Scotland, Probiotics (220.000 £)
- 2015, NSC (National Science Centre Poland), Poland, 2 projects linked to diet, intestinal microbiota and cardiovascular disease
- 2015, FWF (Austria Science Fund), Austria, Archaea and human microbiotas (350.000€)
- 2017, FWF (Austria Science Fund), Austria, Archaea and human skin

Scientific Publications (international peer-reviewed scientific journals only)

1. **Brugère J-F., Cornillot E., Méténier G., Bensimon A. and C.P. Vivarès** (2000). *Encephalitozoon cuniculi* (Microspora) genome: physical map and evidence for telomere-associated rDNA units on all the chromosomes. *Nucleic Acids Res.* 28, 10, 2026-2033. PMID: 10773069
2. **Brugère J-F., Cornillot E., Méténier G. and C.P. Vivarès** (2000). In-gel DNA radiolabelling and two-dimensional pulsed-field gel electrophoresis procedures suitable for fingerprinting and mapping small eukaryotic genomes. *Nucleic Acids Res.* 28, 10, e48. PMID: 10773096
3. **Brugère J-F., Cornillot E., Méténier G. and C.P. Vivarès** (2000). Occurrence of subtelomeric rearrangements in the genome of the microsporidian parasite *Encephalitozoon cuniculi*, as revealed by a new fingerprinting procedure based on two-dimensional pulsed-field gel electrophoresis. *Electrophoresis.* 21, 2576-2581. PMID: 10939475
4. **Brugère J-F., Bourbon T., Cornillot E., Méténier G. and C.P. Vivarès** (2001). Inter-strain variability of insertion/Deletion events in the *Encephalitozoon cuniculi* genome: a comparative KARD 2D-PFGE analysis. *J. Eukaryot. Microbiol. Suppl* :50S-55S. PMID: 11906078
5. **Berthet N., Faure O., Bakri A., Ambroise-Thomas P., Grillot R. and Brugère J-F** (2003). *In vitro* susceptibility of *Aspergillus* spp. clinical isolates to albendazole. *J Antimicrob Chemother.* 51, 6:1419-1422. PMID: 12716778
6. **Shen D. K., Noodeh A, Kazemi H., Grillot R., Robson G. D., Brugère J.-F.** (2004). Characterization of the genes, cDNAs and expression of the phospholipases B from the human pathogenic fungus *Aspergillus fumigatus*. *FEMS Microbiol Lett.* 239:87-93. PMID: 15451105
7. **Mihajlovski A., Alric M., Brugère J.-F.** (2008). A putative new order of methanogenic Archaea inhabiting the human gut revealed by molecular analyses of the *mcrA* gene. *Res. Microbiol.* 159: 516-521. PMID: 18644435
8. **Brugère J.-F., Baud E., Gobron E., Cailloux F.** (2008). Single-tube genotyping using a solid-phase method that combines Γ -phosphorothioate-mediated primer extension and ExoIII: proof of concept with the F508del cystic fibrosis diagnosis. *Mol. Cell. Probes*, 22(5-6):320-3. PMID: 18657606
9. **Brugère J.-F., Mihajlovski A., Missaoui M., Peyret P.** (2009). Tools for stools: the challenge of assessing human intestinal microbiota using molecular diagnostics. *Expert Rev. Mol. Diagn.* 9 (4), 353-365. PMID: 19435456
10. **Mihajlovski A., Doré J., Levenez F., Alric M., Brugère J.-F.** (2010). Molecular evaluation of the human gut methanogenic archaeal microbiota reveals an age-associated increase of the diversity. *Environ Microbiol Rep.* 2 (2), 272-280. PMID: 23766078
11. **Feria-Gervasio D., Denis S., Alric M., Brugère J.-F.** (2011). *In vitro* maintenance of a human proximal colon microbiota using the continuous fermentation system P-ECSIM. *Appl Microbiol Biotechnol.* 91(5),1425-1433. PMID: 21773764
12. **Borrel G., Harris H.M.B., Tottey W., Mihajlovski A., Parisot N., Peyretailade E., Peyret P., Gribaldo S., O'Toole P.W., Brugère J.-F.** (2012). Genome sequence of "*Candidatus* Methanomethylophilus alvus" Mx1201, a methanogenic archaeon from the human gut belonging to a seventh order of methanogens. *J.Bacteriol.* 194(24):6944-5. PMID: 23209209
13. **Brugère J.-F., Gobron S., Baud E., Cailloux F.** (2013). Design and validation of a colorimetric test for the genetic diagnosis of hemochromatosis using Γ -phosphorothioate nucleotides. *Biochem. Genet.* 51(7-8):635-43. PMID: 2367408
14. **Tottey W., Denonfoux J., Jaziri F., Parisot N., Missaoui M., Hill D., Borrel G., Peyretailade E., Alric M., Harris H.M.B., Jeffery I.B., Claesson M.J., O'Toole P.W., Peyret P., Brugère J.-F.** (2013). The human Gut Chip "HuGChip", an explorative phylogenetic microarray for determining gut microbiome diversity at Family level. *PlosONE*, 8(5): e62544. PMID: 23690942
15. **Borrel G., Harris H.M.B., Parisot N., Gaci N., Tottey W., Mihajlovski A., Deane J., Gribaldo S., Bardot O., Peyretailade E., Peyret P., O'Toole P.W., Brugère J.-F.** (2013). Genome sequence of "*Candidatus*

- Methanomassiliicoccus intestinalis” Issoire-Mx1, a third Thermoplasmatales-related methanogenic archaeon from human feces. *Genome Announc.* 1(4): e00453-13. PMID: 23846268
16. **Borrel G., O’Toole P.W., Peyret P., Brugère J.-F., Gribaldo S.** (2013). Phylogenomic data support a seventh order of methylophilic methanogens and provide insights into the evolution of methanogenesis. *Genome Biol. Evol.* 5(10): 1769-1780. PMID: 23985970
 17. **Brugère J.-F., Borrel G., Gaci N., Tottey W., O’Toole P.W., Malpuech-Brugère C.** (2014) Archaeobiotics: proposed therapeutic use of archaea to prevent trimethylaminuria and cardiovascular disease. *Gut Microbes.* 5(1): 5-10. PMID: 2424728
 18. **Borrel G., Gaci N., Peyret P., O’Toole P.W., Gribaldo S., Brugère J.-F.,** (2014) Unique characteristics of the pyrrolysine system in the 7th order of methanogens: implications for the evolution of a genetic code expansion cassette. *Archaea.* Article ID 374146. PMID: 24669202
 19. **Feria-Gervasio D., Tottey W., Gaci N., Alric M., Cardot J.-M., Peyret P., Martin J.-F., Pujos E., Sébédio J.-L., Brugère J.-F.,** (2014) Three-stage continuous culture system with a self-generated anaerobia to study the regionalized metabolism of the human gut microbiota. *J. Microbiol. Methods* 96(1): 111-118. PMID: 24333608
 20. **Parisot N., Faouzi J., Abid A., Denonfoux J., Ribière C., Boucher D., Brugère J.-F., Mahul A., Hill D., Peyretailade P., Peyret P.** (2014) PhyLOPDB: a 16S rRNA oligonucleotide probe database for prokaryotic identification. *Database.* 2014(0):bau036. PMID: 25124552.
 21. **Borrel G., Parisot N., Harris H.M., Peyretailade E., Gaci N., Tottey W., Bardot O., Raymann K., Gribaldo S., Peyret P., O’Toole P.W., Brugère J.-F.** (2014) Comparative genomics highlights the unique biology of Methanomassiliicoccales, a Thermoplasmatales-related seventh order of methanogenic archaea that encodes pyrrolysine. *BMC Genomics.* 15(1):679. PMID: 25124552, DOI: 10.1186/1471-2164-15-679
 22. **Gaci N., Borrel G., Tottey W., O’Toole P.W., Brugère J.-F.** (2014) Archaea and the human gut: New beginning of an old story. *World J. Gastroenterol.* 20(43): 16062-16078. PMID: 25473158, DOI: 10.3748/wjg.v20.i43.16062
 23. **Tottey W., Gaci N., Borrel B., Alric M., O’Toole P.W., Brugère J.-F.** (2015) *In-vitro* model for studying methanogens in human gut microbiota. *Anaerobe.* 34: 50-52. 10.1016/j.anaerobe.2015.04.009
 24. **Chaudhary P. P., Gaci N., Borrel G., O’Toole P. W., Brugère J.-F.** (2015). Molecular methods for studying methanogens of the human gastrointestinal tract: current status and future directions. *Appl Microbiol Biotechnol.* 99(14), 5801-5815. PMID: 26088176, DOI: 10.1007/s00253-015-6739-2
 25. **Ounnas F., Privé F., Salen P., Gaci N., Tottey W., Calani L., Bresciani L., Lopez-Gutierrez N., Hazane-Puch F., Laporte F., Brugère J.-F., Del Rio D., Demeillers C., de Lorgeril M.** (2016). Whole Rye Consumption Improves Blood and Liver n-3 Fatty Acid Profile and Gut Microbiota Composition in Rats. *PLoS one*, 11(2), e0148118.
 26. **Belkorchia A., Pombert J.-F., Polonais V., Parisot N., Delbac F., Brugère J.-F., Peyret P., Gaspin C., Peyretailade E.** (2016) Comparative genomics of microsporidian genomes reveals a minimal non-coding RNA set and new insights for transcription in minimal eukaryotic genomes. *DNA Res*, dsx002
 27. **Tottey W., Feria-Gervasio D., Gaci N., Laillet B., Pujos-Guillot E., Martin J.-F., Sébédio J.-L., Sion B., Jarrige J.-F., Alric M., Brugère J.-F.** (2017) Colonic transit time is a driven force of the gut microbiota composition and metabolism: *in vitro* evidence. *J. Neurogastroenterol. Motil.*, 23(1), 124-134.
Dedicated Editorial: Kim S-E. Colonic Slow Transit Can Cause Changes in the Gut Environment Observed in the Elderly. 3-4. doi:10.5056/jnm16215.
 28. **Borrel G., McCann A., Deane J., Neto M.C., Lynch D.B., Brugère J.-F., O’Toole P.W.** (2017) Genomics and metagenomics of trimethylamine-utilizing Archaea in the human gut microbiome. *ISME J.* 11(9):2059-2074.
 29. **Gaci N., Flemer B., Borrel G., Sanderson I.R., Chaudhary P.P., Tottey W., O’Toole P.W., Brugère J.-F.** (2017) Fecal microbiota variation across the lifespan of healthy laboratory rat. *Gut Microb.*, 8(5):428-439.
 30. **Batut B., Gravouil K., Defois C., Hiltmann S., Brugère J.-F., Peyretailade E., Peyret P.** (2017) ASaiM: a Galaxy-based framework to analyze raw shotgun data from microbiota. *BioRxiv*, 183970. doi:10.1101/183970.
 31. **Gaci N., Chaudhary P.P., Tottey W., Alric M., Brugère J.-F.** (2017) Functional amplification and preservation of human gut microbiota. *Microb. Ecol. Health D.*, 28(1):1308070.
 32. **Brugère J.-F., Ben Hania W., Arnal M.-E., Ribière C., Ballet N., Vandekerckove P., Ollivier B., O’Toole P.W.** (2018) Archaea: microbial candidates in next generation probiotics development. *J. Clin. Gastroenterol.* 2018, MCG.000000000001043 (PMID:29668558)
 33. **Brugère J. F., Atkins J. F., O’Toole P. W., Borrel, G.** (2018). Pyrrolysine in archaea: a 22nd amino acid encoded through a genetic code expansion. *Emerg. Top. Life Sci.*, 2(4), 607-618. doi: 10.1042/ETLS20180094
 34. **Fadhlaoui K., Arnal M.-E., Martineau M., Camponova P., Ollivier B., O’Toole P.W., Brugère J.-F.** (2020) Archaea, specific genetic traits and development of improved bacterial live biotherapeutic products: another face of next-generation probiotics. *Appl. Microb. Biotechnol.*, 104(11): 4705–4716. doi: 10.1007/s00253-020-10599-8
 35. **Borrel G., Brugère J.-F., Gribaldo S., Schmitz R. & Moissl-Eichinger C.** (2020).The host-associated archaeome. *Nat. Rev. Microbiol.* doi:10.1038/s41579-020-0407-y

Other publications (*Book chapters, proceedings, popularization ...*):

1. **Shen D.K., Noodeh A., Kazemi H., Grillot R., Robson G.D., Brugere J.F.** (2003). Complete cDNA sequence of affPLB1, a phospholipase B from *Aspergillus fumigatus*. 9th Congress of the European Confederation of Medical Mycology & 7th Trends in Invasive Fungal Infections, Amsterdam, The Netherlands, September 28 – October 1, 2003.
2. **Shen D.K., Noodeh A., Kazemi H., Grillot R., Robson G.D., Brugere J.F.** (2003). Complete cDNA sequence of affPLB1, a phospholipase B from *Aspergillus fumigatus*. *Trends in Medical Mycology*, D929C0046: 103-107.
3. **Brugère J-F, Mihajlovski A., Alric M.** (2008). StabyCloning based molecular methods for the identification of novel microbial strains. *In DelphiGenetics Technical Note*.
4. **Feria-Gervasio D., Tottey W., Cardot J.M., Vandekerckove P., Denis S., Alric M., Brugère J.F.** (2011). Influence segment-dépendante d'une souche probiotique de *Lactobacillus plantarum* sur le microbiote colique humain analysé en système *in vitro* 3S-ECSIM. *Cahiers de nutrition et de diététique* (46) S83.
5. **Feria-Gervasio D., Tottey W., Pujos-Guillot E., Martin J.F., Sébédio J.L., Cardot J.M., Denis S., Alric M., Brugère J.F.** (2011). Le temps de transit colique simulé en modèle tri-étagé de fermentation continue (3S-ECSIM) influence la structure et le métabolisme d'un microbiote humain. *Cahiers de nutrition et de diététique* (46) S83.
6. **Brugère J.-F., D. Feria-Gervasio, Z. Popse, W. Tottey and M. Alric** (2011). The ECSIM concept (Environmental Control System for Intestinal Microbiota) and its derivative versions to help better understand human gut biology. *In Biomedical Engineering / Book 1, Intech Edition, ISBN 978-953-307-256-2*.
7. **Ounnas F., Privé F., Tottey W., Salen P., Hazane-Puch F., Laporte F., Del Rio D., Calani L., Melegari C., Brugère J-F., Demeilliers C., de Lorgeril M.** (2014). P191: La consommation de seigle complet augmente les acides gras à chaîne longue oméga-3 et modifie le profil du microbiote intestinal chez le rat. *Nutrition Clinique et Métabolisme* (28) S168.
8. **Brugère J.-F.** (2016) Une approche rationnelle pour des probiotiques de nouvelle génération : exemple des archaeobiotics pour prévenir les maladies cardiovasculaires. CNRIUT 2016, 50 ans de recherche en IUT.
9. **Ben Hania W., Ballet N., Vandekerckove P., Ollivier B., O'Toole P.W., Brugère J.-F.** (2017) Archaeobiotics: archaea as pharmabiotics for treating chronic disease in humans? *In Archaea - New Biocatalysts, Novel Pharmaceuticals and Various Biotechnological Applications*, Intech Edition, ISBN 978-953-51-5243-9.

Popularization articles (in French)

- **Contribution to the journal « l'Opéron »** : Volume 74, « *Les extrémophiles : des microorganismes très convoités* » d'Alphonse Meyer (2016).
- Journal « **La Recherche** » about archaeal pharmabiotics (« Archaeobiotics ») and their possible benefits for cardiovascular disease. *La Recherche*, n° 532, pp.55-58 (February 2018).