Infection metallomics as a tool for functional studies in *Aspergillus fumigatus*

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PURPOSE

During proliferation into the host, pathogenic toxins, proteases, extracellular vesicles, quorum sensing molecules, metallophores, etc., modulate the inter-microbial interactions, and host-cell response, which may alter the immune or somatic cell secretomes. **Infection metallomics (IM)** was developed as a novel analytical portfolio for functional studies in host-pathogen-therapy and virus-bacterium-fungus interactomes. The platform affords emerging diagnostic approaches with clinically relevant features as a welcome side-product.

METHOD: INFECTION METALLOMICS

A tool based on the clinical analysis of metal-containing microbial virulence factors, specifically, analysis of metal-containing infection biomarkers using a combination of elemental and molecular mass spectrometry applicable in a wide range of pathogen-related functional studies.

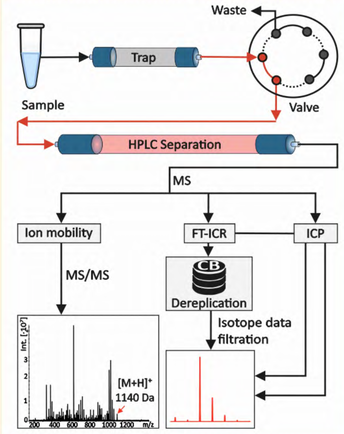


Figure 1. Key instruments and concepts on the infection met

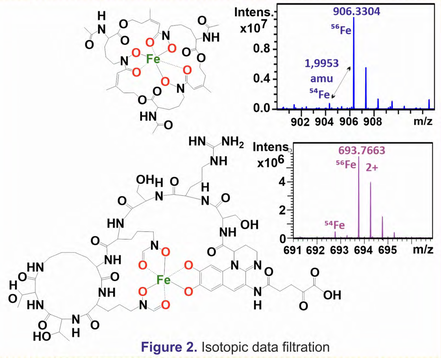
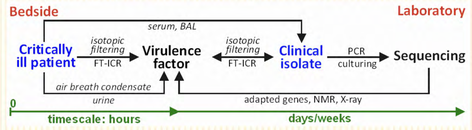
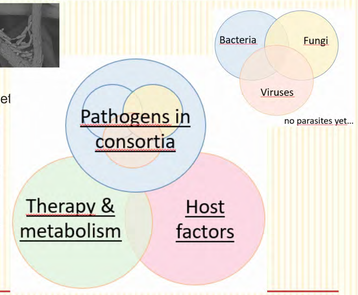


Figure 2. Isotopic data filtration





APPLICATION AREAS

In vitro experiments

Conidia
Pellet
Supernatant

Animal models

Infection medicine

Acknowledgement

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References

European Journal of Nuclear Medicine and Molecular Imaging (2021) 48:355–362
https://doi.org/10.1007/s00259-020-04984-y
ORIGINAL ARTICLE
^{68}Ga-labelled desferrioxamine-B for bacterial infection imaging
Milos Petrik[1] · Eva Urbankova[1] · Vladislav Keckesky[1] · Andrea Palyzova[2] · Vladimir Havlicek[2] · Joachim Pfister[3] · Christian Wan[3] · Zbynek Novy[4] · Miroslav Poppe[4] · Marian Hajduch[1] · Clemens Decristoforo[1]

analytical chemistry
pubs.acs.org/ac
Technical Note
CycloBranch 2: Molecular Formula Annotations Applied to imzML Data Sets in Bimodal Fusion and LC-MS Data Files
Jiří Novák, Anton Sloba, and Vladimír Havlíček*

Metallophores from a historical perspective

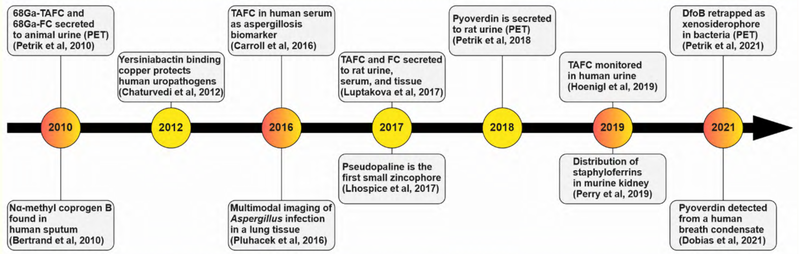


Figure 3. Landmarks of infection metallomics

Pathogen routing by infection metallomics

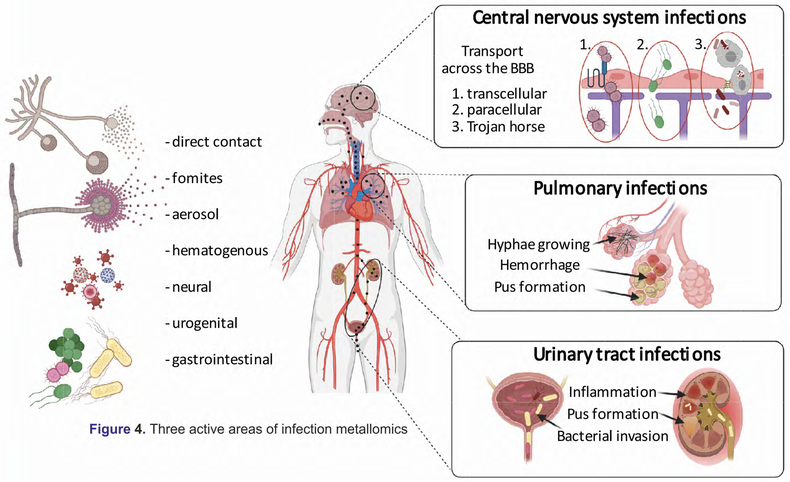


Figure 4. Three active areas of infection metallomics

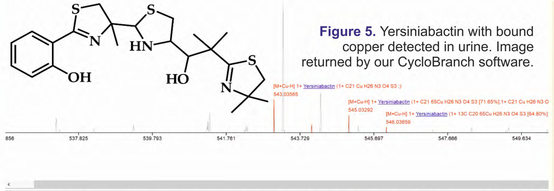
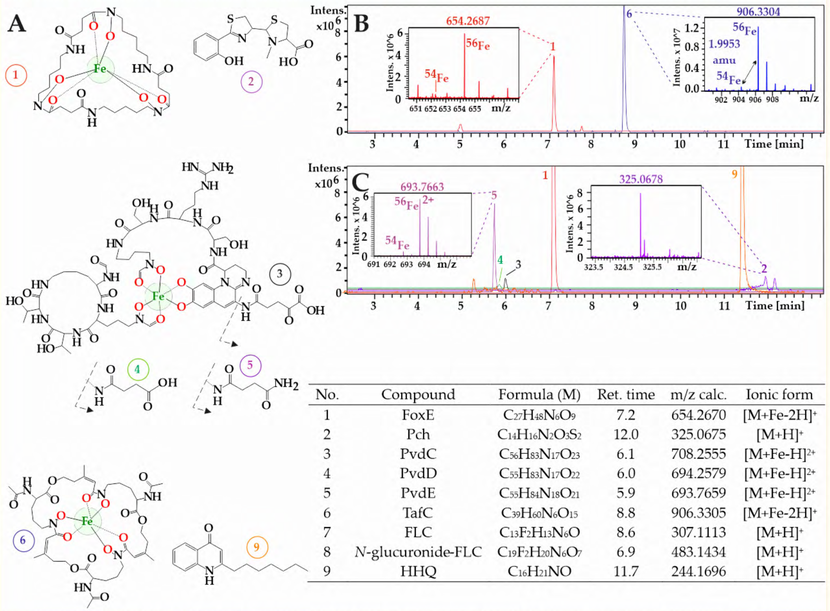


Figure 5. Yersiniabactin with bound copper detected in urine. Image returned by our CycloBranch software.

A. fumigatus & *P. aeruginosa* in coinfection (man)



No.	Compound	Formula (M)	Ret. time	m/z calc.	Ionic form
1	FoxE	$C_{27}H_{48}N_6O_9$	7.2	654.2670	$[M+Fe-2H]^+$
2	Pch	$C_{14}H_{16}N_2O_2S_2$	12.0	325.0675	$[M+H]^+$
3	PvdC	$C_{56}H_{83}N_{17}O_{23}$	6.1	708.2555	$[M+Fe-H]^{2+}$
4	PvdD	$C_{55}H_{83}N_{17}O_{22}$	6.0	694.2579	$[M+Fe-H]^{2+}$
5	PvdE	$C_{53}H_{84}N_{18}O_{21}$	5.9	693.7659	$[M+Fe-H]^{2+}$
6	TafC	$C_{39}H_{60}N_6O_{15}$	8.8	906.3305	$[M+Fe-2H]^+$
7	FLC	$C_{13}F_2H_{13}N_6O$	8.6	307.1113	$[M+H]^+$
8	N-glucuronide-FLC	$C_{19}F_2H_{20}N_6O_7$	6.9	483.1434	$[M+H]^+$
9	HHQ	$C_{16}H_{21}NO$	11.7	244.1696	$[M+H]^+$

Figure 6. Molecules (**A**) monitored on the same day patient's sampling of urine (**B**) and breath condensate (**C**)

Table 1: AspICU diagnostics performance versus Infection Metallomics (excellent, fair, poor; u: urine, s: serum, b: BAL)

Method	Sensitivity	Specificity	Invasivity	Timeliness
sCulturing				
sGM/sPCR				
bGM/bPCR				
bMicroscopy				
uMetallomics				

FEATURES OF INFECTION METALLOMICS

The advantages of IM are affordable dynamic range, specificity, noninvasiveness, high sampling-to-result speed, and the ability to handle mixed infections. As secondary metabolism events represent time-resolved processes, metallophores' molecular leakage into the urine may indicate an angioinvasion process reflecting distant lung, urinal tract, or even central nervous system infections triggered by a bacterial, mycobacterial, or fungal invader.

Article
Freeing *Aspergillus fumigatus* of Polymycovirus Infection Renders It More Resistant to Competition with *Pseudomonas aeruginosa* Due to Altered Iron-Acquiring Tactics
Rutuja H. Patil[1,2], Iolyt Kotta-Loizou[3], Andrea Palyzová[1], Tomáš Pluháček[1,2], Robert H. A. Coutts[4], David A. Stevens[5,6,+] and Vladimír Havlíček[1,2]

Case Report
Noninvasive Combined Diagnosis and Monitoring of *Aspergillus* and *Pseudomonas* Infections: Proof of Concept
Radim Dobiáš[1,2,4], Anton Škriba[3,4], Tomáš Pluháček[3,4], Miloš Petřík[3], Andrea Palyzová[3], Marcela Kaňková[5,7,8], Eva Čubová[9], Jiří Houšť[3,4], Jiří Novák[3], David A. Stevens[10,11], Goran Mitulović[12], Eva Krejčí[1,2], Petr Hubáček[13] and Vladimír Havlíček[3,4]

MassSpectrometryReviews
REVIEW ARTICLE Open Access
Infection metallomics for critical care in the post-COVID era
Rutuja H. Patil, Dominika Luptáková, Vladimír Havlíček
First published: 02 December 2021 | https://doi.org/10.1002/mas.21755