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I. General Objectives

New members of the genus *Malassezia* have been identified during the last 10 years and the genus now comprises 11 species. Their ubiquitous presence and their involvement in skin diseases besides constituting a possible financial burden for patients may also affect their quality of life. Data on the epidemiology and pathogenicity of individual species and the role of strains with distinct genotypes are either sparse or absent. Studying the global epidemiology of *Malassezia* species and their potential to cause disease in humans and animals will highlight aspects of the association of these commensal and pathogenic organisms with their habitat, which is the skin of humans and animals (Figure 1).

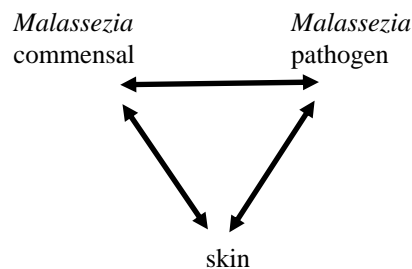


Figure 1. Factors that underlie the transformation of *Malassezia* yeasts from commensals to pathogens are still poorly understood. Establishing an ISHAM Working Group is among the primary necessities for achieving this objective.

a. Epidemiology of *Malassezia* yeasts.

There are many problems that have been encountered in epidemiological studies. Investigations on the isolation of a mixture of species from healthy and diseased skin have indicated that the fastidious species *M. globosa*, *M. restricta* and *M. obtusa* may be overgrown in culture by those which are more amenable to laboratory conditions, i.e. *M. furfur* and *M. sympodialis*. Also, interlaboratory variations in the procedures for isolation, recovery and identification of *Malassezia* species may have a significant impact on the reported recovery rates for these organisms. Nevertheless, from the worldwide reports, current data suggest that individual *Malassezia* species have different geographical distributions. *M. sympodialis* is isolated at high rates from healthy volunteers and patients suffering from atopic or seborrheic dermatitis in the North of Europe, whereas in the South of Europe *M. globosa* has been the predominant species in healthy subjects as well as in pityriasis versicolor and seborrheic dermatitis patients. Moreover, *M. obtusa* is frequently isolated from atopic dermatitis patients and healthy volunteers in the North and no *M. obtusa* isolation has been reported in the South of Europe. In Japan, extensive use of sequencing of isolates from epidemiological studies of healthy volunteers and atopic dermatitis patients have resulted in the description of the new species *M. dermatis*, *M. japonica* and *M. nana*. In the molecular epidemiology of *Malassezia* species several techniques have been applied, each one demonstrating interesting aspects of the dispersion and ecology of this genus. Amplified fragment length polymorphism analysis (AFLP), sequencing of the rDNA, PCR-fingerprinting, PCR-single strand conformational polymorphism analysis (PCR-SSCP) and PCR-restriction fragment length polymorphism analysis (PCR-RFLP), Fourier transform infrared

spectroscopy (FT-IRS) and the terminal fragment length polymorphism (tFLP) method have been used by independent groups for typing *Malassezia* strains, as well as for identification and typing directly from skin specimens. Furthermore, the identification and typing potential of novel methods, such as the Luminex xMap and multilocus sequencing typing (MLST) remain to be evaluated.

The results so far have highlighted an association of *M. globosa* subtypes with atopic dermatitis and pityriasis versicolor lesions, as well as a correlation between certain *M. furfur* subtypes and certain geographical areas. *M. sympodialis* displayed little variation within the species. There are few data on *M. japonica*, *M. nana* and *M. dermatis* subtypes which have been almost exclusively reported from Japan. However, based on nucleotide sequence analysis of the D1/D2 and ITS1 regions, strains of *M. nana* isolated from animals in Brazil have displayed some divergence among themselves as well as showing differences from the Japanese isolate.

On the whole, the molecular methodology employed so far has produced seemingly unequivocal results. However, these are not always directly comparable because the protocols for sampling, inoculation media, colony identification and further processing of the *Malassezia* isolates vary extensively. Only a few data are available about the distribution of *Malassezia* yeasts on the skin of domestic or wild animals. Most studies have been concerned with the non lipid- dependent species *M. pachydermatis* in dogs. These investigations highlighted the common association of *M. pachydermatis* with otitis externa and canine seborrhic dermatitis and canine atopic dermatitis. *M. pachydermatis* is also an occasional cause of otitis and dermatitis in cats. Further surveys have demonstrated that lipid-dependent yeasts may be isolated from other animals (cats, ungulates or birds) and there are sporadic reports of skin disease caused by *Malassezia* in horses and goats. Recently, two new species, *M. equina* and *M. caprae*, have been isolated from healthy animals in Spain. The risk of a transfer of *Malassezia* yeasts from some animal species to humans should be evaluated.

b. Pathobiology.

Malassezia yeasts possess species specific properties which have not been fully explored. The expression of genes coding for allergenic proteins, restricted within certain species such as *M. globosa*, *M. restricta* and *M. sympodialis*, has shown different allergenic protein profiles thus indicating a possible variable between these species in their contribution to the pathogenesis of atopic dermatitis. Also, very few studies on the intraspecific variations of allergenic proteins have been carried out leaving much to be elucidated about the role of each *Malassezia* species in the pathogenesis of diseases, such as atopic dermatitis. Furthermore, the mechanism leading to the depigmentation observed in pityriasis versicolor alba has not been clarified. In that respect, factors such as the indole derivative pityriacitrin, produced by *M. furfur* and *M. pachydermatis*, which has been shown to be a potent UV filter and the observation that *Malassezia* yeasts display variation, both inter and intraspecific in their effect on melanin production encourage wholesale multidisciplinary studies. All of these have the aim of producing lasting results conducive to the realisation of the Working Group's objectives.

II. Specific objectives

1. Determine appropriate sampling, isolation, identification and antifungal susceptibility testing procedures for *Malassezia* yeasts isolated from humans or animals and determine the zoonotic risk of *M. pachydermatis*, by collecting and typing strains associated to *M. pachydermatis* catheter-related fungaemia.
2. Create a list of reference strains and characterize them by use of the agreed standard methods that would be chosen. A database will be created to provide tools to perform online identifications.
3. Determine the most suitable typing method, or set of complementary typing methods.
4. Examine possible associations of *Malassezia* species-specific distribution patterns on healthy and diseased human skin. Evaluate whether geographical and/or disease-specific *Malassezia* species occur, and if so, whether they are associated with certain genotypes. Explore the occurrence of episodic or consistently mixed *Malassezia* species occurrence in related human dermatoses.

5. Review the pathobiology of *Malassezia* strains from multiple geographical locations. Assess *Malassezia* pathophysiology with respect to the tryptophan-derived secondary metabolism of, in particular, *M. furfur* and *M. pachydermatis*.
6. Define the factors that determine the distribution of *Malassezia* species amongst different animal hosts, and also the factors that render individual animals susceptible to the diseases caused by *Malassezia*.

III. Time schedule, verifiable and quantifiable objectives

If accepted, launching of the Group's activities will be pursued at the TIMM meeting, Torino, Italy, 2007 to increase participation of colleagues from different countries and set suitable evaluation measures regarding procedures and results.

Presentation of results on objective items 1, 2 and 3 above is not anticipated until 2 years (ISHAM Congress, Tokyo, Japan, 2009). Items 4 to 6 described in the Specific Objectives paragraph is expected to be concluded in year 3-4. Report writing will commence from year 2 onwards.

IV. Expansion of the Working Group

Colleagues from different parts of the world, with special research interests in *Malassezia* epidemiology and pathobiology can contact the convener.

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