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Charles University

# Differential gene expression of species from *Trichophyton benhamiae* clade

Lenka Machova

# Introduction

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## Faculty of Science, Charles University in Prague

Department of Botany



FACULTY OF SCIENCE  
Charles University

# Introduction

Institute of Microbiology of the Czech Academy of Sciences

Laboratory of fungal genetics and metabolism



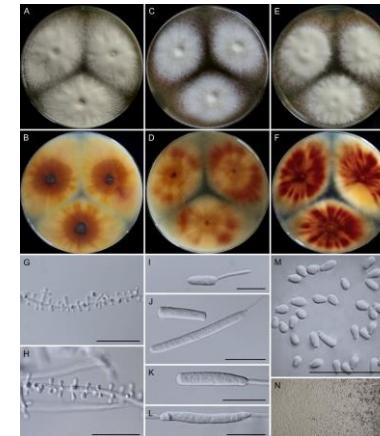
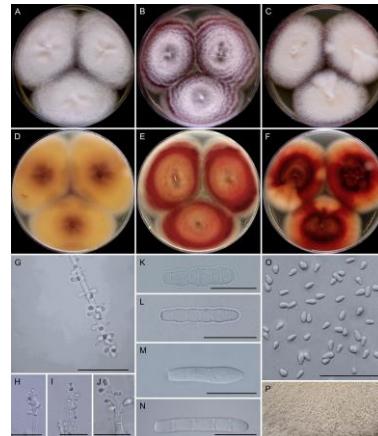
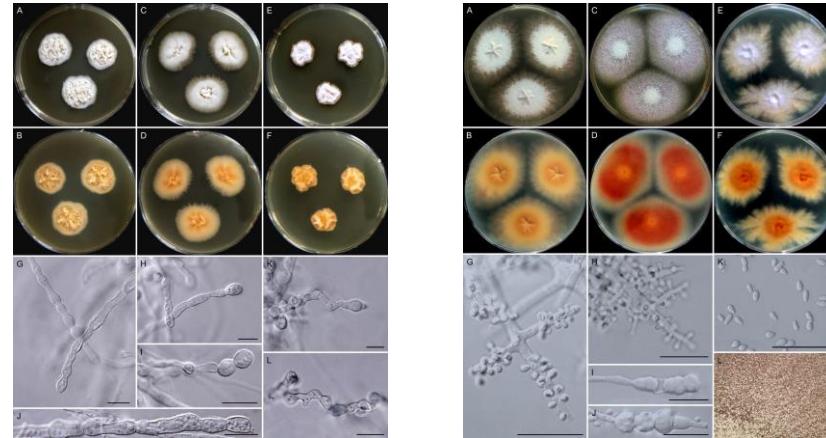
Czech Academy  
of Sciences



# *Trichophyton benhamiae*

= *Arthroderma benhamiae*

- *Arthrodermataceae*
- *Onygenales*
- *Ascomycota*



# *Trichophyton benhamiae*

- Clinical manifestation

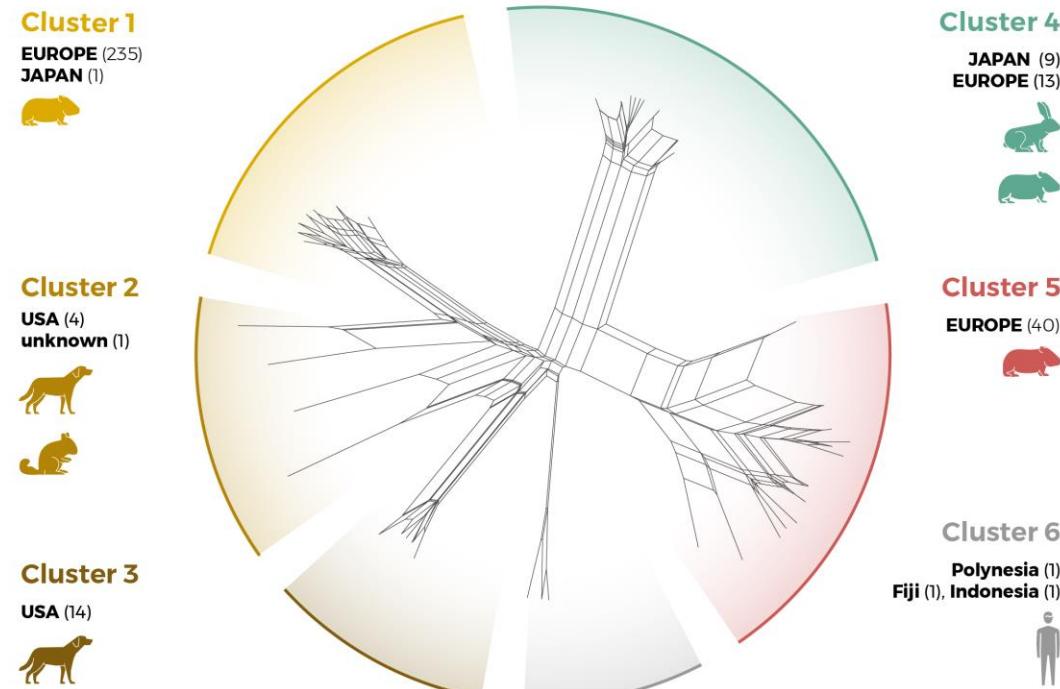


Experimentally infected guinea pig



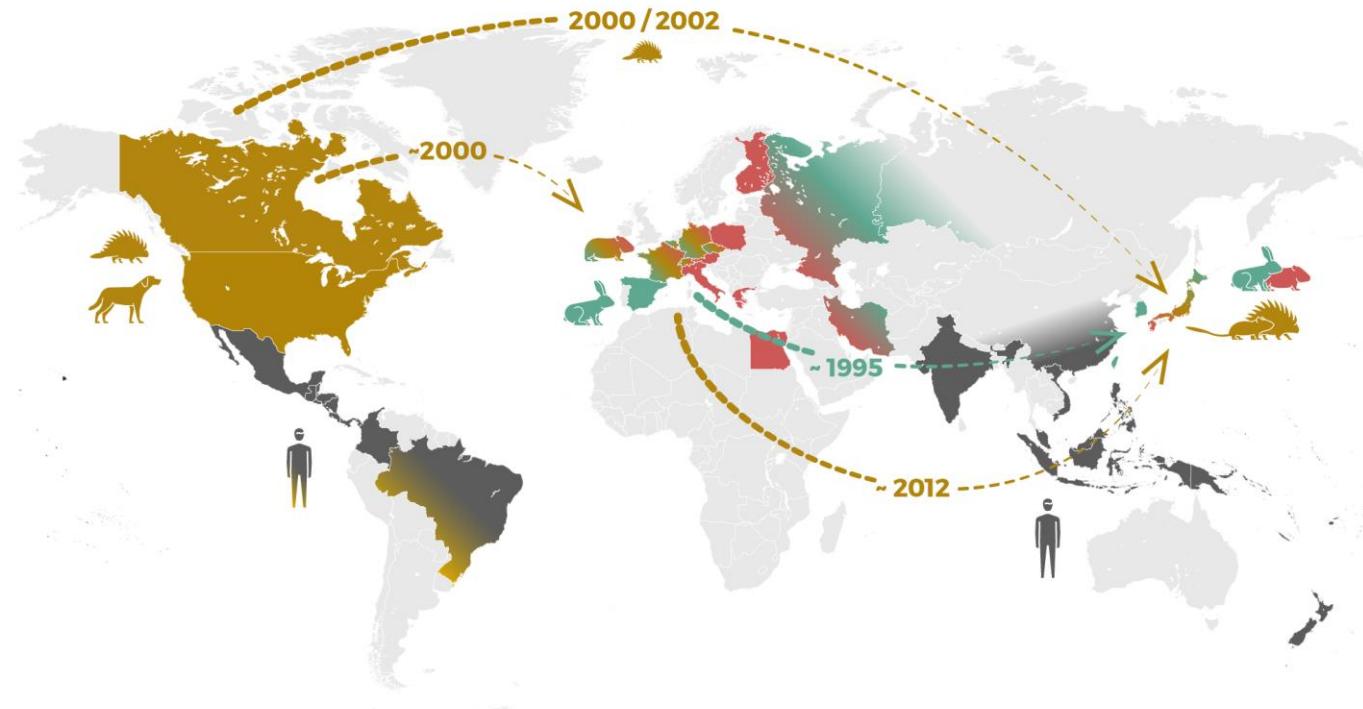
Lesion caused by *T. benhamiae*, young women

# *Trichophyton benhamiae*



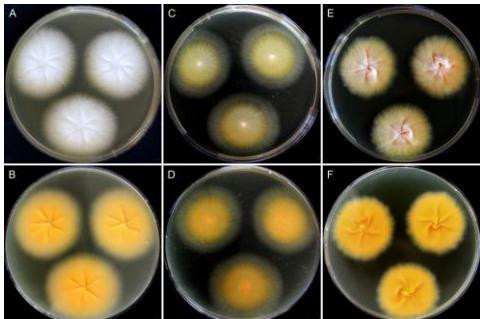
*T. benhamiae* var. *luteum* / *T. benhamiae* var. *benhamiae* C2 / *T. benhamiae* var. *benhamiae* C3  
*T. japonicum* / *T. europaeum* / *T. concentricum*

# *Trichophyton benhamiae*



*T. benhamiae* / *T. japonicum* / *T. europaeum* / *T. concentricum*

# *Trichophyton benhamiae*



## Yellow Phenotype



2002 – 2012 : **Switzerland**  
Symoens et al. (2013)



~ since 2010 : **Germany, Czechia**  
Hubka et al. (2014), Nenoff et al. (2014),  
Uhrlaß et al. (2012)

## epidemic spread in Europe



2012 : **Japan**  
Hiruma et al. (2015)



2016 : **Brazil**  
de Freitas et al. (2019)

## White Phenotype

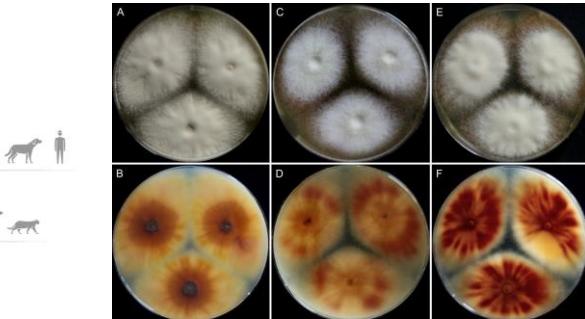
before 1967 : **USA**

Ajello & Cheng (1967)



1960 – 1970 : **Belgium, Spain, France**

Takahashi (1974)



1977 – 1980 : **Finland**

Aho (1980)



1989 : **Czechia**

Hejtmánek & Hejtmánková (1989)



1989 – 2009 : **USA**

Sieklucki et al. (2014)



since 1996 : **Japan**

Kimura et al. (2015),  
Takahashi et al. (2008)



2002 – 2004 : **France, Switzerland**

Fumeaux et al. (2004),  
Fréalle et al. (2007)



## various European countries



before 2010 : **Taiwan**  
Sun et al. (2010)

2011 – 2014 : **Iran, Russia**

Rezaei-Matehkolaei et al. (2013),  
Pchelin et al. (2016)



2010 - 2017 : **USA**

Needle et al. (2019)



# *Aims of the study*

- To answer:

What stands behind epidemic spread of yellow phenotype?

How does gene expression of virulence factors differ?



# Current knowledge - gene expression

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## RNA Sequencing-Based Genome Reannotation of the Dermatophyte *Arthroderma benhamiae* and Characterization of Its Secretome and Whole Gene Expression Profile during Infection

Van Du T. Tran,<sup>a</sup> Niccolò De Coi,<sup>b</sup> Marc Feuermann,<sup>c</sup> Emanuel Schmid-Siegert,<sup>a</sup> Elena-Tatiana Băguț,<sup>d</sup> Bernard Mignon,<sup>d</sup> Patrice Waridel,<sup>e</sup> Corinne Peter,<sup>f</sup> Sylvain Pradervand,<sup>f</sup> Marco Pagni,<sup>a</sup> Michel Monod<sup>b</sup>

*Microbiology* (2010), **156**, 884–895

DOI 10.1099/mic.0.033464-0



## Differential gene expression in the pathogenic dermatophyte *Arthroderma benhamiae* *in vitro* versus during infection

Peter Staib,<sup>1</sup> Christophe Zaugg,<sup>2</sup> Bernard Mignon,<sup>3</sup> Johann Weber,<sup>4</sup> Maria Grumbt,<sup>1</sup> Sylvain Pradervand,<sup>4</sup> Keith Harshman<sup>4</sup> and Michel Monod<sup>2</sup>

Burmester et al. *Genome Biology* 2011, **12**:R7  
<http://genomebiology.com/2011/12/1/R7>



RESEARCH

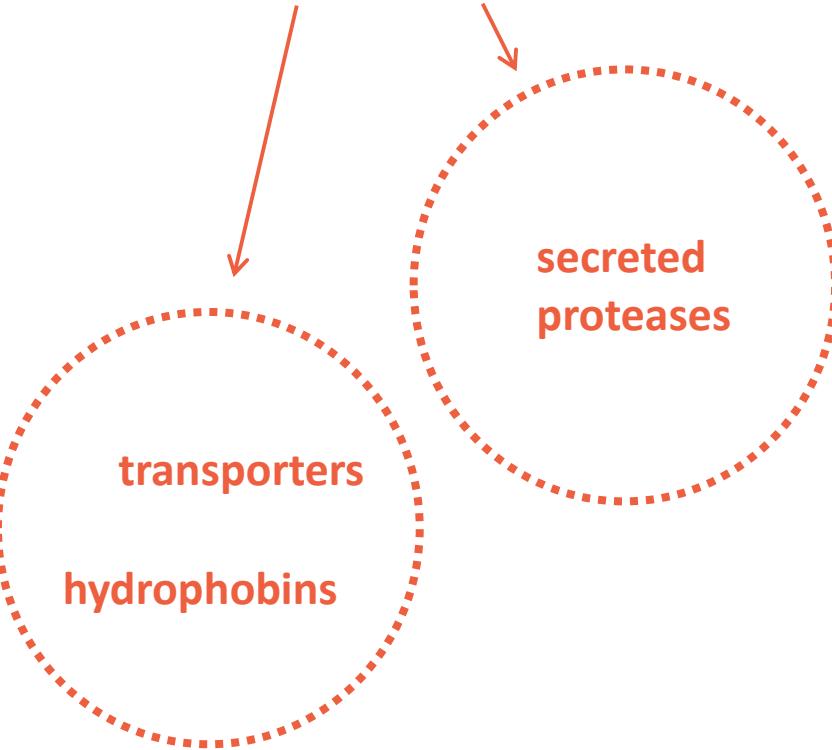
Open Access

## Comparative and functional genomics provide insights into the pathogenicity of dermatophytic fungi

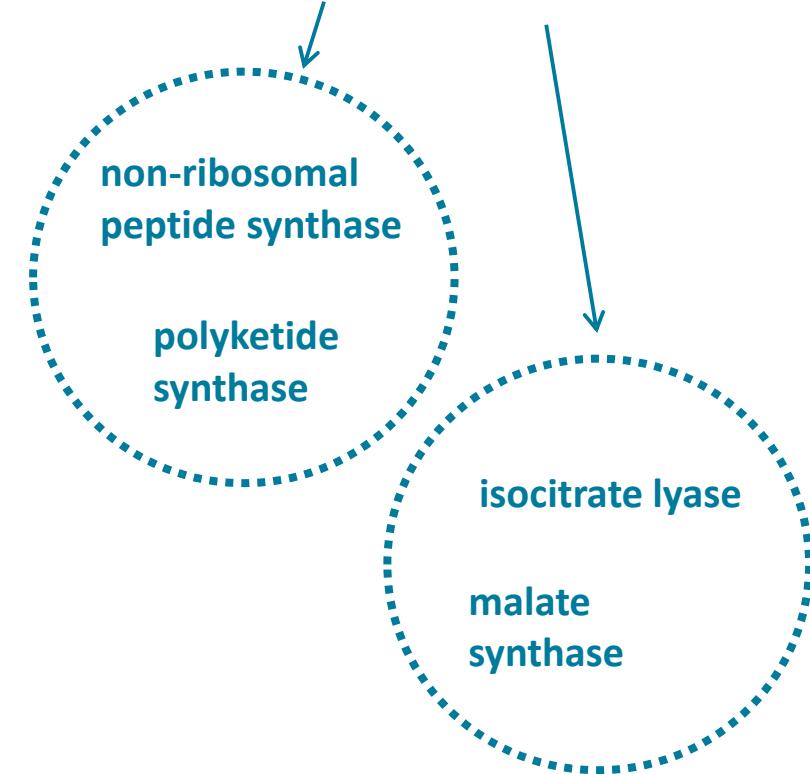
Anke Burmester<sup>1,2†</sup>, Ekaterina Shelest<sup>3†</sup>, Gernot Glöckner<sup>4†</sup>, Christoph Heddergott<sup>1,2†</sup>, Susann Schindler<sup>5,6</sup>, Peter Staib<sup>7</sup>, Andrew Heidel<sup>4</sup>, Marius Felder<sup>4,8</sup>, Andreas Petzold<sup>4</sup>, Karol Szafranski<sup>4</sup>, Marc Feuermann<sup>9</sup>, Ivo Pedruzzi<sup>9</sup>, Steffen Priebe<sup>3</sup>, Marco Groth<sup>4</sup>, Robert Winkler<sup>5,10</sup>, Wenjun Li<sup>11</sup>, Olaf Kniemeyer<sup>1</sup>, Volker Schroeckh<sup>1</sup>, Christian Hertweck<sup>6,10</sup>, Bernhard Hube<sup>6,12</sup>, Theodore C White<sup>13</sup>, Matthias Platzer<sup>4</sup>, Reinhard Guthke<sup>3</sup>, Joseph Heitman<sup>11</sup>, Johannes Wöstemeyer<sup>2</sup>, Peter F Zipfel<sup>5,6</sup>, Michel Monod<sup>14</sup>, Axel A Brakhage<sup>1,2\*</sup>

# Current knowledge - gene expression

putative **virulence factors**



**enzymes** from **metabolic pathways**

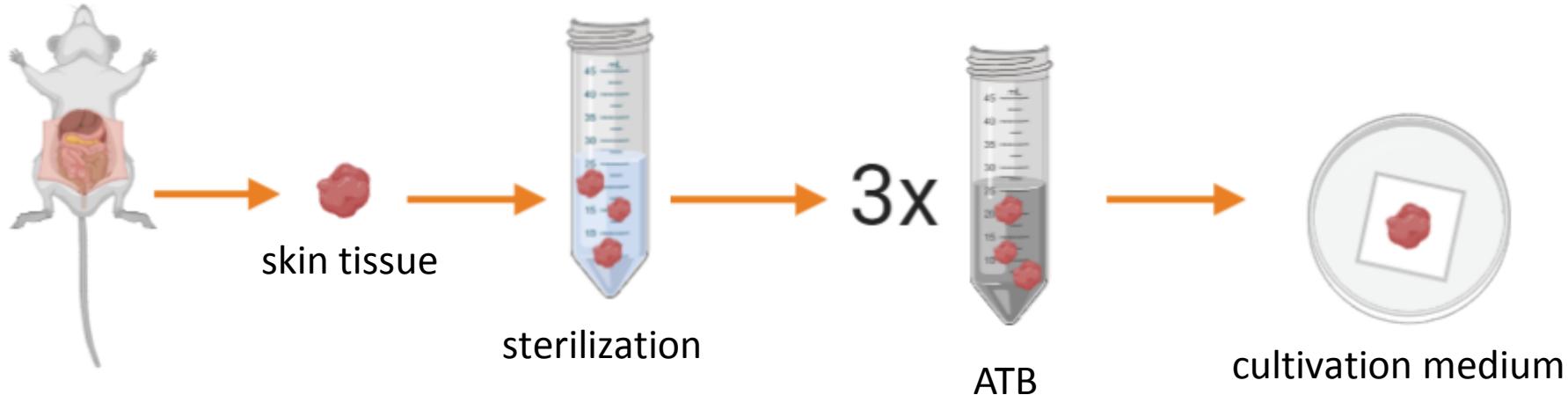


- Cultivation:  
liquid medium  
mouse skin explants

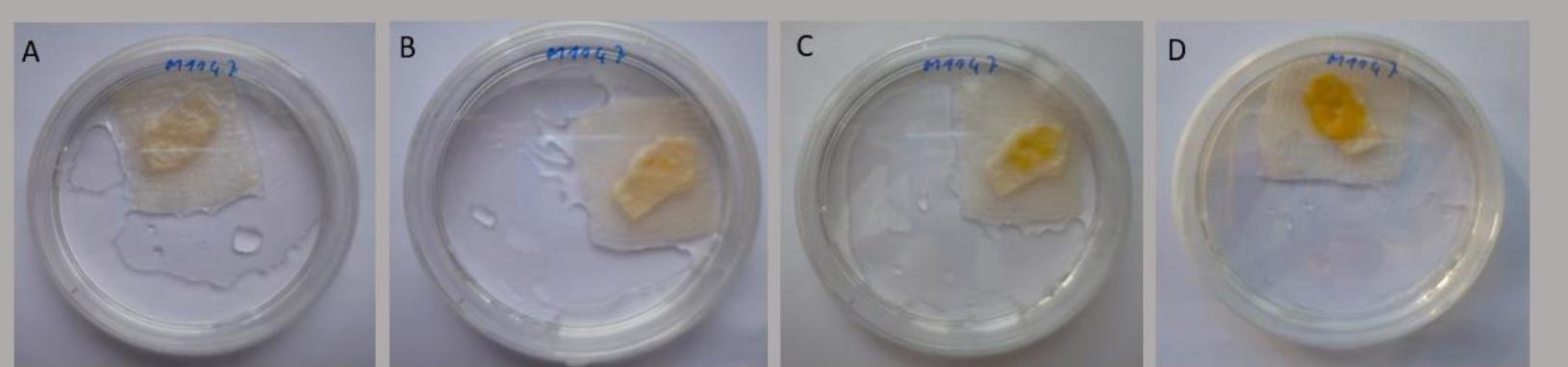
- Transcriptome analysis:  
RNAseq  
RT-qPCR



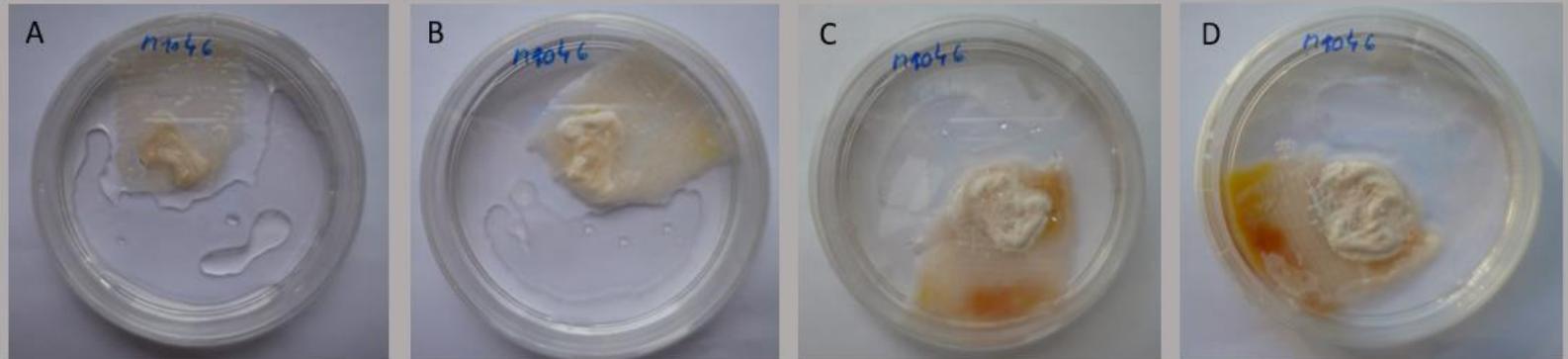
# Mouse skin explants



# Mouse skin explants

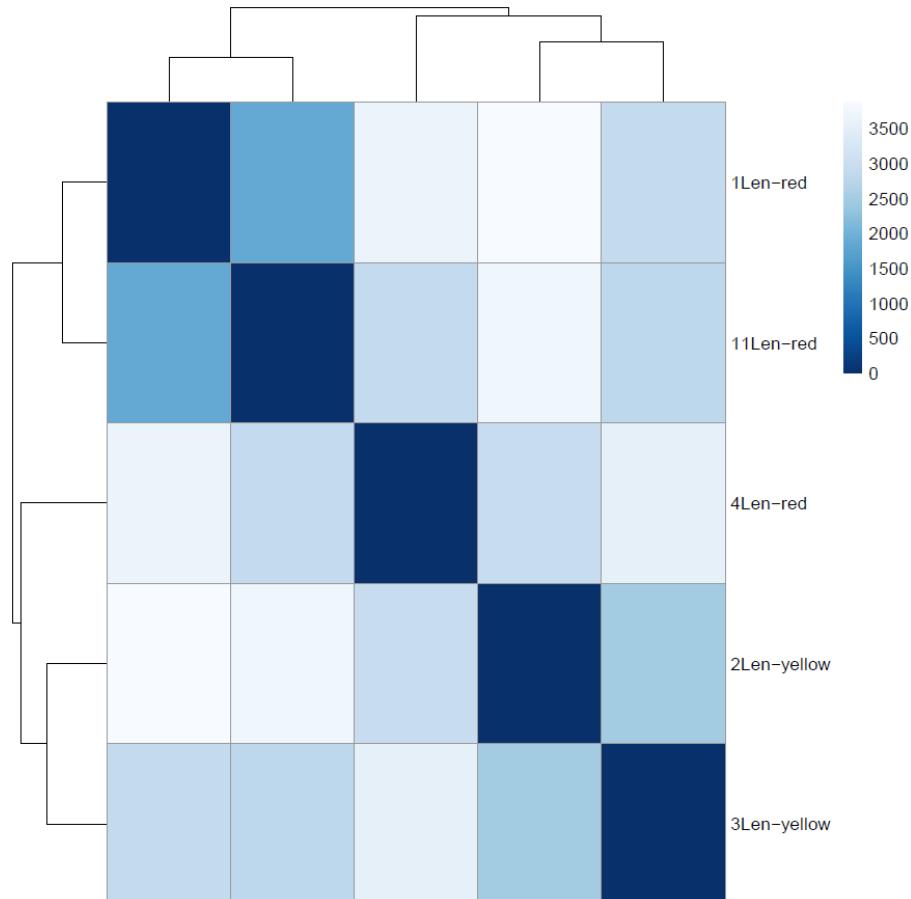


*T. luteum* cultivated on MSE: A) freshly inoculated, B) after 4 days, C) after 6 days, D) after 8 days; grown at 30°C



*T. japonicum* cultivated on MSE: A) freshly inoculated, B) after 4 days, C) after 6 days, D) after 8 days; grown at 30°C

# RNAseq - preliminary data



White phenotype

1Len-red = mouse skin after 6 days

4Len-red = liquid medium after 6 days

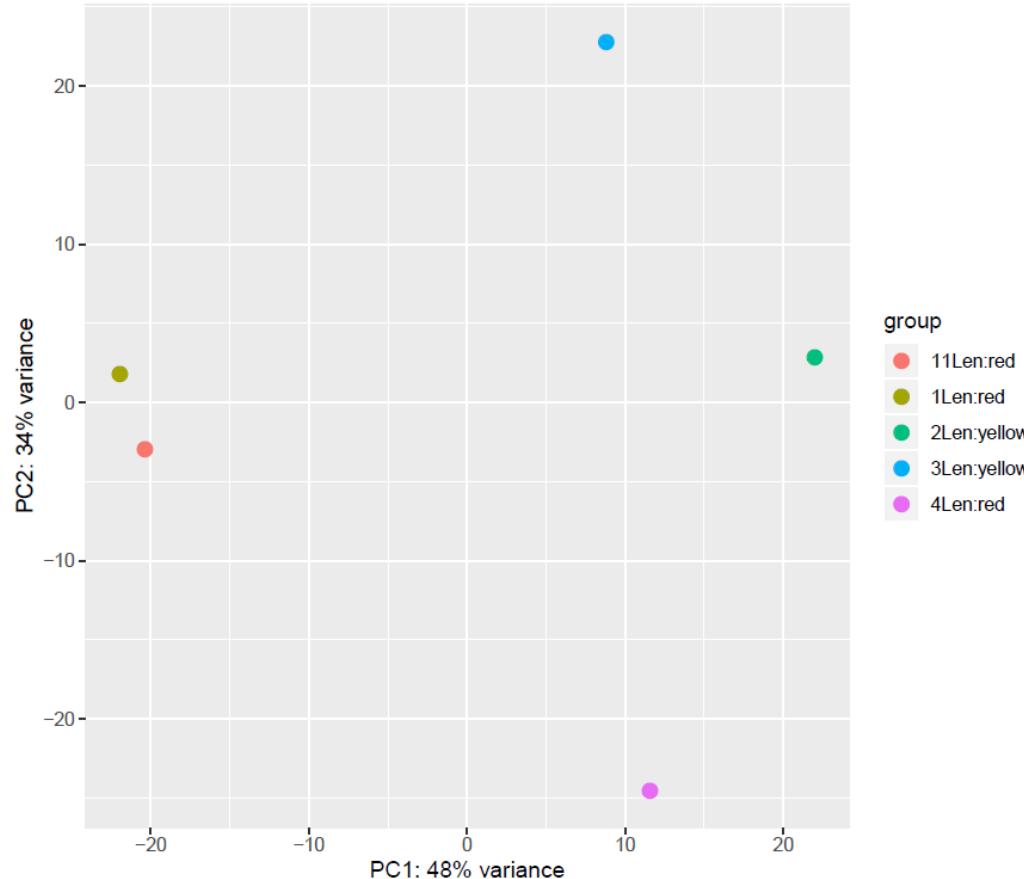
11Len-red = liquid medium after 8 days

Yellow phenotype

3Len-yellow = mouse skin after 6 days

2Len-yellow = liquid medium after 6 days

# RNAseq - preliminary data



White phenotype

1Len:red = mouse skin after 6 days

4Len:red = liquid medium after 6 days

11Len:red = liquid medium after 8 days

Yellow phenotype

3Len:yellow = mouse skin after 6 days

2Len:yellow = liquid medium after 6 days

# Take home message

- *T. benhamie* clade consists of several clusters
- One of the clusters is epidemically spreading in Europe
- This cluster probably differs from others in gene expression

# Thank you for your attention



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and Ministry of Health of the Czech Republic (AZV CR)

# References

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Staib, P., Zaugg, C., Mignon, B., Weber, J., Grumblt, M., Pradervand, S., Harshman, K., Monod, M., Monod MichelMonod, M., 2010. Differential gene expression in the pathogenic dermatophyte *Arthroderma benhamiae* in vitro versus during infection. *Microbiology* 156, 884–895. <https://doi.org/10.1099/mic.0.033464-0>