

Erasmus University Rotterdam, the Netherlands
CSC PhD 2015 Project Description

School/Department:	ErasmusMC, Department of Medical Microbiology and Infectious Diseases
Project Title:	Improving the diagnosis and treatment of mycetoma
Abstract:	<p><i>Mycetoma is an implantation mycosis, characterized by large tumour-like swellings, highly endemic in Africa. Also in India and even China, cases have been reported. It has recently attracted the attention of the World Health Organisation (WHO) as a neglected disease. It can be caused by 56 different micro-organisms. Currently the management of mycetoma is disappointing, resulting in high recurrence (25-50%) and amputation (2.8-25%) rates, which in its turn leads to social isolation and economic dependence on the family. According to the WHO, first focus for this disease needs to be to determine the true burden of disease in terms of prevalence and incidence. For this a proper diagnostic tool is needed which is currently lacking. This tool needs to be cheap and easy to perform with limited equipment. The recombinase polymerase amplification and in situ hybridisation are excellent tools for this purpose and will be developed for the 11 most common causative agents in ErasmusMC and validated in cooperation with the mycetoma clinic in Sudan. Next to that this tool will be used in different countries to determine the prevalence and incidence. To optimise treatment, focus will be on eliminating residual pathogens after surgery. To this purpose the use of photodynamic therapy (PDT) will be assessed. For this the most successful combination of light-activated agents (photosensitizers) and light of a proper wavelength will be determined in vitro and in vivo in our larvae model and later in a clinical trial.</i></p>
Requirements of candidate:	<p>Master degree: Yes</p> <p>Background: the candidate must possess a master's degree in either biology, medical biology or medicine. The candidate needs to be innovative and keen to learn. He or she also needs to have an interest in tropical diseases</p> <p>IELTS Grade: 7.0 (minimal 6.0 per component) or TOEFL: 100 (minimal 20 per component)</p>
Supervisor information:	<p>Co-promotor: Dr. Wendy W.J. van de Sande Email address: w.vandesande@erasmusmc.nl</p> <p>Promotor: Prof. Dr. Annelies Verbon Email address: a.verbon@erasmusmc.nl</p>

Literature list (co-promotor)

- 1) S. Abdalla Ahmed, **W.W.J. van de Sande**, D.A. Stevens, A.H. Fahal, G.S. de Hoog. Taxonomic revision of agents of black grain eumycetoma in the order *Pleosporales*. *Persoonia* (accepted).
- 2) **W.W.J. van de Sande**, A.H. Fahal, M. Goodfellow, El-S. Mahgoub, O. Welsh, E.E. Zijlstra, Merits and pitfalls of currently used diagnostic tools in mycetoma. *Plos Negl trop Dis* 8 (2014) e2918
- 3) S. Abdalla Ahmed, W. Kloezen, F. Duncanson, E.E. Zijlstra, G.S. de Hoog, A.H. Fahal, **W.W.J. van de Sande**. *Madurella mycetomatis* is highly susceptible towards ravuconazole. *Plos Negl trop Dis* 8 (2014) e2942
- 4) N.A. Mhmoud, A.H. Fahal, El-S. Mahgoub, **W.W.J. van de Sande**. The combination of Amoxicillin-clavulanic acid and ketoconazole proved to be effective and safe for the treatment of *Madurella mycetomatis* eumycetoma patients with *Staphylococcus aureus* co-infection. *Plos Negl trop Dis* 8 (2014) e2959
- 5) K. Geneugelijk, W. Kloezen, A.H. Fahal, **W.W.J. van de Sande**. Active matrix metalloprotease-9 is associated with the collagen capsule surrounding the *M. mycetomatis* grain in mycetoma. *Plos Negl trop Dis* 8 (2014) e2754
- 6) P.E.B. Verwer, W.B. van Leeuwen, V. Girard, V. Monnin, A. van Belkum, J.F. Staab, H.A. Verbrugh, I.A.J.M. Bakker-Woudenberg, **W.W.J. van de Sande**. Discrimination of *Aspergillus lentulus* from *Aspergillus fumigatus* by Raman spectroscopy and MALDI-TOF MS, *Eur J Clin Microbiol* 33 (2014) 245-251
- 7) **W.W.J. Van de Sande**, E. Mahgoub, A.H. Fahal, M. Goodfellow, O. Welsh, E.E. Zijlstra. The mycetoma knowledge gap: identification of research priorities. *Plos Negl trop Dis* 8 (2014) e2667
- 8) **W.W.J. van de Sande** (2013). Global burden of human mycetoma: a systematic review and meta-analysis. *Plos Negl trop Dis*, 7(11): e2550
- 9) J. M. Refos, A.G. Vonk, K. Eadie, J.R. Lo-Ten-Foe, H.A. Verbrugh, A.D. van Diepeningen, **W.W.J. van de Sande** (2013). Double-stranded RNA mycovirus infection of *Aspergillus fumigatus* is not dependent on the genetic make-up of the host, *PlosOne* 8(10): e77381
- 10) P.E.B. Verwer, M.T. ten Kate, F.H. Falcone, S. Morroll, H.A. Verbrugh, I.A.J.M. Bakker-Woudenberg, **W.W.J. van de Sande** (2013). Evidence Supporting a Role for Mammalian Chitinases in Efficacy of Caspofungin against Experimental Aspergillosis in Immunocompromised Rats. *PlosOne* 8(10):e75848
- 11) N. Mhmoud, A.H. Fahal, **W.W.J. van de Sande**. Association of IL-10 and CCL5 single nucleotide polymorphisms with tuberculosis in the Sudanese population. *Trop Med Int Health* 18 (2013) 1119-1127
- 12) M. Bruins, J.W. Gerrisen, **W.W.J. van de Sande WWJ**, A. van Belkum, A. Bos A (2013). Enabling a transferable calibration model for metal-oxide type electronic noses. *Sens. Actuator B-Chem* 188: 1187-1195
- 13) J.J. van Hellemond, A.G. Vonk, C. de Vogel, R. Koelewijn, N. Vaessen, A.H. Fahal, A. van Belkum, **W.W.J. van de Sande**. Association of eumycetoma and schistosomiasis. *Plos Negl trop Dis* 7 (2013) e2241
- 14) G.S. De Hoog, S.A. Ahmed, M.J. Najafzadeh, D.A. Sutton, M.S. Keisari, A.H. Fahal, U. Eberhardt, G.J. Verkleij, L. Xin, B. Stielow, **W.W.J. van de Sande**. Phylogenetic findings suggest possible new habitat and routes of infection of human eumycetoma. *PloS Negl Trop Dis* 7 (2013) e2229
- 15) A. Van Belkum, A.H. Fahal, **W.W.J. van de Sande**. Mycetoma caused by *Madurella mycetomatis*: a completely neglected medico-social dilemma. *Adv Exp Med Biol* 764 (2013) 179-189
- 16) E.A.M. Elagab, M.M. Mukhtar, A.H. Fahal, **W.W.J. van de Sande**. Peripheral Blood Mononuclear Cells of mycetoma patients react different to *M. mycetomatis* antigens than healthy endemic controls, *Plos Negl trop Dis* 7

	<p>(2013) e2081</p> <p>17) A.I. Ibrahim, A.M. El Hassan, A. Fahal, W.W.J. van de Sande. A histopathological exploration of the <i>Madurella mycetomatis</i> grain. PloSOne 8 (2013) e57774</p> <p>18) N.A. Mhmoud, A.H. Fahal, W.W.J. van de Sande. The association between interleukin-10 cytokine and CC chemokine ligand 5 polymorphisms and mycetoma granuloma formation. Med Mycol 51 (2013) 524-533</p> <p>19) M. Bruins, Rahim Z, Bos A, van de Sande WWJ, Endtz H, van Belkum A. Diagnosis of active tuberculosis by e-nose analysis of exhaled air. Tuberculosis 93(2013) 232-238</p> <p>20) A.H. Fahal, W.W.J. van de Sande. The epidemiology of mycetoma, Curr Fungal Infect Rep 6 (2012) 320-326</p> <p>21) W. Kloezen, J.F. Meis, I. Curfs Breuker, A.H. Fahal, W.W.J. van de Sande. <i>In vitro</i> antifungal activity of Isavuconazole against <i>Madurella mycetomatis</i>. Antimicrob Agents Chemotherapy 56 (2012) 6054-6055</p> <p>22) M. Dhingra, N. Kaistha, N. Bansal, L.S. Solanki, J. Chander, G.P.Thami, W.W.J. van de Sande. <i>Nocardia nova</i> mycetoma over forehead in a lepromatous leprosy patient. Dermatol Online J 18 (2012) 3</p> <p>23) N.A. Mhmoud, A.H. Fahal, W.W.J. van de Sande. CD4+ T-lymphocytopenia in HIV-negative tuberculosis patients in Sudan. J Infect 65 (2012) 370-372</p> <p>24) N.A. Mhmoud, S.A. Ahmed, A.H. Fahal, G.S de Hoog, A.H. Gerrits van den Ende and W.W.J. van de Sande, <i>Pleurostomophora ochracea</i>, a novel agent of human eumycetoma with yellow grains. J Clin Microbiol 50 (2012) 2987-2994</p> <p>25) W.W.J. van de Sande, Phylogenetic analysis of the complete mitochondrial genome of <i>Madurella mycetomatis</i> confirms its taxonomic position within the order Sordariales. PloSOne. 7 (2012) e38654</p> <p>26) P. Datta, S. Arora, R. Jain, J. Chander and W.W.J. van de Sande, Secondary peritonitis caused by <i>Streptomyces viridis</i>: case report and review of the literature. J Clin Microbiol. 50 (2012) 1813-1814</p> <p>27) G.S. de Hoog, A. D. van Diepeningen, S. el-Mahgoub, W. W. J. van de Sande, New species of <i>Madurella</i>, causative agents of black-grain mycetoma. J. Clin. Microbiol. 50 (2012) 988-994</p> <p>28) P.E. Verwer, M.L. van Duijn, M. Tavakol, I.A.J.M. Bakker-Woudenberg, and W.W.J. van de Sande, Reshuffling of <i>Aspergillus fumigatus</i> cell wall components chitin and β-glucan under the influence of caspofungin or nikkomycin Z alone or in combination. Antimicrob Agents Chemother. 56 (2012) 1595-1598</p> <p>29) R.G. Vitale, G.S. de Hoog, P. Schwarz, E. Dannaoui, S. Deng, M. Machouart, K. Voigt, W.W.J. van de Sande, S. Dolatabadi, J. F. Meis, and G. Walther, Antifungal susceptibility and phylogeny of opportunistic members of the order mucorales, J Clin Microbiol 50 (2012) 66-75</p> <p>30) N. de Klerk, C.P. de Vogel, A. Fahal, A. Van Belkum, and W.W.J. Van de Sande, Fructose-Bisphosphate Aldolase and Pyruvate Kinase, two novel immunogens in <i>Madurella mycetomatis</i> Med Mycol. 50 (2012) 143-151</p> <p>31) P.E. Verwer, M.C. Woodle, T. Boekhout, F. Hagen, I.A. Bakker-Woudenberg, and W.W.J van de Sande, Cryptococcus and Trichosporon spp. are susceptible in vitro to branched histidine- and lysine-rich peptides (BHKPs). J Antimicrob Chemother. 66 (2011) 1649-1652.</p> <p>32) A. van Belkum, A.H. Fahal, and W.W.J van de Sande, In vitro susceptibility of <i>Madurella mycetomatis</i> to posaconazole and terbinafine. Antimicrob Agents Chemother. 55 (2011) 1771-1773.</p> <p>33) M.G. de Boer, L.B. Gelinck, B.D. van Zelst, W.W.J. van de Sande, L.N. Willems, J.T. van Dissel, R. de Jonge, and F.P. Kroon, beta-D-glucan and S-adenosylmethionine serum levels for the diagnosis of <i>Pneumocystis pneumonia</i></p>
--	---

- in HIV-negative patients: a prospective study. *J Infect.* 62 (2011) 93-100.
- 34) **W.W.J. van de Sande**, J.R. Lo-Ten-Foe, A. van Belkum, M.G. Netea, B.J. Kullberg, and A.G. Vonk, Mycoviruses: future therapeutic agents of invasive fungal infections in humans? *Eur J Clin Microbiol Infect Dis.* 29 (2010) 755-763.
- 35) **W.W.J. van de Sande**, A.H. Fahal, I.A.J.M. Bakker-Woudenberg, and A. van Belkum, *Madurella mycetomatis* is not susceptible to the echinocandin class of antifungal agents. *Antimicrob Agents Chemother.* 54 (2010) 2738-2740.
- 36) **W.W.J. van de Sande**, A. Fahal, M. Tavakol, and A. van Belkum, Polymorphisms in catechol-O-methyltransferase and cytochrome p450 subfamily 19 genes predispose towards *Madurella mycetomatis*-induced mycetoma susceptibility. *Med Mycol.* 48 (2010) 959-968.
- 37) **W.W. J. van de Sande**, M. Tavakol, W. van Vianen, and I.A. Bakker-Woudenberg, The effects of antifungal agents to conidial and hyphal forms of *Aspergillus fumigatus*. *Med Mycol.* 48 (2010) 48-55.
- 38) L.Y. Chai, M.G. Netea, J. Sugui, A.G. Vonk, **W.W.J. van de Sande**, A. Warris, K.J. Kwon-Chung, and B.J. Kullberg, *Aspergillus fumigatus* conidial melanin modulates host cytokine response. *Immunobiology.* 215 (2010) 915-920.

Literature list (promotor)

- R.S. Boersma, K.S. Jie, A.C. Voogd, K. Hamulyak, **A. Verbon**, H.C. Schouten. Concentrated citrate locking in order to reduce the long-term complications of central venous catheters: a randomized controlled trial in patients with hematological malignancies. *Support Care Cancer* (2014)
- C. Rokx, **A. Verbon**, B. Rijnders. Successful switch to rilpivirine/tenofovir/emtricitabine in HIV-1-infected patients with an isolated K103N mutation acquired during prior nonnucleoside reverse transcriptase inhibitor therapy. *HIV Med* (2014)
- R.J. Hassing, W.H. Goessens, W. van Pelt W, D.J. Mevius, B.H. Stricker, N. Molhoek, **A. Verbon**, P.J. van Genderen. Salmonella subtypes with increased MICs for azithromycin in travelers returned to The Netherlands. *Emerg Infect Dis.* 20 (2014) 705-708.
- M. Haeseker, T. Havenith, L. Stolk, C. Neef, C. Bruggeman, **A. Verbon**. Is the standard dose of amoxicillin-clavulanic acid sufficient? *BMC Pharmacol Toxicol.* 15 (2014) 38
- B.H. Wittekamp, M. Chalabi, W.N. van Mook, B. Winkens, **A. Verbon**, D.C. Bergmans. Catheter-related bloodstream infections: a prospective observational study of central venous and arterial catheters. *Scand J Infect Dis.* 45 (2013) 738-745.
- A. Verbon**. [The Health Council of the Netherlands' advice on Lyme disease] Gezondheidsraadadvies over lymeziekte. *Ned Tijdschr Geneesk.* 157 (2013) A6626.
- M. Schouten, A.J. van Velde, I.J. Snijders, **A. Verbon**, B.J. Rijnders, M.E. van der Ende. [Late diagnosis of HIV positive patients in Rotterdam, the Netherlands: risk factors and missed opportunities] Late diagnose van hiv-patienten in Rotterdam: risicofactoren en gemiste kansen. *Ned Tijdschr Geneesk.* 157 (2013) A5731.
- C. Rokx, M.E. van der Ende, **A. Verbon**, B.J. Rijnders. Peginterferon alfa-2a for AIDS-associated Kaposi sarcoma: experience with 10 patients. *Clin Infect Dis.* 57 (2013) 1497-1499.
- E.A. Misch, **A. Verbon**, J.M. Prins, S.J. Skerrett, T.R. Hawn. A TLR6 polymorphism is associated with increased risk of Legionnaires' disease. *Genes Immun.* 14 (2013) 420-426.

	<p>R.J. Hassing, W.H. Goessens, D.J. Mevius, W. van Pelt, J.W. Mouton, A. Verbon, P.J. van Genderen. Decreased ciprofloxacin susceptibility in <i>Salmonella</i> Typhi and Paratyphi infections in ill-returned travellers: the impact on clinical outcome and future treatment options. <i>Eur J Clin Microbiol Infect Dis</i>. 32 (2013) 1295-1301.</p> <p>M.B. Haeseker, E. Pijpers, N.H. Dukers-Muijrers, P. Nelemans, C.J. Hoebe, C.A. Bruggeman CA, A. verbon, V.J. Goosens. Association of cytomegalovirus and other pathogens with frailty and diabetes mellitus, but not with cardiovascular disease and mortality in psycho-geriatric patients; a prospective cohort study. <i>Immun Ageing</i>. 10 (2013) 30.</p> <p>M. Haeseker, L. Stolk, F. Nieman, C. Hoebe, C. Neef, C. Bruggeman C, A. Verbon. The ciprofloxacin target AUC : MIC ratio is not reached in hospitalized patients with the recommended dosing regimens. <i>Br J Clin Pharmacol</i>. 2013 Jan;75(1):180-5.</p> <p>F.N. Frakking, W.C. Rottier, J.W. Dorigo-Zetsma, J.M. van Hattem, B.C. van Hees, J.A. Kluytmans, S.P. Iutgens, J.M. Prins, S.F. Thijsen, A. Verbon, B.J. Vlamincx, J.W. Cohen Stuart, M.A. Leverstein-van hall, M.J. Bonten. Appropriateness of empirical treatment and outcome in bacteremia caused by extended-spectrum-beta-lactamase-producing bacteria. <i>Antimicrob Agents Chemother</i>. 57 (2013) 3092-3099.</p> <p>C.S. Andeweg, I.M. Mulder, R.J. Felt-Bersma, A. Verbon, G.J. van der Wilt, H. van Goor, J.F. Lange, J. Stoker, M.A. Boermeester, R.P. Bleichrodt. Guidelines of diagnostics and treatment of acute left-sided colonic diverticulitis. <i>Dig Surg</i>. 30 (2013) 278-292.</p> <p>C.S. Andeweg, R. Felt-Bersma, A. Verbon, J. Stoker, M. Boermeester, R. Bleichrodt. [Summary of the practice guideline on diverticulitis in the colon: diagnostics and treatment in specialty care]. <i>Samenvatting richtlijn diverticulitis van het colon: diagnostiek en behandeling in de tweede lijn</i>. <i>Ned Tijdschr Geneesk</i>. 157 (2013) A6124.</p> <p>J. Potjewijd, R.A. de Paus, A. van Wengen, J. Damoiseaux, A. Verbon, E. van de Vosse. Disseminated <i>Mycobacterium genavense</i> infection in a patient with a novel partial interleukin-12/23 receptor beta1 deficiency. <i>Clin Immunol</i>. 144 (2012) 83-86.</p> <p>W.L. Hansen, J. Beuving, A. Verbon, P.F. Wolffs. One-day workflow scheme for bacterial pathogen detection and antimicrobial resistance testing from blood cultures. <i>J Vis Exp</i>. 65 (2012).</p> <p>M.B. Haeseker, N.H. Dukers-Muijrers, C.J. Hoebe, C.A. Bruggeman, J.W. Cals, A. Verbon. Trends in antibiotic prescribing in adults in Dutch general practice. <i>PLoS One</i>. 7 (2012) e51860.</p> <p>M.L. Grijzen, R. Steingrover, F.W. Wit, S. Jurriaans, A. Verbon, K. Brinkman, M.E. van der Ende, R. Soetekouw, F. de Wolf, J.M. Lange, H. Schuitemaker, J.M. Prins. No treatment versus 24 or 60 weeks of antiretroviral treatment during primary HIV infection: the randomized Primo-SHM trial. <i>PLoS Med</i>. 9 (2012) e1001196.</p> <p>A.L. Cruz, A. Verbon, L.J. Geurink, P.J. Verheijen, J.J. Heijnen, W.M. van Gulik. Use of sequential-batch fermentations to characterize the impact of mild hypothermic temperatures on the anaerobic stoichiometry and kinetics of <i>Saccharomyces cerevisiae</i>. <i>Biotechnol Bioeng</i>. 109 (2012):1735-1744.</p> <p>J. Bierau, J.A. Bakker, J.A. Schippers, J.A. Grashorn, M. Lindhout, S.H. Lowe, A.D. Paulussen, A. Verbon. Erythrocyte inosine triphosphatase activity is decreased in HIV-seropositive individuals. <i>PLoS One</i>. 7(2012) e30175.</p> <p>M.A. Beerepoot, G ter Riet, S. Nys, W.M. van der Wal, C.A. de Borgie, T.M. de Reijke TM, J.M. Prins, J. Koeijers, A. Verbon, E. Stobberingh, S.E. Geerlings. Lactobacilli vs antibiotics to prevent urinary tract infections: a randomized, double-blind, noninferiority trial in postmenopausal women. <i>Arch Intern Med</i>.</p>
--	--

Erasmus University Rotterdam, the Netherlands

CSC PhD 2015 Project Description

	<p>14 (2012) 704-712.</p> <p>C.M. van Nispen tot Pannerden, A. Verbon, E.J. Kuipers. Recurrent Clostridium difficile infection: what are the treatment options? Drugs. 71 (2011) 853-868.</p> <p>G.J. Oudhuis, D.C. Bergmans, A. Verbon. Probiotics for prevention of nosocomial infections: efficacy and adverse effects. Curr Opin Crit Care. 17(2011) 487-492.</p> <p>G.J. Oudhuis, D.C. Bergmans, T. Dormans, J.H. Zwaveling, A. Kessels, M.H. Prins, E.E. Stobberingh, A. Verbon. Probiotics versus antibiotic decontamination of the digestive tract: infection and mortality. Intensive Care Med. 37 (2011) 110-117.</p> <p>A. Kesselring, L. Gras, C. Smit, G. van Twillert, A. Verbon, F. de Wolf, P. Reiss, F. Wit. Immunodeficiency as a risk factor for non-AIDS-defining malignancies in HIV-1-infected patients receiving combination antiretroviral therapy. Clin Infect Dis. 52 (2011) 1458-1465.</p> <p>J. Beuving, A. Verbon, F.A. Gronthoud, E.E. Stobberingh, P.F. Wolffs. Antibiotic susceptibility testing of grown blood cultures by combining culture and real-time polymerase chain reaction is rapid and effective. PLoS One. 6 (2011) e27689.</p> <p>J. Beuving, C.F. van der Donk, C.F. Linssen, P.F. Wolffs, A. Verbon. Evaluation of direct inoculation of the BD PHOENIX system from positive BACTEC blood cultures for both Gram-positive cocci and Gram-negative rods. BMC Microbiol. 11 (2011) 156.</p> <p>M.A. Beerepoot, G. ter Riet, S. Nys, W.M. van der Wal, C.A. de Borgie, T.M. de Reijke, J.M. Prins, J. Koeijers, A. Verbon, E. Stobberingh, S.E. Geerlings. Cranberries vs antibiotics to prevent urinary tract infections: a randomized double-blind noninferiority trial in premenopausal women. Arch Intern Med. 171 (2011): 1270-1278.</p> <p>A. Verbon, J.M. Prins. Shoulder pain in two HIV-seropositive patients. Avascular necrosis (AVN) of the bone. Neth J Med. 68 (2010) 322-325.</p> <p>L. van Dommelen, A. Verbon, H.R. van Doorn, V.J. Goossens. Acute hepatitis B virus infection with simultaneous high HBsAg and high anti-HBs signals in a previously HBV vaccinated HIV-1 positive patient. J Clin Virol. 47 (2010):293-296.</p> <p>J.J. Koeijers, A. Verbon, A.G. Kessels, A. Bartelds, G. Donkers, S. Nys, E.E. Stobberingh. Urinary tract infection in male general practice patients: uropathogens and antibiotic susceptibility. Urology. 76 (2010) 336-340.</p>
--	---