

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/22939> holds various files of this Leiden University dissertation.

Author: Franken, Adriana Cornelia Wilhelmina

Title: Heme biosynthesis and regulation in the filamentous fungus *Aspergillus niger*

Issue Date: 2013-12-17

References

- Allen G, Bromley M, Kaye SJ, Keszenman-Pereyra D, Zucchi TD, Price J, Birch M, Oliver JD, Turner G (2011) Functional analysis of a mitochondrial phosphopantetheinyl transferase (PPTase) gene *pptB* in *Aspergillus fumigatus*. *Fungal Genet Biol* 48(4):456-464
- Amich J, Vicentefranqueira R, Leal F, Calera JA (2010) *Aspergillus fumigatus* survival in alkaline and extreme zinc-limiting environments relies on the induction of a zinc homeostasis system encoded by the *zrfC* and *aspf2* genes. *Eukaryot Cell* 9(3):424-437
- Amillet JM, Buisson N, Labbe-Bois R (1995) Positive and negative elements involved in the differential regulation by heme and oxygen of the HEM13 gene (coproporphyrinogen oxidase) in *Saccharomyces cerevisiae*. *Curr Genet* 28(6):503-511
- Amillet JM, Buisson N, Labbe-Bois R (1996) Characterization of an upstream activation sequence and two Rox1p-responsive sites controlling the induction of the yeast *HEM13* gene by oxygen and heme deficiency. *J Biol Chem* 271(40):24425-24432
- Amillet JM, Labbe-Bois R (1995) Isolation of the gene *HEM4* encoding uroporphyrinogen III synthase in *Saccharomyces cerevisiae*. *Yeast* 11(5):419-424
- Andersen HD, Jensen EB, Welinder KG (1992) A process for producing heme proteins. European Patent Application no. 0505311A2 PCT/DK1993/000094
- Banerjee R, Zou CG (2005) Redox regulation and reaction mechanism of human cystathionine- β -synthase: a PLP-dependent hemesensor protein. *Arch Biochem Biophys* 433(1):144-156
- Bennet JW, Lasure LL (1991) More gene manipulations in fungi. Academic Press, San Diego, CA
- Bien CM, Espenshade PJ (2010) Sterol regulatory element binding proteins in fungi: hypoxic transcription factors linked to pathogenesis. *Eukaryot Cell* 9(3):352-359
- Blanco M, Becerra M, González-Siso MI, Cerdán ME (2005) Functional characterization of *KIHEM13*, a hypoxic gene of *Kluyveromyces lactis*. *Can J Microbiol* 51(3):241-249
- Blatzer M, Binder U, Haas H (2011a) The metalloreductase FreB is involved in adaptation of *Aspergillus fumigatus* to iron starvation. *Fungal Genet Biol* 48(11):1027-33
- Blatzer M, Schrettl M, Sarg B, Lindner HH, Pfaller K, Haas H (2011b) SidL, an *Aspergillus fumigatus* transacetylase involved in biosynthesis of the siderophores ferricrocin and hydroxyferricrocin. *Appl Environ Microbiol* 77(14):4959-66

-
- Bonkovsky HL, Wood SG, Howell SK, Sinclair PR, Lincoln B, Healey JF, Sinclair JF (1986) High-performance liquid chromatographic separation and quantitation of tetrapyrroles from biological materials. *Anal Biochem* 155(1):56-64
- Bos CJ, Debets AJ, Swart K, Huybers A, Kobus G, Slakhorst SM (1988) Genetic analysis and the construction of master strains for assignment of genes to six linkage groups in *Aspergillus niger*. *Curr Genet* 14(5):437-443
- Braaksma M, Punt PJ (2008) *Aspergillus* as a cell factory for protein production: controlling protease activity in fungal production. In: Goldman GH, Osmani SA (eds) *The Aspergilli: Genomics, Medical Aspects, Biotechnology, and Research Methods*. CRC Press, Boca Raton, pp 441-455
- Braaksma M, Smilde AK, van der Werf MJ, Punt PJ (2009) The effect of environmental conditions on extracellular protease activity in controlled fermentations of *Aspergillus niger*. *Microbiology* 155(Pt 10):3430-3439
- Bradshaw RE, Dixon SW, Raitt DC, Pillar TM (1993) Isolation and nucleotide sequence of the 5-aminolevulinate synthase gene from *Aspergillus nidulans*. *Curr Genet* 23(5-6):501-507
- Camadro J-M, Labbe P (1996) Cloning and characterization of the yeast *HEM14* gene coding for protoporphyrinogen oxidase, the molecular target of diphenyl ether-type herbicides. *J Biol Chem* 271(15):9120-9128
- Carvalho ND, Arentshorst M, Kooistra R, Stam H, Sagt CM, van den Hondel CA, Ram AF (2011) Effects of a defective ERAD pathway on growth and heterologous protein production in *Aspergillus niger*. *Appl Microbiol Biotechnol* 89(2):357-373
- Chandrika SR, Padmanaban G (1980) Purification, properties and synthesis of δ -aminolaevulinate dehydratase from *Neurospora crassa*. *Biochem J* 191(1):29-36
- Chang PK, Ehrlich KC, Linz JE, Bhatnagar D, Cleveland TE, Bennett JW (1996) Characterization of the *Aspergillus parasiticus niaD* and *niiA* gene cluster. *Curr Genet* 30(1):68-75
- Chang YC, Bien CM, Lee H, Espenshade PJ, Kwon-Chung KJ (2007) Sre1p, a regulator of oxygen sensing and sterol homeostasis, is required for virulence in *Cryptococcus neoformans*. *Mol Microbiol* 64(3):614-629
- Chang YC, Ingavale SS, Bien C, Espenshade P, Kwon-Chung KJ (2009) Conservation of the sterol regulatory element-binding protein pathway and its pathobiological importance in *Cryptococcus neoformans*. *Eukaryot Cell* 8(11):1770-1779
- Claros MG, Vincens P (1996) Computational method to predict mitochondrially imported proteins and their targeting sequences. *Eur J Biochem* 241(3):779-786

-
- Conesa A, Jeenes D, Archer DB, van den Hondel CAMJJ, Punt PJ (2002a) Calnexin overexpression increases manganese peroxidase production in *Aspergillus niger*. *Appl Environ Microbiol* 68(2):846-851
- Conesa A, Punt PJ, van den Hondel CAMJJ (2002b) Fungal peroxidases: molecular aspects and applications. *J Biotechnol* 93(2):143-158
- Conesa A, van den Hondel CAMJJ, Punt PJ (2000) Studies on the production of fungal peroxidases in *Aspergillus niger*. *Appl Environ Microbiol* 66(7):3016-3023
- Corrick CM, Twomey AP, Hynes MJ (1987) The nucleotide sequence of the *amdS* gene of *Aspergillus nidulans* and the molecular characterization of 5' mutations. *Gene* 53(1):63-71
- Crane BR, Getzoff ED (1996) The relationship between structure and function for the sulfite reductases. *Curr Opin Struct Biol* 6(6):744-756
- Dailey HA (2002) Terminal steps of haem biosynthesis. *Biochem Soc Trans* 30(4):590-595
- Dailey HA, Wu C-K, Horanyi P, Medlock AE, Najahi-Missaoui W, Burden AE, Dailey TA, Rose J (2007) Altered orientation of active site residues in variants of human ferrochelatase. Evidence for a hydrogen bond network involved in catalysis. *Biochem* 46(27):7973-7979
- Dailey TA, Dailey HA (1998) Identification of an FAD superfamily containing protoporphyrinogen oxidases, monoamine oxidases, and phytoene desaturase. Expression and characterization of phytoene desaturase of *Myxococcus xanthus*. *J Biol Chem* 273(22):13658-13662
- Dailey TA, Dailey HA (2002) Identification of [2Fe-2S] clusters in microbial ferrochelatases. *J Bacteriol* 184(9):2460-2464
- Dailey TA, Dailey HA, Meissner P, Prasad ARK (1995) Cloning, sequence, and expression of mouse protoporphyrinogen oxidase. *Arch Biochem Biophys* 324(2):379-384
- Dailey TA, Woodruff JH, Dailey HA (2005) Examination of mitochondrial protein targeting of haem synthetic enzymes: in vivo identification of three functional haem-responsive motifs in 5-aminolaevulinic synthase. *Biochem J* 386(Pt 2):381-386
- de Ruiter-Jacobs YM, Broekhuijsen M, Unkles SE, Campbell EI, Kinghorn JR, Contreras R, Pouwels PH, van den Hondel CA (1989) A gene transfer system based on the homologous *pyrG* gene and efficient expression of bacterial genes in *Aspergillus oryzae*. *Curr Genet* 16(3):159-163
- De Weert S, Lokman BC (2010) Heterologous Expression of Peroxidases. In: Torres E, Ayala M (eds) *Biocatalysis Based on Heme Peroxidases*. Springer-Verlag Berlin Heidelberg, pp 315-334
- Douma RD, de Jonge LP, Jonker CT, Seifar RM, Heijnen JJ, van Gulik WM (2010) Intracellular metabolite determination in the presence of extracellular abundance: Application to the penicillin biosynthesis pathway in *Penicillium chrysogenum*. *Biotechnol bioeng* 107(1):105-115

-
- Eibes GM, Lu-Chau TA, Ruiz-Duenas FJ, Feijoo G, Martinez MJ, Martinez AT, Lema JM (2009) Effect of culture temperature on the heterologous expression of *Pleurotus eryngii* versatile peroxidase in *Aspergillus* hosts. *Bioprocess Biosyst Eng* 32(1):129-134
- Eisendle M, Oberegger H, Zadra I, Haas H (2003) The siderophore system is essential for viability of *Aspergillus nidulans*: functional analysis of two genes encoding L-ornithine N⁵-monooxygenase (*sidA*) and a non-ribosomal peptide synthetase (*sidC*). *Mol Microbiol* 49(2):359-375
- Elrod SL, Cherry JR, Jones A (1997) A Method for Increasing Hemoprotein Production in Filamentous Fungi. International Patent Application WO 97/47746 PCT/US97/10003
- Elrod SL, Jones A, Berka RM, Cherry JR (2000) Cloning of the *Aspergillus oryzae* 5-aminolevulinate synthase gene and its use as a selectable marker. *Curr Genet* 38(5):291-298
- Emanuelsson O, Brunak S, von Heijne G, Nielsen H (2007) Locating proteins in the cell using TargetP, SignalP and related tools. *Nat Protoc* 2(4):953-971
- Erskine PT, Senior N, Maignan S, Cooper J, Lambert R, Lewis G, Spencer P, Awan S, Warren M, Tickle IJ, Thomas P, Wood SP, Shoolingin-Jordan PM (1997) Crystallization of 5-aminolaevulinic acid dehydratase from *Escherichia coli* and *Saccharomyces cerevisiae* and preliminary X-ray characterization of the crystals. *Protein Sci* 6(8):1774-1776
- Espenshade PJ, Hughes AL (2007) Regulation of sterol synthesis in eukaryotes. *Annu Rev Genet* 41:401-427
- Ferreira GC (1999) Ferrochelataze. *Int J Biochem Cell Biol* 31(10):995-1000
- Ferreira GC, Gong J (1995) 5-Aminolevulinate synthase and the first step of heme biosynthesis. *J Bioenerg Biomembr* 27(2):151-159
- Ferreira GC, Neame PJ, Dailey HA (1993) Heme biosynthesis in mammalian systems: evidence of a Schiff base linkage between the pyridoxal 5'-phosphate cofactor and a lysine residue in 5-aminolevulinate synthase. *Protein Sci* 2(11):1959-1965
- Franken AC, Lokman BC, Ram AF, Punt PJ, van den Hondel CA, de Weert S (2011) Heme biosynthesis and its regulation: towards understanding and improvement of heme biosynthesis in filamentous fungi. *Appl Microbiol Biotechnol* 91(3):447-460
- Franken ACW, Lechner BE, Werner ER, Haas H, Lechner B, Lokman BC, van den Hondel CAMJJ, Weert Sd, Punt PJ Derepression of siderophore production does and heme biosynthesis does not increase intracellular heme availability in *Aspergillus niger*. *Submitted*
- Franken ACW, Lokman BC, Ram AFJ, van den Hondel CAMJJ, de Weert S, Punt PJ (2012) Analysis of the role of the *Aspergillus niger* aminolevulinic acid synthase (*hemA*) gene illustrates the difference between regulation of yeast and fungal haem- and sirohaem-dependent pathways. *FEMS Microbiol Lett* 335(2):104-112

-
- Franken ACW, Werner ER, Haas H, Lokman BC, van den Hondel CAMJJ, Ram AFJ, Weert Sd, Punt PJ (2013) The role of coproporphyrinogen III oxidase and ferrochelatase genes in heme biosynthesis and regulation in *Aspergillus niger*. *Appl Microbiol Biotechnol* DOI: 10.1007/s00253-013-5274-2 *In Press*
- Fujino E, Fujino T, Karita S, Kimura T, Sakka K, Ohmiya K (1999) Purification and characterization of the *Clostridium josui* porphobilinogen deaminase encoded by the *hemC* gene from a recombinant *Escherichia coli*. *J Biosci Bioeng* 87(4):535-537
- Gibson SL, Havens JJ, Metz L, Hilf R (2001) Is δ -aminolevulinic acid dehydratase rate limiting in heme biosynthesis following exposure of cells to δ -aminolevulinic acid? *Photochem Photobiol* 73(3):312-317
- Gollub EG, Liu K-P, Dayan J, Adlersberg M, Sprinson DB (1977) Yeast mutants deficient in heme biosynthesis and a heme mutant additionally blocked in cyclization of 2,3-oxidosqualene. *J Biol Chem* 252(9):2846-2854
- González-Domínguez M, Freire-Picos MA, Cerdán ME (2001) Haem regulation of the mitochondrial import of the *Kluyveromyces lactis* 5-aminolaevulinate synthase: an organelle approach. *Yeast* 18(1):41-48
- González-Domínguez M, Freire-Picos MA, Ramil E, Guiard B, Cerdán ME (2000) Heme-mediated transcriptional control in *Kluyveromyces lactis*. *Curr Genet* 38(4):171-177
- González-Domínguez M, Méndez-Carro C, Cerdán ME (1997) Isolation and characterization of the *KIHEM1* gene in *Kluyveromyces lactis*. *Yeast* 13(10):961-971
- Góra M, Pluta K, Chelstowska A, Żołądek T (2000) Suppressors of translation initiation defect in *hem12* locus of *Saccharomyces cerevisiae*. *Acta Biochim Pol* 47(1):181-190
- Graf SA, Haigh SE, Corson ED, Shirihai OS (2004) Targeting, import, and dimerization of a mammalian mitochondrial ATP binding cassette (ABC) transporter, ABCB10 (ABC-me). *J Biol Chem* 279(41):42954-42963
- Grünberg-Etkovitz N, Greenbaum L, Grinblat B, Malik Z (2006) Proteasomal degradation regulates expression of porphobilinogen deaminase (PBGD) mutants of acute intermittent porphyria. *Biochim Biophys Acta* 1762(9):819-827
- Guan Z, Chai X, Yu S, Hu H, Jiang Y, Meng Q, Wu Q (2010) Synthesis, molecular docking, and biological evaluation of novel triazole derivatives as antifungal agents. *Chem Biol Drug Des* 76(6):496-504
- Guillemette T, van Peij NNME, Goosen T, Lanthaler K, Robson GD, van den Hondel CAMJJ, Stam H, Archer DB (2007) Genomic analysis of the secretion stress response in the enzyme-producing cell factory *Aspergillus niger*. *BMC Genomics* 8:158

-
- Guo GG, Gu M, Etlinger JD (1994) 240-kDa proteasome inhibitor (CF-2) is identical to delta-aminolevulinic acid dehydratase. *J Biol Chem* 269(17):12399-12402
- Haas H (2003) Molecular genetics of fungal siderophore biosynthesis and uptake: the role of siderophores in iron uptake and storage. *Appl Microbiol Biotechnol* 62(4):316-330
- Haas H (2012) Iron – a key nexus in the virulence of *Aspergillus fumigatus*. *Frontiers in Microbiology* 3(28)
- Haas H, Eisendle M, Turgeon BG (2008) Siderophores in fungal physiology and virulence. *Annu Rev Phytopathol* 46:149-187
- Hagag S, Kubitschek-Barreira P, Neves GW, Amar D, Nierman W, Shalit I, Shamir R, Lopes-Bezerra L, Oshero N (2012) Transcriptional and proteomic analysis of the *Aspergillus fumigatus* Δ *prtT* protease-deficient mutant. *PLoS one* 7(4):e33604
- Hakala TK, Hildén K, Maijala P, Olsson C, Hatakka A (2006) Differential regulation of manganese peroxidases and characterization of two variable MnP encoding genes in the white-rot fungus *Physisporinus rivulosus*. *Appl Microbiol Biotechnol* 73(4):839-849
- Hammel KE, Cullen D (2008) Role of fungal peroxidases in biological ligninolysis. *Curr Opin Plant Biol* 11(3):349-355
- Hamza I (2006) Intracellular trafficking of porphyrins. *ACS Chem Biol* 1(10):627-629
- Hanley PJ, Drose S, Brandt U, Lareau RA, Banerjee AL, Srivastava DK, Banaszak LJ, Barycki JJ, Van Veldhoven PP, Daut J (2005) 5-Hydroxydecanoate is metabolised in mitochondria and creates a rate-limiting bottleneck for beta-oxidation of fatty acids. *J Physiol* 562(Pt 2):307-318
- Harris D, DeBolt S (2010) Synthesis, regulation and utilization of lignocellulosic biomass. *Plant Biotechnol J* 8(3):244-262
- Hiner ANP, Ruiz JH, López JNRg, Cánovas FGa, Brisset NC, Smith AT, Arnao MB, Acosta M (2002) Reactions of the Class II Peroxidases, Lignin Peroxidase and *Arthromyces ramosus* Peroxidase, with Hydrogen Peroxide. *J Biol Chem* 277(30):26879-26885
- Hoffman M, Góra M, Rytka J (2003) Identification of rate-limiting steps in yeast heme biosynthesis. *Biochem Biophys Res Commun* 310(4):1247-1253
- Hofrichter M, Ullrich R, Pecyna M, Liers C, Lundell T (2010) New and classic families of secreted fungal heme peroxidases. *Appl Microbiol Biotechnol* 87(3):871-897
- Horton P, Park KJ, Obayashi T, Fujita N, Harada H, Adams-Collier CJ, Nakai K (2007) WoLF PSORT: protein localization predictor. *Nucleic Acids Res* 35(Web Server issue):W585-7

-
- Hortschansky P, Eisendle M, Al Abdallah Q, Schmidt AD, Bergmann S, Thon M, Kniemeyer O, Abt B, Seeber B, Werner ER, Kato M, Brakhage AA, Haas H (2007) Interaction of HapX with the CCAAT-binding complex--a novel mechanism of gene regulation by iron. *EMBO J* 26(13):3157-3168
- Hou S, Reynolds MF, Horrigan FT, Heinemann SH, Hoshi T (2006) Reversible binding of heme to proteins in cellular signal transduction. *Acc Chem Res* 39(12):918-924
- Hughes AL, Todd BL, Espenshade PJ (2005) SREBP pathway responds to sterols and functions as an oxygen sensor in fission yeast. *Cell* 120(6):831-842
- Ildurm A, Heitman J (2010) Ferrochelatase is a conserved downstream target of the blue light-sensing White collar complex in fungi. *Microbiology* 156(Pt 8):2393-2407
- Inoue H, Nojima H, Okayama H (1990) High efficiency transformation of *Escherichia coli* with plasmids. *Gene* 96(1):23-28
- James MFM, Hift RJ (2000) Porphyrins. *Br J Anaesth* 85(1):143-153
- Jiang Y, Vasconcelles MJ, Wretzel S, Light A, Gilooly L, McDaid K, Oh C-S, Martin CE, Goldberg MA (2002) Mga2p processing by hypoxia and unsaturated fatty acids in *Saccharomyces cerevisiae*: impact on LORE-dependent gene expression. *Eukaryot Cell* 1(3):481-490
- Jordan PM, Berry A (1980) Preuroporphyrinogen, a universal intermediate in the biosynthesis of uroporphyrinogen III. *FEBS Lett* 112(1):86-88
- Jorgensen TR, Park J, Arentshorst M, van Welzen AM, Lamers G, Vankuyk PA, Damveld RA, van den Hondel CA, Nielsen KF, Frisvad JC, Ram AF (2011) The molecular and genetic basis of conidial pigmentation in *Aspergillus niger*. *Fungal Genet Biol* 48(5):544-553
- Jung WH, Saikia S, Hu G, Wang J, Fung CK, D'Souza C, White R, Kronstad JW (2010) HapX positively and negatively regulates the transcriptional response to iron deprivation in *Cryptococcus neoformans*. *PLoS Pathog* 6(11):e1001209
- Kabe Y, Ohmori M, Shinouchi K, Tsuboi Y, Hirao S, Azuma M, Watanabe H, Okura I, Handa H (2006) Porphyrin accumulation in mitochondria is mediated by 2-oxoglutarate carrier. *J Biol Chem* 281(42):31729-31735
- Kelly JM, Hynes MJ (1985) Transformation of *Aspergillus niger* by the *amdS* gene of *Aspergillus nidulans* *EMBO J* 4(2):475-479
- Keng T (1992) HAP1 and ROX1 form a regulatory pathway in the repression of *HEM13* transcription in *Saccharomyces cerevisiae*. *Mol Cell Biol* 12(6):2616-2623
- Keng T, Guarente L (1987) Constitutive expression of the yeast *HEM1* gene is actually a composite of activation and repression. *Proc Natl Acad Sci U S A* 84(24):9113-9117

-
- Keng T, Richard C, Larocque R (1992) Structure and regulation of yeast *HEM3*, the gene for porphobilinogen deaminase. *Mol Gen Genet* 234(2):233-243
- Kim SJ, Lee JA, Joo JC, Yoo YJ, Kim YH, Song BK (2010) The development of a thermostable CiP (*Coprinus cinereus* peroxidase) through *in silico* design. *Biotechnol Prog* 26(4):1038-1046
- Kim SJ, Lee JA, Kim YH, Song BK (2009) Optimization of the functional expression of *Coprinus cinereus* peroxidase in *Pichia pastoris* by varying the host and promoter. *J Microbiol Biotechnol* 19(9):966-971
- Klinkenberg LG, Mennella TA, Luetkenhaus K, Zitomer RS (2005) Combinatorial repression of the hypoxic genes of *Saccharomyces cerevisiae* by DNA binding proteins Rox1 and Mot3. *Eukaryot Cell* 4(4):649-660
- Kolar M, Punt PJ, van den Hondel CA, Schwab H (1988) Transformation of *Penicillium chrysogenum* using dominant selection markers and expression of an *Escherichia coli lacZ* fusion gene. *Gene* 62(1):127-134
- Kragl C, Schrettl M, Abt B, Sarg B, Lindner HH, Haas H (2007) EstB-mediated hydrolysis of the siderophore triacetylfusarinine C optimizes iron uptake of *Aspergillus fumigatus*. *Eukaryot Cell* 6(8):1278-1285
- Krishnamurthy P, Xie T, Schuetz JD (2007) The role of transporters in cellular heme and porphyrin homeostasis. *Pharmacol Ther* 114(3):345-358
- Krishnamurthy PC, Du G, Fukuda Y, Sun D, Sampath J, Mercer KE, Wang J, Sosa-Pineda B, Murti KG, Schuetz JD (2006) Identification of a mammalian mitochondrial porphyrin transporter. *Nature* 443(7111):586-589
- Kurlandzka A, Źołądek T, Rytka J, Labbe-Bois R, Urban-Grimal D (1988) The effects *in vivo* of mutationally modified uroporphyrinogen decarboxylase in different *hem12* mutants of baker's yeast (*Saccharomyces cerevisiae*). *Biochem J* 253(1):109-116
- Labbe-Bois R (1990) The ferrochelatase from *Saccharomyces cerevisiae*. Sequence, disruption, and expression of its structural gene *HEM15*. *J Biol Chem* 265(13):7278-7283
- Lamas-Maceiras M, Núñez L, Rodríguez-Belmonte E, González-Siso MI, Cerdán ME (2007) Functional characterization of *KIHAP1*: a model to foresee different mechanisms of transcriptional regulation by Hap1p in yeasts. *Gene* 405(1-2):96-107
- Lathrop JT, Timko MP (1993) Regulation by heme of mitochondrial protein transport through a conserved amino acid motif. *Science* 259(5094):522-525
- Layer G, Reichelt J, Jahn D, Heinz DW (2010) Structure and function of enzymes in heme biosynthesis. *Protein Sci* 19(6):1137-1161

-
- Leonowicz A, Cho N-S, Luterek J, Wilkolazka A, Wojtas-Wasilewska M, Matuszewska A, Hofrichter M, Wesenberg D, Rogalski J (2001) Fungal laccase: properties and activity on lignin. *J Basic Microbiol* 41(3-4):185-227
- Leustek T, Smith M, Murillo M, Singh DP, Smith AG, Woodcock SC, Awan SJ, Warren MJ (1997) Siroheme biosynthesis in higher plants. Analysis of an S-adenosyl-L-methionine-dependent uroporphyrinogen III methyltransferase from *Arabidopsis thaliana*. *J Biol Chem* 272(5):2744-2752
- Limongi P, Kjalke M, Vind J, Tams JW, Johansson T, Welinder KG (1995) Disulfide bonds and glycosylation in fungal peroxidases. *Eur J Biochem* 227(1-2):270-276
- Liu H, Gravelat FN, Chiang LY, Chen D, Vanier G, Ejzykowicz DE, Ibrahim AS, Nierman WC, Sheppard DC, Filler SG (2010) *Aspergillus fumigatus* AcuM regulates both iron acquisition and gluconeogenesis. *Mol Microbiol* 78(4):1038-1054
- Lokman BC, Joosten V, Hovenkamp J, Gouka RJ, Verrips CT, van den Hondel CAMJJ (2003) Efficient production of *Arthromyces ramosus* peroxidase by *Aspergillus awamori*. *J Biotechnol* 103(2):183-190
- Lorenz RT, Parks LW (1987) Regulation of ergosterol biosynthesis and sterol uptake in a sterol-auxotrophic yeast. *J Bacteriol* 169(8):3707-3711
- Luzzani C, Cardillo SB, Bermúdez Moretti M, Correa García S (2007) New insights into the regulation of the *Saccharomyces cerevisiae* UGA4 gene: two parallel pathways participate in carbon-regulated transcription. *Microbiology* 153(11):3677-3684
- Martínez AT (2002) Molecular biology and structure-function of lignin- degrading heme peroxidases. *Enzyme Microb Technol* 30(4):425-444
- Martínez ÁT, Ruiz-Dueñas FJ, Martínez MJ, del Río JC, Gutiérrez A (2009) Enzymatic delignification of plant cell wall: from nature to mill. *Curr Opin Biotech* 20(3):348-357
- Masuo S, Terabayashi Y, Shimizu M, Fujii T, Kitazume T, Takaya N (2010) Global gene expression analysis of *Aspergillus nidulans* reveals metabolic shift and transcription suppression under hypoxia. *Mol Genet Genomics* 284(6):415-424
- Mathews MA, Schubert HL, Whitby FG, Alexander KJ, Schadick K, Bergonia HA, Phillips JD, Hill CP (2001) Crystal structure of human uroporphyrinogen III synthase. *EMBO J* 20(21):5832-5839
- Mattern IE, van Noort JM, van den BP, Archer DB, Roberts IN, van den Hondel CAMJJ (1992) Isolation and characterization of mutants of *Aspergillus niger* deficient in extracellular proteases. *Mol Genet* 234(2):332-336
- Mclvaine TC (1921) A buffer solution for colorimetric comparison. *J Biol Chem* 49(1):183-186

-
- McNicholas PM, Javor G, Darie S, Gunsalus RP (1997) Expression of the heme biosynthetic pathway genes *hemCD*, *hemH*, *hemM*, and *hemA* of *Escherichia coli*. *FEMS Microbiol Lett* 146(1):143-148
- Mercier A, Watt S, Bähler J, Labbé S (2008) Key function for the CCAAT-binding factor Php4 to regulate gene expression in response to iron deficiency in fission yeast. *Eukaryot Cell* 7(3):493-508
- Meyer V, Ram AF, Punt PJ (2010) Genetics, genetic manipulation, and approaches to strain improvement of filamentous fungi. In: Davies JE, Demain AL (eds) *Manual of industrial microbiology and biotechnology*. 3 edn. Wiley, New York, pp 318-329
- Moore MR (2009) An historical introduction to porphyrin and chlorophyll synthesis. In: Warren MJ, Smith AG, Moore MR (eds) *Tetrapyrroles, their birth, life and death*. Molecular Biology Intelligence Unit. Springer New York, pp 1-28
- Moretti MB, Garcia SC, Batlle A (2000) Porphyrin biosynthesis intermediates are not regulating δ -aminolevulinic acid transport in *Saccharomyces cerevisiae*. *Biochem Biophys Res Commun* 272(3):946-950
- Murphy MJ, Siegel LM (1973) Siroheme and sirohydrochlorin. The basis for a new type of porphyrin-related prosthetic group common to both assimilatory and dissimilatory sulfite reductases. *J Biol Chem* 248(19):6911-6919
- Muthukrishnan S, Malathi K, Padmanaban G (1972) δ -aminolaevulinic acid dehydratase, the regulatory enzyme of the haem-biosynthetic pathway in *Neurospora crassa* *Biochem J* 129(1):31-37
- Muthukrishnan S, Padmanaban G, Sarma PS (1969) Regulation of heme biosynthesis in *Neurospora crassa*. *J Biol Chem* 244(15):4241-4246
- Myers AM, Crivellone MD, Koerner TJ, Tzagoloff A (1987) Characterization of the yeast *HEM2* gene and transcriptional regulation of *COX5* and *COR1* by heme. *J Biol Chem* 262(35):16822-16829
- Núñez L, González-Siso I, Becerra M, Cerdán ME (2004) Functional characterisation and transcriptional regulation of the *KIHEM12* gene from *Kluyveromyces lactis*. *Curr Genet* 46(3):147-157
- Núñez L, Rodríguez-Torres A, Cerdán ME (2008) Regulatory elements in the *KIHEM1* promoter. *Biochim Biophys Acta* 1779(2):128-133
- Oberegger H, Schoeser M, Zadra I, Abt B, Haas H (2001) SREA is involved in regulation of siderophore biosynthesis, utilization and uptake in *Aspergillus nidulans*. *Mol Microbiol* 41(5):1077-1089
- Pae HO, Son Y, Kim NH, Jeong HJ, Chang KC, Chung HT (2010) Role of heme oxygenase in preserving vascular bioactive NO. *Nitric oxide* 23(4):251-257

-
- Pandak WM, Ren S, Marques D, Hall E, Redford K, Mallonee D, Bohdan P, Heuman D, Gil G, Hylemon P (2002) Transport of cholesterol into mitochondria is rate-limiting for bile acid synthesis via the alternative pathway in primary rat hepatocytes. *J Biol Chem* 277(50):48158-48164
- Panek H, O'Brian MR (2002) A whole genome view of prokaryotic haem biosynthesis. *Microbiology* 148(Pt 8):2273-2282
- Parish T, Schaeffer M, Roberts G, Duncan K (2005) HemZ is essential for heme biosynthesis in *Mycobacterium tuberculosis*. *Tuberculosis (Edinb)* 85(3):197-204
- Paterson JK, Shukla S, Black CM, Tachiwada T, Garfield S, Wincovitch S, Ernst DN, Agadir A, Li X, Ambudkar SV, Szakacs G, Akiyama S-i, Gottesman MM (2007) Human ABCB6 localizes to both the outer mitochondrial membrane and the plasma membrane. *Biochem* 46(33):9443-9452
- Pauly M, Keegstra K (2010) Plant cell wall polymers as precursors for biofuels. *Curr Opin Plant Biol* 13(3):305-312
- Pendrak ML, Chao MP, Yan SS, Roberts DD (2004) Heme oxygenase in *Candida albicans* is regulated by hemoglobin and is necessary for metabolism of exogenous heme and hemoglobin to α -biliverdin. *J Biol Chem* 279(5):3426-3433
- Pérez-Boada M, Doyle WA, Ruiz-Dueñas FJ, Martínez MJ, Martínez AT, Smith AT (2002) Expression of *Pleurotus eryngii* versatile peroxidase in *Escherichia coli* and optimisation of in vitro folding. *Enzyme Microb Technol* 30(4):518-524
- Phillips JD, Whitby FG, Warby CA, Labbe P, Yang C, Pflugrath JW, Ferrara JD, Robinson H, Kushner JP, Hill CP (2004) Crystal structure of the oxygen-dependant coproporphyrinogen oxidase (Hem13p) of *Saccharomyces cerevisiae*. *J Biol Chem* 279(37):38960-38968
- Philpott CC (2006) Iron uptake in fungi: a system for every source. *Biochim Biophys Acta* 1763(7):636-645
- Polo CF, Frisardi AL, Resnik ER, Schoua AE, del C. Batlle AM (1988) Factors influencing fluorescence spectra of free porphyrins. *Clin Chem* 34(4):757-760
- Pontecorvo G, Roper JA, Hemmons LM, Macdonald KD, Bufton AW (1953) The genetics of *Aspergillus nidulans*. *Adv Genet* 5:141-238
- Posey JE, Gherardini FC (2000) Lack of a role for iron in the Lyme disease pathogen. *Science* 288(5471):1651-1653
- Power T, Ortoneda M, Morrissey JP, Dobson AD (2006) Differential expression of genes involved in iron metabolism in *Aspergillus fumigatus*. *Int Microbiol* 9(4):281-287
- Prasad ARK, Dailey HA (1995) Effect of cellular location on the function of ferrochelatase. *J Biol Chem* 270(31):18198-18200

-
- Protchenko O, Philpott CC (2003) Regulation of intracellular heme levels by *HMX1*, a homologue of heme oxygenase, in *Saccharomyces cerevisiae*. *J Biol Chem* 278(38):36582-36587
- Protchenko O, Rodriguez-Suarez R, Androphy R, Bussey H, Philpott CC (2006) A screen for genes of heme uptake identifies the FLC family required for import of FAD into the endoplasmic reticulum. *J Biol Chem* 281(30):21445-21457
- Protchenko O, Shakoury-Elizeh M, Keane P, Storey J, Androphy R, Philpott CC (2008) Role of PUG1 in inducible porphyrin and heme transport in *Saccharomyces cerevisiae*. *Eukaryot Cell* 7(5):859-871
- Punt PJ, Oliver RP, Dingemans MA, Pouwels PH, van den Hondel CA (1987) Transformation of *Aspergillus* based on the hygromycin B resistance marker from *Escherichia coli*. *Gene* 56(1):117-124
- Punt PJ, Schuren FH, Lehmbeck J, Christensen T, Hjort C, van den Hondel CA (2008) Characterization of the *Aspergillus niger prtT*, a unique regulator of extracellular protease encoding genes. *Fungal Genet Biol* 45(12):1591-1599
- Punt PJ, van Biezen N, Conesa A, Albers A, Mangnus J, van den Hondel CAMJJ (2002) Filamentous fungi as cell factories for heterologous protein production. *Trends Biotechnol* 20(5):200-206
- Rao AU, Carta LK, Lesuisse E, Hamza I (2005) Lack of heme synthesis in a free-living eukaryote. *Proc Natl Acad Sci U S A* 102(12):4270-4275
- Raux E, Leech HK, Beck R, Schubert HL, Santander PJ, Roessner CA, Scott AI, Martens JH, Jahn D, Thermes C, Rambach A, Warren MJ (2003) Identification and functional analysis of enzymes required for precorrin-2 dehydrogenation and metal ion insertion in the biosynthesis of sirohaem and cobalamin in *Bacillus megaterium*. *Biochem J* 370(Pt 2):505-516
- Raux E, McVeigh T, Peters SE, Leustek T, Warren MJ (1999) The role of *Saccharomyces cerevisiae* Met1p and Met8p in sirohaem and cobalamin biosynthesis. *Biochem J* 338 (Pt 3):701-708
- Reiber K, Reeves EP, Neville CM, Winkler R, Gebhardt P, Kavanagh K, Doyle S (2005) The expression of selected non-ribosomal peptide synthetases in *Aspergillus fumigatus* is controlled by the availability of free iron. *FEMS Microbiol Lett* 248(1):83-91
- Sakaino M, Ishigaki M, Ohgari Y, Kitajima S, Masaki R, Yamamoto A, Taketani S (2009) Dual mitochondrial localization and different roles of the reversible reaction of mammalian ferrochelatase. *FEBS J* 276(19):5559-5570
- Sambrook, Fritsch, Maniatis (1989) *Molecular cloning: a laboratory manual*, vol 3, 2nd edn. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY
- Sambrook J, Russell DW (2001) *Molecular cloning: a laboratory manual*, 3rd edn. Spring Harbor Press, Cold Spring Harbor, NY

-
- Santos R, Buisson N, Knight S, Dancis A, Camadro JM, Lesuisse E (2003) Haemin uptake and use as an iron source by *Candida albicans*: role of *CaHMx1*-encoded haem oxygenase. *Microbiology* 149(Pt 3):579-588
- Schlaepfer IR, Mattoon JR, Bajszar G (1994) The Sequence and Potential Regulatory Elements of the *Hem2* Promoter of *Saccharomyces cerevisiae*. *Yeast* 10(2):227-229
- Schrettl M, Beckmann N, Varga J, Heinekamp T, Jacobsen ID, Jochl C, Moussa TA, Wang S, Gsaller F, Blatzer M, Werner ER, Niermann WC, Brakhage AA, Haas H (2010) HapX-mediated adaptation to iron starvation is crucial for virulence of *Aspergillus fumigatus*. *PLoS Pathog* 6(9)
- Schrettl M, Bignell E, Kragl C, Joechl C, Rogers T, Arst HN, Jr., Haynes K, Haas H (2004) Siderophore biosynthesis but not reductive iron assimilation is essential for *Aspergillus fumigatus* virulence. *J Exp Med* 200(9):1213-1219
- Schrettl M, Bignell E, Kragl C, Sabiha Y, Loss O, Eisendle M, Wallner A, Arst HN, Jr., Haynes K, Haas H (2007) Distinct Roles for Intra- and Extracellular Siderophores during *Aspergillus fumigatus* Infection. *PLoS Pathog* 3(9):e128
- Schrettl M, Kim HS, Eisendle M, Kragl C, Nierman WC, Heinekamp T, Werner ER, Jacobsen I, Illmer P, Yi H, Brakhage AA, Haas H (2008) SreA-mediated iron regulation in *Aspergillus fumigatus*. *Mol Microbiol* 70(1):27-43
- Schubert HL, Raux E, Brindley AA, Leech HK, Wilson KS, Hill CP, Warren MJ (2002a) The structure of *Saccharomyces cerevisiae* Met8p, a bifunctional dehydrogenase and ferrochelatase. *EMBO J* 21(9):2068-2075
- Schubert HL, Raux E, Matthews MA, Phillips JD, Wilson KS, Hill CP, Warren MJ (2002b) Structural diversity in metal ion chelation and the structure of uroporphyrinogen III synthase. *Biochem Soc Trans* 30(4):595-600
- Senior NM, Brocklehurst K, Cooper JB, Wood SP, Erskine P, Shoolingin-Jordan PM, Thomas PG, Warren MJ (1996) Comparative studies on the 5-aminolaevulinic acid dehydratases from *Pisum sativum*, *Escherichia coli* and *Saccharomyces cerevisiae*. *Biochem J* 320 (Pt 2):401-412
- Sharon H, Hagag S, Osherov N (2009) Transcription factor PrtT controls expression of multiple secreted proteases in the human pathogenic mold *Aspergillus fumigatus*. *Infect Immun* 77(9):4051-4060
- Shirihai OS, Gregory T, Yu C, Orkin SH, Weiss MJ (2000) ABC-me: a novel mitochondrial transporter induced by GATA-1 during erythroid differentiation. *EMBO J* 19(11):2492-2502
- Simmons BA, Loqué D, Ralph J (2010) Advances in modifying lignin for enhanced biofuel production. *Curr Opin Plant Biol* 13(3):313-320

-
- Smith AT, Doyle WA (2006) Engineered peroxidases with veratryl alcohol oxidase activity. WO/2006/114616
- Smith AT, Doyle WA, Dorlet P, Ivancich A (2009) Spectroscopic evidence for an engineered, catalytically active Trp radical that creates the unique reactivity of lignin peroxidase. Proc Natl Acad Sci U S A 106(38):16084-16089
- Smith AT, Santama N, Dacey S, Edwards M, Bray RC, Thorneley RN, Burke JF (1990) Expression of a synthetic gene for horseradish peroxidase C in *Escherichia coli* and folding and activation of the recombinant enzyme with Ca²⁺ and heme. J Biol Chem 265(22):13335-13343
- Susa S, Daimon M, Ono H, Li S, Yoshida T, Kato T (2002) Heme inhibits the mitochondrial import of coproporphyrinogen oxidase. Blood 100(13):4678-4679
- Takaya N (2009) Response to hypoxia, reduction of electron acceptors, and subsequent survival by filamentous fungi. Biosci Biotechnol Biochem 73(1):1-8
- Taketani S, Adachi Y, Nakahashi Y (2000) Regulation of the expression of human ferrochelatase by intracellular iron levels. Eur J Biochem 267(15):4685-4692
- Tanaka A, Kato M, Nagase T, Kobayashi T, Tsukagoshi N (2002) Isolation of genes encoding novel transcription factors which interact with the Hap complex from *Aspergillus* species. Biochim Biophys Acta 1576(1-2):176-182
- te Biesebeke R, Boussier A, van Biezen N, Braaksma M, van den Hondel CA, de Vos WM, Punt PJ (2006) Expression of *Aspergillus* hemoglobin domain activities in *Aspergillus oryzae* grown on solid substrates improves growth rate and enzyme production. Biotechnol J 1(7-8):822-827
- Todd BL, Stewart EV, Burg JS, Hughes AL, Espenshade PJ (2006) Sterol regulatory element binding protein is a principal regulator of anaerobic gene expression in fission yeast. Mol Cell Biol 26(7):2817-2831
- Tripathy BC, Sherameti I, Oelmüller R (2010) Siroheme: an essential component for life on earth. Plant Signal Behav 5(1):14-20
- Tsuchida M, Emi Y, Kida Y, Sakaguchi M (2008) Human ABC transporter isoform B6 (ABCB6) localizes primarily in the Golgi apparatus. Biochem Biophys Res Commun 369(2):369-375
- Urban-Grimal D, Labbe-Bois R (1981) Genetic and biochemical characterization of mutants of *Saccharomyces cerevisiae* blocked in six different steps of heme biosynthesis. Mol Gen Genet 183(1):85-92
- Valiante V, Heinekamp T, Jain R, Hartl A, Brakhage AA (2008) The mitogen-activated protein kinase MpkA of *Aspergillus fumigatus* regulates cell wall signaling and oxidative stress response. Fungal Genet Biol 45(5):618-27

-
- van Hartingsveldt W, Mattern IE, van Zeijl CM, Pouwels PH, van den Hondel CA (1987) Development of a homologous transformation system for *Aspergillus niger* based on the *pyrG* gene. *Mol Genet* 206(1):71-75
- Vargas PD, Furuyama K, Sassa S, Shibahara S (2008) Hypoxia decreases the expression of the two enzymes responsible for producing linear and cyclic tetrapyrroles in the heme biosynthetic pathway. *FEBS J* 275(23):5947-5959
- Vasconcelles MJ, Jiang Y, McDaid K, Gilooly L, Wretzel S, Porter DL, Martin CE, Goldberg MA (2001) Identification and characterization of a low oxygen response element involved in the hypoxic induction of a family of *Saccharomyces cerevisiae* genes. Implications for the conservation of oxygen sensing in eukaryotes. *J Biol Chem* 276(17):14374-14384
- Vieira J, Messing J (1991) New pUC-derived cloning vectors with different selectable markers and DNA replication origins. *Gene* 100:189-194
- Vodisch M, Scherlach K, Winkler R, Hertweck C, Braun HP, Roth M, Haas H, Werner ER, Brakhage AA, Kniemeyer O (2011) Analysis of the *Aspergillus fumigatus* proteome reveals metabolic changes and the activation of the psurotin A biosynthesis gene cluster in response to hypoxia. *J Proteome Res* 10(5):2508-2524
- Wariishi H, Valli K, Gold MH (1992) Manganese(II) oxidation by manganese peroxidase from the basidiomycete *Phanerochaete chrysosporium*. Kinetic mechanism and role of chelators. *J Biol Chem* 267(33):23688-23695
- Warren MJ, Scott AI (1990) Tetrapyrrole assembly and modification into the ligands of biologically functional cofactors. *Trends Biochem Sci* 15(12):486-491
- Weenink XO, Punt PJ, van den Hondel CAMJJ, Ram AFJ (2006) A new method for screening and isolation of hypersecretion mutants in *Aspergillus niger*. *Appl Microbiol Biotechnol* 69(6):711-717
- Wilks A (2002) Analysis of heme and hemoproteins. In: Smith AG, Witty M (eds) Heme, chlorophyll, and bilins. Humana Press, Totowa, NJ, pp 157-184
- Willger SD, Puttikamonkul S, Kim KH, Burritt JB, Grahl N, Metzler LJ, Barbuch R, Bard M, Lawrence CB, Cramer RA, Jr. (2008) A sterol-regulatory element binding protein is required for cell polarity, hypoxia adaptation, azole drug resistance, and virulence in *Aspergillus fumigatus*. *PLoS Pathog* 4(11):e1000200
- Yasmin S, Alcazar-Fuoli L, Grundlinger M, Puempel T, Cairns T, Blatzer M, Lopez JF, Grimalt JO, Bignell E, Haas H (2012) Mevalonate governs interdependency of ergosterol and siderophore biosyntheses in the fungal pathogen *Aspergillus fumigatus*. *Proc Natl Acad Sci U S A* 109(8):E497-504

-
- Zagorec M, Buhler J-M, Treich I, Keng T, Guarente L, Labbe-Bois R (1988) Isolation, sequence, and regulation by oxygen of the yeast *HEM13* gene coding for coproporphyrinogen oxidase. *J Biol Chem* 263(20):9718-9724
- Zhou S, Fushinobu S, Kim SW, Nakanishi Y, Maruyama J, Kitamoto K, Wakagi T, Shoun H (2011) Functional analysis and subcellular location of two flavohemoglobins from *Aspergillus oryzae*. *Fungal Genet Biol* 48(2):200-207
- Zhou S, Fushinobu S, Kim SW, Nakanishi Y, Wakagi T, Shoun H (2010) *Aspergillus oryzae* flavohemoglobins promote oxidative damage by hydrogen peroxide. *Biochem Biophys Res Commun* 394(3):558-561
- Zhou S, Fushinobu S, Nakanishi Y, Kim SW, Wakagi T, Shoun H (2009) Cloning and characterization of two flavohemoglobins from *Aspergillus oryzae*. *Biochem Biophys Res Commun* 381(1):7-11
- Zitomer RS, Lowry CV (1992) Regulation of gene expression by oxygen in *Saccharomyces cerevisiae*. *Microbiol Rev* 56(1):1-11