Curriculum vitae Michel Flipphi

Full name: **Michel Johannes Anthonie Flipphi**

Date of Birth: **30 September 1964**

Place of Birth: **Bergh (Gld), The Netherlands**

Nationality: **Netherlands**

Sex: **Male**

Marital status: **Single**

Current E-mail: **drir.michelflipphi@gmail.com**

University Education

Agricultural University Wageningen, Wageningen, The Netherlands
September 1982 – November 1988.

M. Sc. Degree in Agricultural and Environmental Sciences
("Ingenieur in de Landbouw- en Milieu Wetenschappen")

Obtained 22 November 1988 with the highest possible distinction ("cum laude")

Ph.D Degree in Agricultural and Environmental Sciences
("Doctor in de Landbouw- en Milieu Wetenschappen")

Obtained 2 May 1995 after succesfull defence of a thesis entitled: "A Molecular Analysis of L-Arabinan Degradation in *Aspergillus niger* and *Aspergillus nidulans*"

Thesis Supervisor ("Promotor"): Dr. Albert J.J. van Ooyen

Professor in Genetical Techniques in Food Technology at the Dept. of Food Technology, Agricultural University Wageningen, Wageningen, The Netherlands.

Senior Scientist at DSM Food Specialities, Delft, The Netherlands (retired at present).

Curriculum vitae Michel Flipphi

Professional employment (1)

Ph.D Fellow ("Assistent in Opleiding"): **November 1988 – October 1992.**

Agricultural University Wageningen, Wageningen, The Netherlands
Dept. of Genetics, Section Molecular Genetics

Supervisor: Dr. Jaap Visser

Research Assistant**: November 1992 – February 1994.**

Agricultural University Wageningen, Wageningen, The Netherlands
Section Molecular Genetics of Industrial Micro-organisms

(EC programme 'BRIDGE', Grant CT90-0169)
Supervisor: Dr. Jaap Visser

Please note that due to a serious accident in the late summer of 1995, applicant was unable to work for the following one and a half year.

EC Marie Curie Fellow**: April 1997 – March 1999.**

Université Paris-Sud XI, Orsay, France
Institute de Génétique et Microbiologie, CNRS UMR 8621

(EC TMR "Marie Curie" Training Grant BIO4-CT97-5028 – Personal Grant)
Supervisor: Dr. Béatrice Felenbok

Post Doc**: April 1999 – June 1999.**

Université Paris-Sud XI, Orsay, France
Institute de Génétique et Microbiologie, CNRS UMR 8621

(EC RTD Grant BIO4-CT96-0535 – Eurofung)
Supervisor: Prof. Dr. Claudio Scazzocchio

Associated Researcher**: July 1999 – December 1999**.

Université Paris-Sud XI, Orsay, France
Institute de Génétique et Microbiologie, CNRS UMR 8621

(Centre National de la Recherche Scientifique – Poste Rouge – Personal Grant)
Supervisor: Prof. Dr. Michel Duguet (deceased)

Curriculum vitae Michel Flipphi

Professional employment (2)

__Post Doc__: **March 2000 – January 2003**.

Université Paris-Sud XI, Orsay, France
Institute de Génétique et Microbiologie, CNRS UMR 8621

(EC Fifth Framework Programme – Quality of Life and Management of Living Resources – Grant QLK3-CT99-00729 – Eurofung 2)
Supervisor: Dr. Béatrice Felenbok

__Post Doc__: **February 2003 – November 2003**.

Consejo Superior de Investigaciones Científicas (CSIC)
Instituto de Agroquímica y Tecnología de Alimentos (IATA), Paterna, Valencia, Spain

(Instituto Nacional de Investigación y Tecnología Agraria y Alimentaría, VIN01-018-C2-1)
Supervisors: Dr. Paloma Manzanares & Dr. Daniel Ramón

__Post Doc__: **September 2004 – August 2005**

Université Paris-Sud XI, Orsay, France
Institute de Génétique et Microbiologie, CNRS UMR 8621

(Centre National de la Recherche Scientifique – ATIP Microbiologie 2001, Contrat 2JE077)
Supervisor: Dr. Christian Vélot

__Post Doc__: **September 2005 – August 2010**

Consejo Superior de Investigaciones Científicas (CSIC)
Instituto de Agroquímica y Tecnología de Alimentos (IATA), Paterna, Valencia, Spain

(Ministerio de Educación y Ciencia (MEC) – Programa "Ramón y Cajal" – Ref. RYC-2004-003005 – Personal Grant)
(NB. The Ramón y Cajal program provides temporary contracts for young scientists)

NB. In this position, applicant has also participated in another European project of the Eurofung consortium (EU Sixth Framework Programme – Coordinated Action: FP6-2004-LIFESCIHEALTH-5; Grant LSSG-CT-2005-018964) concerning the manual re-annotation of the genome sequence of the filamentous fungus *Aspergillus nidulans*.
Project coordinator: Prof. Dr. Cees A.M.J.J. van den Hondel

Curriculum vitae Michel Flipphi

Professional experience in filamentous fungal biochemistry, genetics, metabolism and physiology (1)

(including technical approaches)

Biochemistry of Enzymes and Porters

1) Characterisation of three L-arabinolytic enzymes produced by *Aspergillus niger*: purification and subsequent physico-chemical and kinetic characterisation of these extracellular enzymes (prior to the cloning of the encoding genes)
2) Characterisation of glucose transporters *in Aspergillus nidulans* by determination of the Km value of the uptake component absent in gene-deleted *A. nidulans* mutants. The low-affinity transporter MstE and the high-affinity transporter MstC are both physiologically relevant glucose transporters whose substrate specificities were addressed with *in vivo* transport inhibition studies. MstC is also a physiological transporter of the toxic keto-sugar L-sorbose, although L-sorbose does not inhibit glucose transport by MstC.
3) The permease of the acetate anion, AcpA, was functionally characterised by comparatively studying acetate transport in gene-deleted strains and wild type *A. nidulans*, determining its Km value in the latter.

Physiology and Metabolism

Pentose catabolism

1) Identification of simple compounds that induce the production of arabinolytic enzymes, L-arabinose and L-arabitol, and their differential effect on the six enzymes of pentose oxido-reductive catabolism and polyol accumulation in *A. niger*.
2) Studies of the physiology of the pentose oxido-reductive catabolism (enzymes, polyol accumulation) in *A. nidulans* in various carbon derepressed mutant backgrounds and in a mutant (*araA1*) unable to grow on L-arabinose. Remarkable are the strongly reduced steady state mannitol concentrations on mixed carbon sources containing L-arabinose in the latter.

Professional experience in filamentous fungal biochemistry, genetics, metabolism and physiology (2)

3) Identification of a physiological phenomenon called autorepression in which L-arabinose effects both an induction and an antagonistic repression of arabinolytic gene expression. A similar effect was later shown for D-xylose and xylanase A.
4) Evidence for the involvement of L-arabitol dehydrogenase in the keto-oxidation of galactitol, part of the (then unknown) alternative, oxido-reductive pathway for D-galactose utilisation.

Acetate utilisation

5) Acetate permease is essential for growth of *A. nidulans* at low acetate concentations at neutral and alkaline medium pH, conditions under which the availability of protonated form (HAc) – that can pass biological membranes by diffusion – is limiting or negligible.

Catabolic networks: metabolism, regulation, physiology, biochemistry

Identification of metabolic networks related to the utilization of ethanol in A. nidulans (alc *regulon)*: *identification of the genes, their regulation and that of other catabolic routes that could involve the participation of* alc *genes*.

1) Physiological studies with catabolic mutants. Demonstration that aldehyde dehydrogenase controls the concentration of the physiological inducer of the *alc* system and thereby, an efficient catabolic flux from ethanol. Acetaldehyde was shown to be the physiological inducer common to ethanol, ethylamine and L-threonine catabolism. At low concentrations (below 1mM), it is inducing *alc* while higher concentrations provoke a toxic effect on cellular functioning.

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Professional experience in filamentous fungal biochemistry, genetics, metabolism and physiology (3)

2) Loss-of-function mutations in the adehyde dehydrogenase (*aldA*) gene result in expression of the *alc* genes under normally non-inducing conditions while this so-called pseudo-constitutive expression can be eliminated *in vivo* with an aldehyde scavenger. The uninduced and non-repressible basal expression of the *aldA* gene is therefore physiologically relevant in order to prevent accumulation of aldehydes.
3) Using alcohols and amines as precursors, it was established that inducing aldehydes have a backbone of 2 to 5 carbon atoms. Small aliphatic esters induce the *alc* genes because their catabolism yields aldehyde intermediates. Small alpha-ketones, however, are direct inducers of the *alc* system.
4) Transient *alc* responses (i.e. temporal aldehyde accumulation) could be detected at the offset of putrescine and D-galacturonic acid catabolism.

Signalling of carbon catabolite repression: genetical, biochemical and physiological approaches

1) The role of glucose-phosphorylating enzymes in carbon catabolite repression (CCR) in *Aspergillus nidulans* was investigated using newly selected hexokinase and glucokinase single and double mutants. Enzyme lesions in these mutants were confirmed with activity assays; hexokinase is trehalose-6-phosphate inhibited.
2) A strong reduction of the glucose repression was demonstrated for double hexose kinase mutants only. Conversily, CCR provoked by growth substrates that do not require the hexose kinases for their catabolisation (e.g. xylose) was not affected in either mutant. Glucose repression in *Aspergillus* thus depends on the sugar's phosphorylation.
3) The important conclusion is that the signalling of CCR is fundamentally different in *A. nidulans* compared to that in *Saccharomyces cerevisiae.*

Curriculum vitae Michel Flipphi

Professional experience in filamentous fungal biochemistry, genetics, metabolism and physiology (4)

Fungal Molecular Genetics

α-L-arabinanan degrading enzymes from Aspergillus niger (pre-genome)

1) Cloning of the α-L-arabinofuranosidase A (*abfA*) and endo-α-L-arabinanase (*abnA*) genes from genomic phage libraries with the aid of cDNA probes selected from L-arabitol-induced cDNA expression libraries with specific antibodies against the purified proteins.
2) Cloning of the α-L-arabinofuranosidase B (*abfB*) genes with the aid of probes amplified off genomic DNA with gene-specific oligonucleotide mixtures based on N-terminal amino acid sequences from the purified protein and cyanogen bromide-generated peptides.
3) Manual sequencing of the *abfA*, *abfB* and *abnA* genes and cDNA of those three genes, using the dideoxy chain-termination method.
4) Functionality was put to evidence upon introduction, by transformation, of extra copies of the cloned genes in *A. niger* as well as in *Aspergillus nidulans*.
5) Physiological study of induction of the three genes at the RNA level included work in transformants carrying multiple copies of either one of the *abf* genes and revealed copy-dilution effects of common regulatory proteins.

Ethanol Utilisation and the alc *Gene Cluster in* Aspergillus nidulans

1) An exhaustive study of the induction profile of the genes (*alc*) previously shown to be under pathway-specific control by the transcriptional activator AlcR, was undertaken at the RNA level (see above)

Professional experience in filamentous fungal biochemistry, genetics, metabolism and physiology (5)

2) Extant classical loss-of-function mutants in aldehyde dehydrogenase (*aldA*) and *alcR* were used as well as artificially obtained gene-deleted mutants and mutants that constitutively overexpressed *aldA* or *alcR* from the glyceraldehyde-3-phosphate dehydrogenase (*gpdA*) promoter. This work included the characterisation of point mutations leading to loss of aldehyde dehydrogenase function and their consequences for *alc* gene expression.
3) *alcS* encodes a plasma membrane protein with six transmembranal domains. A C-terminal GFP fusion expressed from the *alcS* promoter showed the functional localisation of AlcS. *alcS* is dispensable for the catabolism of ethanol, threonine and ethylamine, and its deletion had apparently no effect on the transport of alcohols, acetaldehyde or acetate in physiological assays.
4) Comparative genomics showed that ethanol utilisation (*alc*) gene clusters have evolved independently in *A. nidulans* and *A. fumigatus*. AlcR-regulated alcohol- and/or aldehyde dehydrogenase gene copies recruited to either of these *alc* clusters arose from recent gene duplications. An efficient expression system using the *A. nidulans alcA* promoter works in *A. fumigatus* without the need to co-introduce *alcR* and allows the generation of conditionally lethal mutants. The *alcA*-*alcR* ethanol/acetaldehyde-inducible expression system has been applied succesfully in *A. niger*, plant and mammalian cells (NB. Shown by thirds)

The Acetate Transporter of A. nidulans*, AcpA*

1) The acetate permease (*acpA*) gene encodes a membrane protein of the same class as AlcS and is co-induced with the *alc* genes on ethanol and ethylacetate.
2) *acpA* gene-deleted strains show increasingly bigger growth defects with the decrease of the external acetate concentration and the increase of medium pH but there is no phenoype on ethanol or ethylacetate.

Professional experience in filamentous fungal biochemistry, genetics, metabolism and physiology (6)

3) *acpA* induction by limiting concentrations of acetate and propionate is under control of the acetate catabolic pathway activator FacB while ceasing at higher concentrations. Induction of the malate synthase (*acuE*) gene is absent in *acpA*-deleted mutants on limiting acetate at neutral medium pH but not on ethanol or ethylacetate, further suggesting that AcpA is involved in the active transport of the acetate anion over the plasma membrane (see above).

Glucose Transport in A. nidulans

1) Glucose uptake by *A. nidulans* germlings is conducted by a low-affinity system when grown on glucose and by a high-affinity system when grow on glycerol or ethanol. The genes encoding these transport systems were identified as *mstE* (low-affinity) and *mstC* (high-affinity) and characterised by comparing glucose uptake kinetics in wild-type and gene-deleted strains. *mstE*-deleted strains always take up glucose with MstC-like kinetics. *mstC*-deleted and double deleted strains take up glucose with kinetics that are clearly distinct from those of either previously described uptake component and do not show growth defects on glucose.
2) Expression was studied in wild-type strains and derepressed mutants at the transcript level. *mstE* is only expressed in the presence of a functional carbon catabolite repressor CreA on glucose early in growth and during the exponential phase but ceases later in culture. *mstC* is initially repressed on glucose in wild type but derepressed upon glucose exhaustion. On poor carbon sources and in *creA* mutant strains, *mstC* is always expressed and its mRNA is present in dormant spores. In *creA*-mutants, *mstC* transcript levels are considerably higher on glucose than on galactose, indicating that *mstC* is subject to glucose induction.
3) Functional MstE and MstC localisation in the plasma membrane was shown with GFP fusions under the appropriate growth conditions. Medium transfer to galactose leads to rapid internalisation of MstE-GFP.

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Professional experience in filamentous fungal biochemistry, genetics, metabolism and physiology (7)

4) The *mstC* gene complements L-sorbose- and 2-deoxyglucose resistent mutations at the *sorA* locus upon transformation. Three *sorA* mutations were characterised.
5) The *mstA* gene is a duplication of *mstC* and is uniquely expressed late in culture upon carbon source starvation. The MstA protein was shown capable to transport glucose with MstC-like kinetics when expressed from the *mstC* promoter, with a single copy of the expression cassette integrated at the *uaZ* locus in a background from which the *mstC* locus was previously deleted.

Transcriptomics of the Sugar Porter Complement

1) A macroarray with 120 gene-specific PCR products, representing the annotation-predicted sugar porter complement of *A. nidulans*, was designed and generated on nylon membranes.
2) The array was hybridised with single-strand radiolabelled cDNA probes, either oligo-dT- or randomly primed off total RNA samples from a wild-type strain or a *creA* loss-of-function mutant, grown under a wide range of different growth conditions. Candidate genes for a third glucose transporter were screened for with cDNA-probes primed off RNA isolated from *mstC* gene-deleted mutants.
3) Carbon source-specific responses could be observed and candidate-genes for the transporter(s) of particular sugars or polyols (a.o., xylose, L-arabinose, lactose, galactose, sorbitol) have been selected. A selection of porter genes will be deleted to investigate their function.

Curriculum vitae Michel Flipphi

Professional experience in filamentous fungal biochemistry, genetics, metabolism and physiology (8)

Biotin Biosynthesis in A. nidulans*: Development of a New Transformation System*

1) The three clustered genes, *bioF*, *bioDA* and *bioB*, are responsible for the last four enzymatic steps of biotin biosynthesis, as proven by functional complementation of *E. coli* mutants. Eukaryote BioDA is a bifunctional enzyme converting 7-keto-8-amino perlargonic acid in dethiobiotin via 7,8-diamino perlargonic acid.
2) Regulation of the three *bio* genes was shown to be coordinated by quantitative PCR; constitutive regardless the presence of biotin but upregulated in a biotin-requiring mutant upon mycelial transfer to biotin-deficient medium.
3) Three classical biotin-requiring mutations could be complemented with the *bioDA* gene and were structurally characterised.
4) Transformation of the ortholog *A. fumigatus bioDA* gene into an *A. nidulans biA1* mutant resulted in clearly defined colonies of mitotically stable biotin-prototroph transformants without the need for avidin sequestering. The utility of this new selection system was demonstrated with a gene-replacement experiment.

Bio-informatics: Functional Annotation and Comparative Genomics

1) Applicant was actively involved in the functional re-annotation of the *A. nidulans* FGSC A4 genome sequences, including gene model correction.
2) A comparative genomics study of primary metabolism was conducted utilising the genomes of eight species of the Aspergillus genus.
3) Applicant actively contributed to an integrated genomics and transcriptomics study comparing the biocontrol species *Trichoderma atroviride* and *Trichoderma virens* with their saprophytic relative *Trichoderma reesei*. Mycoparasite responses to the presence of the fungal plant pathogen *Rhizoctonia solani* were analysed at three subsequent stages of attack.

Curriculum vitae Michel Flipphi

Referees

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List of Publications Michel Flipphi (August 2011)

Kubicek, C.P., Herrera-Estrella, A., Seidl, V., Martinez, D.A., Druzhinina, I.S., Thon, M., Zeilinger, S., Casas-Flores, S., Horwitz, B.A., Mukherjee, P.K., Mukherjee, M., Kredics, L., Alcaraz, L.D., Aerts, A., Antal, Z., Atanasova, L., Cervantes-Badillo, M.G., Challacombe, J., Chertkov, O., McCluskey, K., Coulpier, F., Deshpande, N.,von Döhren, H., Ebbole, D.J., Esquivel-Naranjo, E.U., Fekete, E., **Flipphi, M.**, Glaser, F., Gómez-Rodríguez, E.Y., Gruber, S., Han, C., Henrissat, B., Hermosa, R., Hernández-Oñate, M., Karaffa, L., Kosti, I., Le Crom, S., Lindquist, E., Lucas, S., Lübeck, M., Lübeck, P.S., Margeot, A., Metz, B., Misra, M., Nevalainen, H., Omann, M., Packer, N., Perrone, G., Uresti-Rivera, E.E., Salamov, A., Schmoll, M., Seiboth, B., Shapiro, H., Sukno, S., Tamayo-Ramos, J.A., Tisch, D., Wiest, A., Wilkinson, H.H., Zhang, M., Coutinho, P.M., Kenerley, C.M., Monte, E., Baker, S.E., and Grigoriev, I.V. (2011) Comparative genome sequence analysis underscores mycoparasitism as the ancestral life style of *Trichoderma*. Genome Biol. **12** (4): R40

Magliano, P., **Flipphi, M.**, Sanglard, D. and Poirier, Y. (2011) Characterization of the *Aspergillus nidulans* biotin biosynthetic gene cluster and use of the *bioDA* gene as a new transformation marker. Fungal Genet. Biol. **48** (2): 208–215

Flipphi, M., Sun, J., Robellet, X., Karaffa, L., Fekete, E., Zeng, A. P. and Kubicek, C.P. (2009) Biodiversity and evolution of primary carbon metabolism in *Aspergillus nidulans* and other *Aspergillus* spp. Fungal Genet. Biol. **46** Suppl. 1: S19–S44

Wortman, J.R., Gilsenan, J.M., Joardar, V., Deegan, J., Clutterbuck, J., Andersen, M.R., Archer, D., Bencina, M., Braus, G., Coutinho, P., von Döhren, H., Doonan, J., Driessen, A.J.M., Durek, P., Espeso, E., Fekete, E., **Flipphi, M.**, Garcia-Estrada, C., Geysens, S., Goldman, G., de Groot, P.W.J., Hansen, K., Harris, S.D., Heinekamp, T., Helmstaedt, K., Henrissat, B., Hofmann, G., Homan, T., Horio, T., Horiuchi, H., James, S., Jones, M., Karaffa, L., Karányi, Z., Kato, M., Keller, N., Kelly, D.E., Kiel, J.A.K.W., Kim, J-M., van der Klei, I.J., Klis, F.M., Kovalchuk, A., Krasevec, N., Kubicek, C.P., Liu, B., MacCabe, A., Meyer, V., Mirabito, P., Miskei, M., Mos, M., Mullins, J., Nelson, D.R., Nielsen, J., Oakley, B.R., Osmani, S.A., Pakula, T., Paszewski, A., Paulsen, I., Pilsyk,

S., Pócsi, I., Punt, P.J., Ram, A.F.J., Ren, Q., Robellet, X., Robson, G., Seiboth, B., van Solingen, P., Specht, T., Sun, J., Taheri-Talesh, N., Takeshita, N., Ussery, D., vanKuyk, P.A., Visser, H., van de Vondervoort, P.J.I., de Vries, R.P., Walton, J., Xiang, X., Xiong, Y., Zeng, A.P., Brandt, B.W., Cornell, M.J., van den Hondel, C.A.M.J.J., Visser, J., Oliver, S.G., and Turner, G. (2009) The 2008 update of the *Aspergillus nidulans* genome annotation: a community effort. Fungal Genet. Biol. **46** Suppl.1: S2–S13

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Flipphi, M., Robellet, X., Dequier, E., Leschelle, X., Felenbok, B. and Vélot, C. (2006) Functional analysis of *alcS*, a gene of the *alc* cluster in *Aspergillus nidulans*. Fungal Genet. Biol. **43** (4): 247–260

Forment, J.V., **Flipphi, M.**, Ramón, D., Ventura, L., and MacCabe, A.P. (2006) Identification of the *mstE* gene encoding a glucose-inducible, low affinity glucose transporter in *Aspergillus nidulans*. J. Biol. Chem. **281** (13): 8339–8346

Ramón, D., Centeno, J.M., Enrique, M., **Flipphi, M.**, Forment, J.V., Gil, J.V., Herrero, O., Ibañez, E., MacCabe, A.P., Manzanares, P., Orejas, M., Ortiz, M.J., Tamayo, J.A., Ventura, L., Vallés, S., Villanueva, A. and Vila, M. (2005) GMOs: optimism, pessimism, realism. In *Proceedings of the 12th Australian Wine Industry Technical Conference* (Blair, R.J., Williams, P.J. and Pretorius, I.S., eds). Winetitles, Adelaide. pp. 145–148

Flipphi, M., and Felenbok, B. (2004) The Onset of Carbon Catabolite Repression and Interplay between Specific Induction and Carbon Catabolite Repression in *Aspergillus nidulans*. In *The Mycota. III. Biochemistry and Molecular Biology.* 2nd *Edn.* (Brambl, R., and Marzluf, G.A., eds). Springer-Verlag, Berlin- Heidelberg. pp. 403–420

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Flipphi, M., van de Vondervoort, P.J.I., Ruijter, G.J.G., Visser, J., Arst, H.N., Jr., and Felenbok, B. (2003) Onset of carbon catabolite repression in *Aspergillus nidulans*: parallel involvement of hexokinase and glucokinase in sugar signalling. J. Biol. Chem. **278** (14): 11849–11857

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Flipphi, M.J.A., Visser, J., van der Veen, P., and de Graaff, L.H. (1994) Arabinase gene expression in *Aspergillus niger*: indications for coordinated regulation. Microbiology **140** (10): 2673–2682

de Vries, R.P., **Flipphi, M.J.A.**, Witteveen, C.F.B., and Visser, J. (1994) Characterization of an *Aspergillus nidulans* L-arabitol dehydrogenase mutant. FEMS Microbiol. Lett. **123** (1-2): 83–90

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Flipphi, M.J.A., van Heuvel, M., van der Veen, P., Visser, J., and de Graaff, L.H. (1993) Cloning and chraracterization of the *abfB* gene coding for the major *alpha*-L-arabinofuranosidase (ABF B) of *Aspergillus niger*. Curr. Genet. **24** (6): 525–532

Flipphi, M.J.A., Panneman, H., van der Veen, P., Visser, J., and de Graaff, L.H. (1993) Molecular cloning, expression and structure of the endo-1,5-*alpha*-L-arabinase gene of *Aspergillus niger*. Appl. Microbiol. Biotechnol. **40** (2-3): 318–326

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van der Veen, P., **Flipphi, M.J.A.**, Voragen, A.G.J., and Visser, J. (1993) Induction of extracellular arabinases on monomeric substrates in *Aspergillus niger*. Arch. Microbiol. **159** (1): 66–71

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Eur. Pat. Appl. EP 0 506,190

Inventors: Heuvel, M., Bakhuis, J.G., Coutel, Y., Harder, A., de Graaff, L.H., **Flipphi, M.J.A.**, van der Veen, P., Visser, J., and Andreoli, P.M.

Title: Cloning and expression of genes encoding arabinan-degrading enzymes of fungal origin. Priority date: 27-03-1991.

European Patent Office Bulletin 92 / 40, EP 0 506 190 A1 (30.09.1992): 75 pp.

PTC/NL92/00056

Inventors: Heuvel, M., Bakhuis, J.G., Coutel, Y., Harder, A., de Graaff, L.H., **Flipphi, M.J.A.**, van der Veen, P., Visser, J. and Andreoli, P.M.

Title: Cloning and expression of DNA molecules encoding arabinan-degrading enzymes of fungal origin. Priority date: 27-03-1991.

USP 5863783

Inventors: Heuvel, M., Bakhuis, J.G., Coutel, Y., Harder, A., de Graaff, L.H., **Flipphi, M.J.A.**, van der Veen, P., Visser, J. and Andreoli, P.M.

Title: Cloning and expression of DNA molecules encoding arabinan-degrading enzymes of fungal origin. Priority date: 25-11-1992.

USP 5989887

Inventors: Heuvel, M., Bakhuis, J.G., Coutel, Y., Harder, A., de Graaff, L.H., **Flipphi, M.J.A.**, van der Veen, P., Visser, J. and Andreoli, P.M.

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