Elucidating species boundaries between agents of superficial mycoses *Trichophyton interdigitale* and *T. mentagrophytes*

Michaela Švarcová
Dermatophytes = agents causing superficial mycosis

- ecologically and phylogenetically related fungi, pathogens with high prevalence
- order Onygenales, family *Arthrodermataceae*

**Primary pathogenic**
- **anthropophilic**

**zoophilic**

**Geophilic dermatophytes**

**TINEA** (DERMATOPHYTOSIS, RINGWORM)

Zoonotic infections transmit to human
Clinical manifestation
**Taxonomy of dermatophytes**

- Taxonomy of dermatophytes = still developing and adjusting

  - taxonomy based on morphological markers
  - taxonomy based on molecular markers (esp. ITS rDNA)

- Earlier
- 2000
- Nowadays

- species recognition
- recognition of complex
Taxonomy of dermatophytes

- Taxonomy of fungi, especially dermatophytes = still developing and adjusting
  - taxonomy based on morphological markers
  - taxonomy based on molecular markers (esp. ITS rRNA)

2000

- Species recognition nowadays

2017 de Hoog = *Trichophyton interdigitale* and *T. mentagrophytes*
  - ecological differences
  - not so clear
Taxonomy of dermatophytes

- Taxonomy of fungi, especially dermatophytes = still developing and adjusting

  taxonomy based on morphological markers
  earlier

  taxonomy based on molecular markers (esp. ITS rRNA)
  2000
  nowadays

  species recognition

  recognition of complex

  polyphasic approach
  rare

  species recognition
• Dermatophytes are mainly studied by clinicians
• Often identified by morphology or ITS rDNA
Polyphasic approach

Aspergillus, Penicillium, Cryptococcus and others show the way

DNA sequence markers
- sufficiently variable (ITS, β-tubulin, calmodulin, RPB2, mcm7, tsr1)
- available for majority of species
- relatively well-known level of intraspecific variability and minimal genetic distances between species
Polyphasic approach

**Dermatophytes**
- DNA sequence markers (ITS, β-tubulin, tef-1α)
- morphology
- physiological and biochemical tests
- mating experiments
- secondary metabolism
- ecology – host spectrum, distribution
- clinical manifestation
Current approach

*T. interdigitale*

- tinea pedis and onychomycosis in humans
- ITS barcode sequence
- clonal, only MAT1-2 isolates

*T. mentagrophytes*

- infection in rabbit, dogs, cats, rodents
- ITS barcode sequence
- sexual, both MAT genes
Morphology

**T. interdigitale**

- microconidia
- macroconidia

**T. mentagrophytes**

- microconidia
- spiral hyphae
Does the fungi know how to behave?
Does the fungi know how to behave? No!

ONE STRAIN
Does the fungi know how to behave? No!

What about molecular data?

ONE STRAIN
Trichophyton interdigitale and T. mentagrophytes are not monophyletic (Nenoff et al., 2019)
Importance for pathogen recognition

prevention of reinfection and spread of infection by identifying source of mycotic infection

Anthropophilic infection
• sanitary conditions
• treatment of roommates
• prevention of risky hobbies

Zoophilic infection
• finding of infected animal and animal treatment
Hypotheses

• Confirmation of traditional classification = two species
• OR = one species with wide host range and variable phenotype and genotype
Approach with dataset of 130 isolates

- 3 DNA markers: ITS rDNA, β-tubulin, translation elongation factor 1-α (TEF)
- MAT genes
- Microsatellite markers
- Morphology markers
- Clinical data

CORRELATION TOGETHER
Preliminary results

- Phylogenetic tree on dataset of 80 isolates
- Comparison of ITS, TUB and TEF genes
- Pattern
  - Clonal type, "T. interdigitale"
  - Other, gene flow
    "T. mentagrophytes"
Preliminary results

• Pressumption of morphology
  • “T.mentagrophytes”
  • “T.interdigitale”
• many isolates are in transition state
Preliminary results

- violet = age of patient
- average age

“T.interdigitale” > “T.mentagrophytes”
Preliminary results

Clinical manifestation

Onychomycosis are specific for “T.interdigitale”
### Take home message

<table>
<thead>
<tr>
<th>2 species</th>
<th>1 species</th>
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</thead>
<tbody>
<tr>
<td>Low gene flow between populations</td>
<td><em>T. interdigitale</em> is not monophyletic by ITS and TEF markers</td>
</tr>
<tr>
<td><em>T. interdigitale</em> and <em>T. mentagrophytes</em> separated by 3 gene markers</td>
<td>overlapping morphology</td>
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<tr>
<td>Onychomycoses specific for <em>T. interdigitale</em></td>
<td>overlapping clinical manifestation</td>
</tr>
<tr>
<td><em>Trichophyton mentagrophytes</em> † gene diversity by mating</td>
<td><em>tinea</em> infections are not specific for one or another species</td>
</tr>
</tbody>
</table>

**Future:**
- dataset scale up, MAT genes, morphology (micro-, macro), delimitation methods
Thank you for your attention!
References

- www.itol.embl.de
- www.scholar.google.com