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Perspective

Sarcoptes-World Molecular Network (Sarcoptes-WMN): integrating research on scabies

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SUMMARY

Parasites threaten human and animal health globally. It is estimated that more than 60% of people on planet Earth carry at least one parasite, many of them several different species. Unfortunately, parasite studies suffer from duplications and inconsistencies between different investigator groups. Hence, groups need to collaborate in an integrated manner in areas including parasite control, improved therapy strategies, diagnostic and surveillance tools, and public awareness. Parasite studies will be better served if there is coordinated management of field data and samples across multidisciplinary approach plans, among academic and non-academic organizations worldwide. In this paper we report the first 'Living organism-World Molecular Network', with the cooperation of 167 parasitologists from 88 countries on all continents. This integrative approach, the 'Sarcoptes-World Molecular Network', seeks to harmonize Sarcoptes epidemiology, diagnosis, treatment, and molecular studies from all over the world, with the aim of decreasing mite infestations in humans and animals.

1. The parasite and the disease

Sarcoptes scabiei causes sarcoptic mange in companion, livestock, and wild animals, as well as scabies in humans. This parasite has a very broad host range, which includes more than 100 mammalian species belonging to 27 families from 10 orders.[1] In addition to its potential to cause huge economic loss due to reduced production and increased mortality in animals,[1–3] scabies is an emerging/re-emerging infectious disease that threatens human and animal health globally.[4–6] There are no accurate estimates of the prevalence of sarcoptic mange in many of the different animal populations affected worldwide. However, there are several examples of how serious an *S. scabiei* epidemic can be, causing devastating morbidity.[1]

It is estimated that 300 million people are infested with scabies worldwide.[7,8] This conservative estimate is most likely too low considering that the infection is frequently not reported in humans.[9] The prevalence of scabies in African children can be as high as 40–80%,[10,11] and in remote indigenous communities in northern Australia, up to 50% of children and 25% of adults were

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found to be infested.[12] In developing countries, scabies is a significant public health problem because it is highly prevalent and complications are frequent.[13] These may include, in the presence of bacterial superinfection, acute post-streptococcal glomerulonephritis (PSGN). Children appear to be more commonly affected by streptococcal superinfection,[14] and complications such as PSGN may be fatal.[15] A study performed in The Gambia showed that skin lesions associated with scabies were the leading portal of entry for organisms causing septicemia in infants aged 3 months or less.[16] The presence and severity of scabies are often associated with poor living conditions and illiteracy.[17] Introduction of a single case of scabies into crowded living conditions can result in an epidemic.[18,19] The disease is also a curse in high-income countries where the prevalence may be increasing due to diagnostic failures, suspected resistance against some acaricides, and perhaps changes in social habits.[20]

Chemotherapy of scabies is important in clinical work. Cheap, safe, and efficacious drugs are not commonly available in some of the poorer countries. Emerging drug resistance to *S. scabiei* has recently been reported from regions where previously effective acaricides have been used extensively in socially disadvantaged communities and in some developing countries.[21–23] Researchers are addressing this in various ways, e.g., by testing (identifying) novel chemotherapeutics,[24–26] by immunological intervention, and/or by molecular studies of the mite, including, for example, investigating whether glutathione transferases (GSTs) play any role in conferring acaricide resistance to *S. scabiei* and other mechanisms.[27–31]

The diagnosis of Sarcoptes is pivotal for assessing eradication programs[32–34] and for epidemiological studies.[35] For the experienced dermatologist, the clinical diagnosis of scabies may not appear difficult, but in fact scabies continues to be a diagnostic challenge[36] because of its diverging clinical manifestations and many differential diagnoses.[24] The definitive diagnosis of Sarcoptes infestation can be difficult as in many cases only a few mites are present on an infested host, and skin manifestations can be subtle or atypical.[37] There is a lack of accurate diagnostic tests for humans.[24,38] In addition, for many domestic and wild animals, including threatened species such as Chamois and Gorillas,[39,40] better specific Sarcoptes diagnostic methods need to be developed.

For many years, parasitologists have been immersed in an ongoing debate as to "whether or not *S. scabiei* infecting different hosts belong to different species or sub-species, or whether they are, in fact, monospecific".[4] Today, the species *Sarcoptes scabiei* is divided into varieties based on the host species, e.g., *S. scabiei* var. *hominis* and *S. scabiei* var. *canis*. Humans can be infested with animal varieties, but in this case the disease is usually limited to certain topographic sites and is self-limited. It has been shown that an epidemiological relationship does not exist between sarcoptic mange foci,[41] while morphological studies have failed to identify any significant differences between populations of mites.[42] Experimental cross-contamination of hosts with some different *S. scabiei* varieties is commonly unsuccessful,[43] however, cross-transmission/infection is common in some varieties, e.g., *S. scabiei* var. *vulpes/canis* readily infect dogs and other canids as well as felids, including domestic European cats.[2] In addition, this variety of *S. scabiei* also readily infects/infests humans causing pseudoscabies.[2] Research into finding an answer to the question of whether or not *S. scabiei* is a single species and understanding the 'host-specificity' of the mite has advanced in the last decade with the advent of polymerase chain reaction (PCR) technology and molecular marker systems in the genetic era. Molecular studies based on short fragments of mitochondrial or ribosomal DNA spacer regions failed to identify *S. scabiei* populations to the host species level and geographical localities.[42,44–47] Studies on a central fragment of the 16S gene and the complete cytochrome c oxidase subunit I gene gene (COI) in combination with microsatellite markers provided some support for a genetic differentiation of *S. scabiei*. These genetic markers demonstrated significant relationships between *S. scabiei* mitochondrial DNA (mtDNA) haplotypes and microsatellite allele frequencies, and host species and geographical locations, even at skin-scale level.[48–50] Immunological studies have shown that each variety of *S. scabiei* tested produces a range of proteins, both variety-specific and immunologically identical and shared by the different mite sub-types.[51]

Clinical manifestations of scabies range from singular nodules to severe crusted scabies. The underlying causes for these different manifestations may be found in the immunological host response, but are not fully understood.

In summary, there is ongoing debate about the host specificity and range of different Sarcoptes populations on a worldwide scale. The taxonomical status of this important parasite remains unclear. Sensitive diagnostic methods are still not available for many host species, including humans, and new therapeutic options need to be evaluated. Therefore, well-designed studies aimed at better understanding the world epidemiology and transmission dynamics, and the design and development of sensitive and specific diagnostic methods are of paramount importance.

2. Sarcoptes-World Molecular Network initiative

During the last few years we have been working on Sarcoptes mite epidemiology, diagnosis, treatment, control, clinical aspects, and genetics, and we are in touch with colleagues who are working on Sarcoptes mite epidemiology and control worldwide. This has enabled us to create the 'Sarcoptes-World Molecular Network' (WMN), which currently includes 167 parasitologists from 88 countries from all continents. The Sarcoptes-WMN aims to be a facilitator of collaborative, mainly molecular research on Sarcoptes. The network will bring together a wide spectrum of research communities, aiming to share information, expertise, samples, and infrastructure. The Sarcoptes-WMN includes different institutions such as universities, hospitals, centers of animal health, medical colleges, public health institutes, private clinics, medical centers, biological institutes, veterinary research laboratories, animal health services, clinical research centers, public health institutes, and wildlife conservation institutes worldwide.

3. Overall strategy of the Sarcoptes-World Molecular Network

The Sarcoptes-WMN plans to 'pump-prime' a new genetic era of research into this important parasite, with the aim of achieving the following:

1. Technology and knowledge transfer among specialists and human and veterinary practitioners all over the world on the diagnosis, epidemiology, and management of *Sarcoptes scabiei* infestations. This will prevent Sarcoptes research duplication and foster protocol uniformity, which would fast-track world research on Sarcoptes.
2. Increase knowledge on the world epidemiology of this ubiquitous parasite.
3. The design and development of universal and specific Sarcoptes PCR-based and antibody-based diagnostic methods.
4. Create a global open access 'Sarcoptes-Specimens World Bank'.
5. Create a global open access 'Sarcoptes-gDNA World Bank'.
6. Create a global open access database on the world molecular systematics of the species Sarcoptes, inferred from molecular marker data from thousands of individual Sarcoptes specimens worldwide.

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7. Examine the long-term evolutionary history undergone by this ectoparasite, and establish a possible scenario for Sarcoptes migration throughout the world.
8. Formulate public and animal health control policies with the aim of decreasing *S. scabiei* infections in humans and in animals.

4. Conclusions

The concept of 'network' plays a central role in all branches of our life. In the area of parasitology research, it is crucial to realize the importance of standardizing research protocols worldwide. Availability of biological samples is a recognized limiting factor for biological and genetic studies; hence the creation of a global open access 'Living organism-Specimens/gDNA World Bank' is of pivotal interest. Sufficiently robust and well-standardized diagnostic methods are needed in the form of ready-to-use kits in the routine laboratory for many host-derived parasite species. The accurate estimation of parasite host specificity and range will only be achieved by global epidemiology and molecular studies.

Sarcoptes-WMN is just starting its operations in terms of technology and knowledge transfer among its members, Sarcoptes specimen collection, and the design of the epidemiological/molecular studies. We are aware that such a world genetic epidemiology study in different host species, countries, and geographical areas requires wider awareness and collaborations from all sectors concerned in animal/human welfare, and especially from those interested in the disease.

To our knowledge this is the first world molecular network, which we hope will serve as a framework around which further 'Living being-World Molecular Networks' (Anima-WMN) will be constructed.

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