

## Review of Doctoral Thesis

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Name: **Mgr. Adéla ČMOKOVÁ**  
study programme Botanika

Thesis name: One Health approach to understand emerging zoonotic pathogens in the *Trichophyton benhamiae* complex

The candidate chose as the format of her dissertation a commentary on the results of five selected articles, in which she appeared as the first author (in three) or co-author (in two). The work is at a very good level in terms of language and formality (personally, I would divide the introduction by thematic parts, see below). The dissertation is divided into two main parts: Introduction (pp. 17 to 53), which is a synthesis of the acquired knowledge into several thematic chapters (One Health approach; taxonomic, phylogenetic, phenotypic, ecological, and biological concept). The second part consists of the articles with clearly documented results in the form of tables and images. It is worth noting the precise technical aspect of displaying the results, especially the quality of the photomicrographs of dermatophytes, the clarity of the taxonomic schemes and the photographic documentation of the clinical manifestations of dermatophytosis in humans and their pets. The candidate avoided mechanically commenting on the results by dividing the comments according to thematic groups and not only according to individual papers. This enabled her to comment on the results across the individual articles in a comprehensive and contextual manner and thus supported the advantages of a polyphasic approach to the studied issue. The elaboration of a new method used for intraspecific typing based on 10 microsatellites and 4 sequencing markers deserves special attention, as well. It proved to be beneficial for the study of dermatophyte variability and provided a number of interesting results of two in many aspects similar groups of dermatophytes represented by the *Trichophyton benhamiae* complex and *T. erinacei* complex. While research of the former lead to the description of five new species (*T. europeum*, *T. japonicum*, *T. africanum*, *T. persicum* and *T. spiraliforme*) and a new variety of *Trichophyton benhamiae* var. *luteum* (apart from the existing white variety *Trichophyton benhamiae* var. *benhamiae*), in the latter the data obtained did not discriminate new species. On the other hand, the findings pointed to the ongoing evolution of *T. erinacei* complex, which was also indicated by a different antifungal profile between two candidate subpopulations related to the hedgehogs of European (*Erinaceus europeus*) and African (*Aterelix albiventris*) origin. In this way the candidate's work reveals an evolution in "direct transmission" that is likely related to the expansion of the original population to northern latitudes and adaptation to new host - the European hedgehog. In contrast, the situation with the yellow variant *Trichophyton benhamiae* is somewhat more complex and a bit mysterious, perhaps also because human being entered the "game" through the animal trade (see Questions).

As with any meaningful research, the results often provide not only answers, but also new questions that, like a relay, push the boundaries of general knowledge. I am convinced that

the work of the candidate significantly opened the imaginary door of knowledge and contributed to a better understanding of the complexity of the relationship between man and fungal parasites.

I have the following questions for the candidate:

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1. On page 17 you state that clinicians prefer a taxonomic system based on ease of diagnosis. In terms of the impact on the renaming of pathogenic fungi, I would rather prefer the term reliability and stability of diagnosis. Anyway, what is your solution to the contradiction between the natural science (molecular) and medical approach to the taxonomy of pathogenic fungi?
2. To what extent, if at all, can the spread of the yellow variant of *T. benhamiae* be considered an evolutionary process driven by human interventions (in this case by animal trade)?
  - Sub-question a/: If it is assumed that the yellow variant of *T. benhamiae* came from North America and evolved in Europe - why in Europe (in other words – guinea pigs are kept as pets in the US as well)?
  - Sub-question b/: Given that the yellow variant of *T. benhamiae* is strongly associated with guinea pigs in Europe, the question arises, what about an occurrence of *T. benhamiae* in the original homeland of guinea pigs - South America? Shouldn't we rather consider that this variant got to Europe from South America with guinea pigs?
  - Sub-question c/: Is there any research on *T. benhamiae* in guinea pigs in South America or in human population that domesticated them?
3. The current state of development of the *T. erinacei* complex can be viewed as a process that is on the trajectory of the emergence of two species. Is clinical manifestation of dermatophytosis different in humans infected with strains from European versus African hedgehog? If so, any difference between the clinical response in European and African human population?
4. Collection strains are used in the study of dermatophytes. Long-term maintenance of fungal cultures usually requires their regular passage on culture media. However, as you state, pleomorphism of the isolates can often be observed. This could complicate experiments if the isolates lost or changed the trait under investigation. Can we consider collection strains the same as fresh isolates from a physiological point of view? How do you deal with this phenomenon if you encounter it?

Overall, the work presented met the stated goals by bringing a number of valuable insights into the taxonomy and evolution of dermatophytes, including the introduction of a new method and the use of a polyphasic approach to the study of this group of fungi. The erudition of the candidate, and last but not least, the entire team, is a guarantee of future research into the evolutionary processes of human pathogenic fungi.

I recommend Adéla Čmelová to defend the dissertation thesis and obtain the title of Ph.D.

Hradec Králové, January 3, 2024

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