

Új felismerések az infekciós szövődmények diagnosztikájában és kezelésében onko-hematológiai betegekben

Sinkó János PhD FECMM

Dél-pesti Centrumkórház – Szent László Kórház Telephely

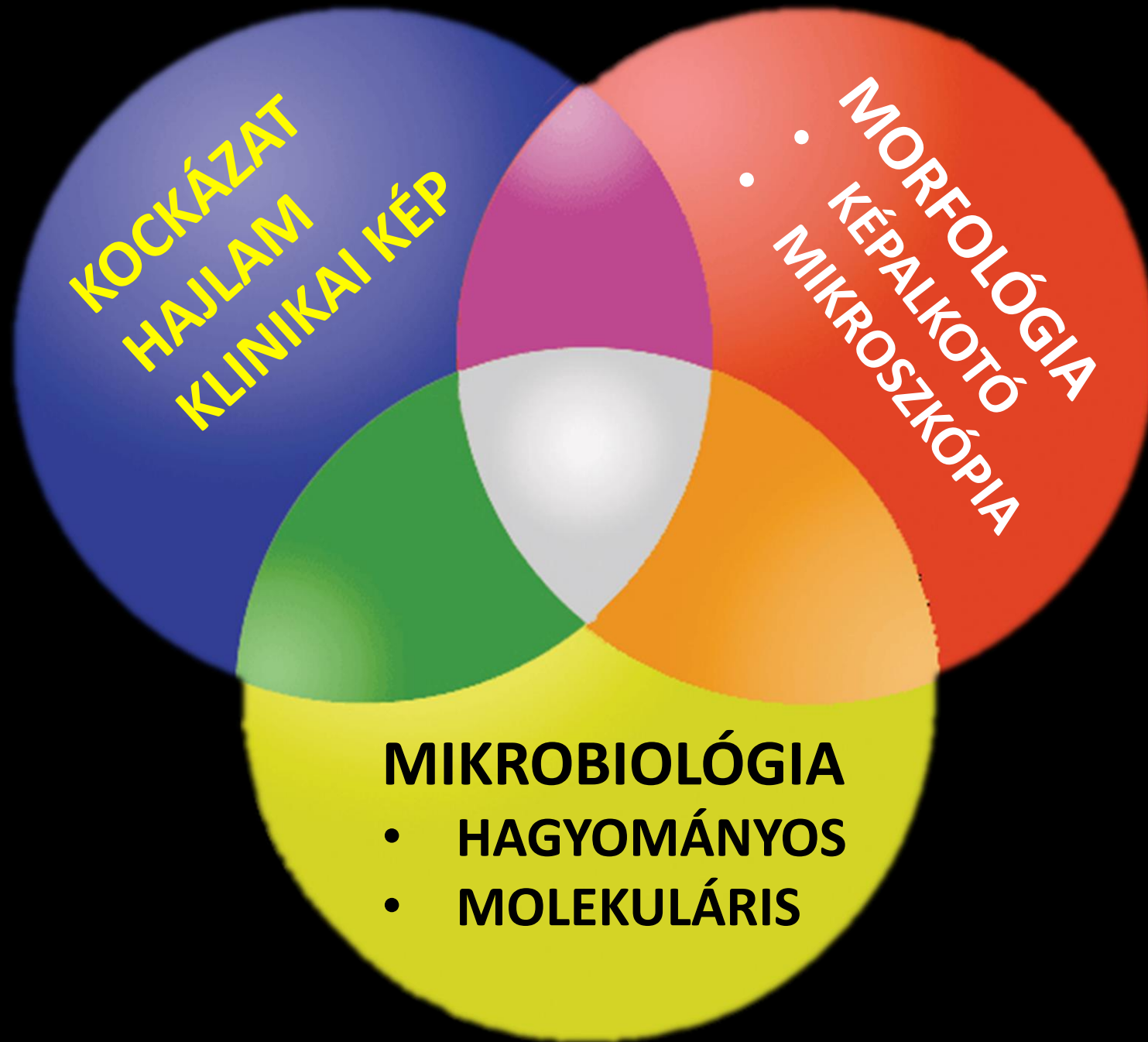
Budapest

2025

- Jelen prezentáció elkészültét gyógyszeripari szereplő nem támogatta.
- Az előadó korábban támogatásban /szakértői díjazásban részesült az alábbi vállalatok részéről: MSD, Pfizer, Fresenius-Gilead, Takeda, Janssen, Medis, Sobi.
- Az elhangzó információk az előadó saját véleményét tükrözik.
- A terápiás eljárások során követni kell az alkalmazási előiratokat, irányelveket és a vonatkozó jogszabályokat.



DIAGNOSZTIKA



Mikrobiológiai diagnosztika a hematológiában

Módszerek általában

- Mikroszkópia, tenyésztés, biokémia, spektrometria, antigén-, antitest-, nukleinsav-alapú módszerek

Alkalmazhatóság szempontjai

- Érzékenység, specificitás
- Hozzáférhetőség, fajlagos költség, szükséges infrastruktúra
- Leletmegfordulási idő

A vizsgálat célja

- Szűrés
- Betegség megállapítása
- Terápia eredményének monitorozása, prognosztika

A jelen ellentmondásai

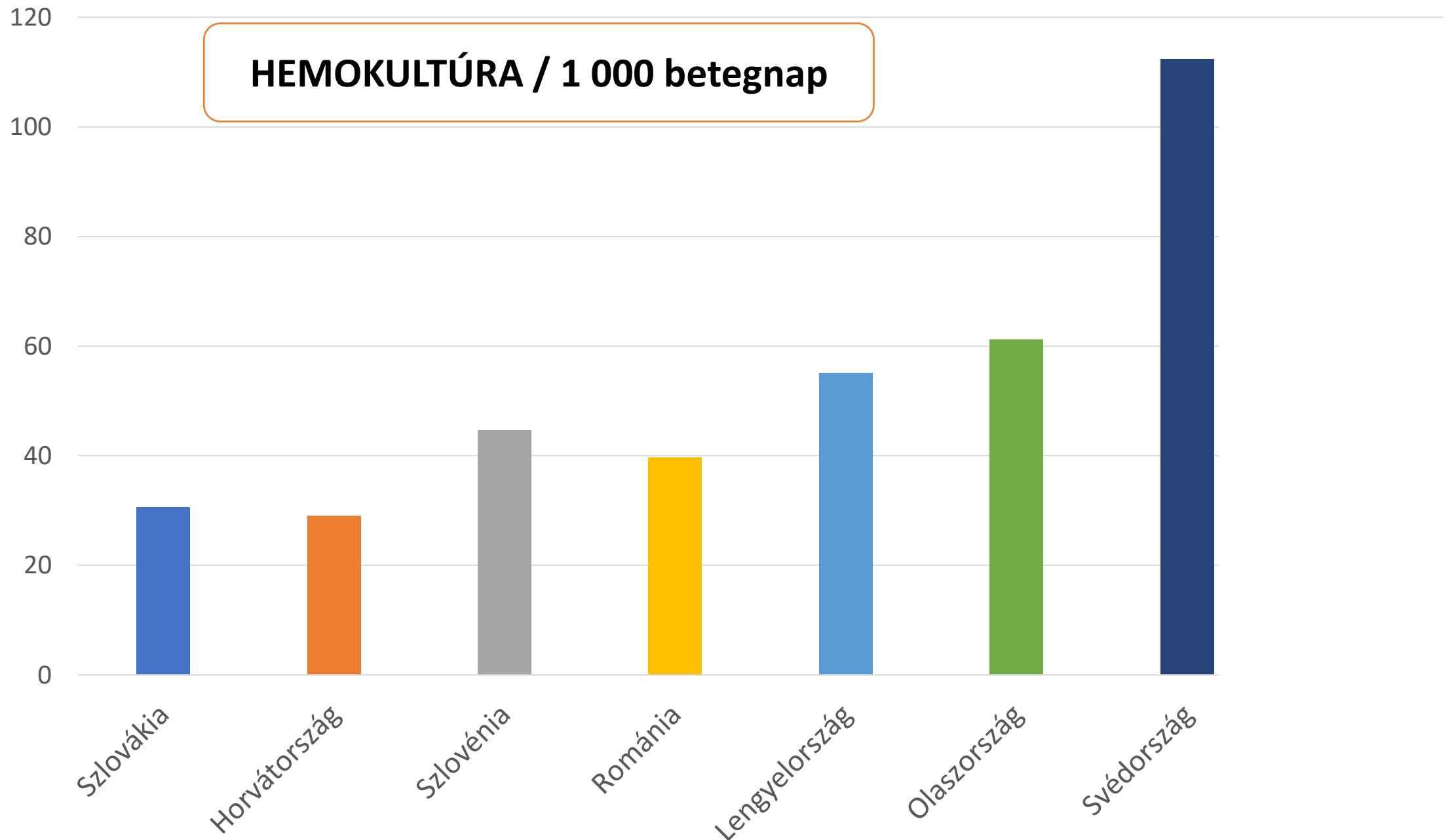
Világszerte

- Számottevő helyi különbségek a fejlettségben
- Az új módszerek eltérő mértékű befogadása
- Evidenciák és finanszírozhatóság: a terápiához hasonlóan nyílik az olló

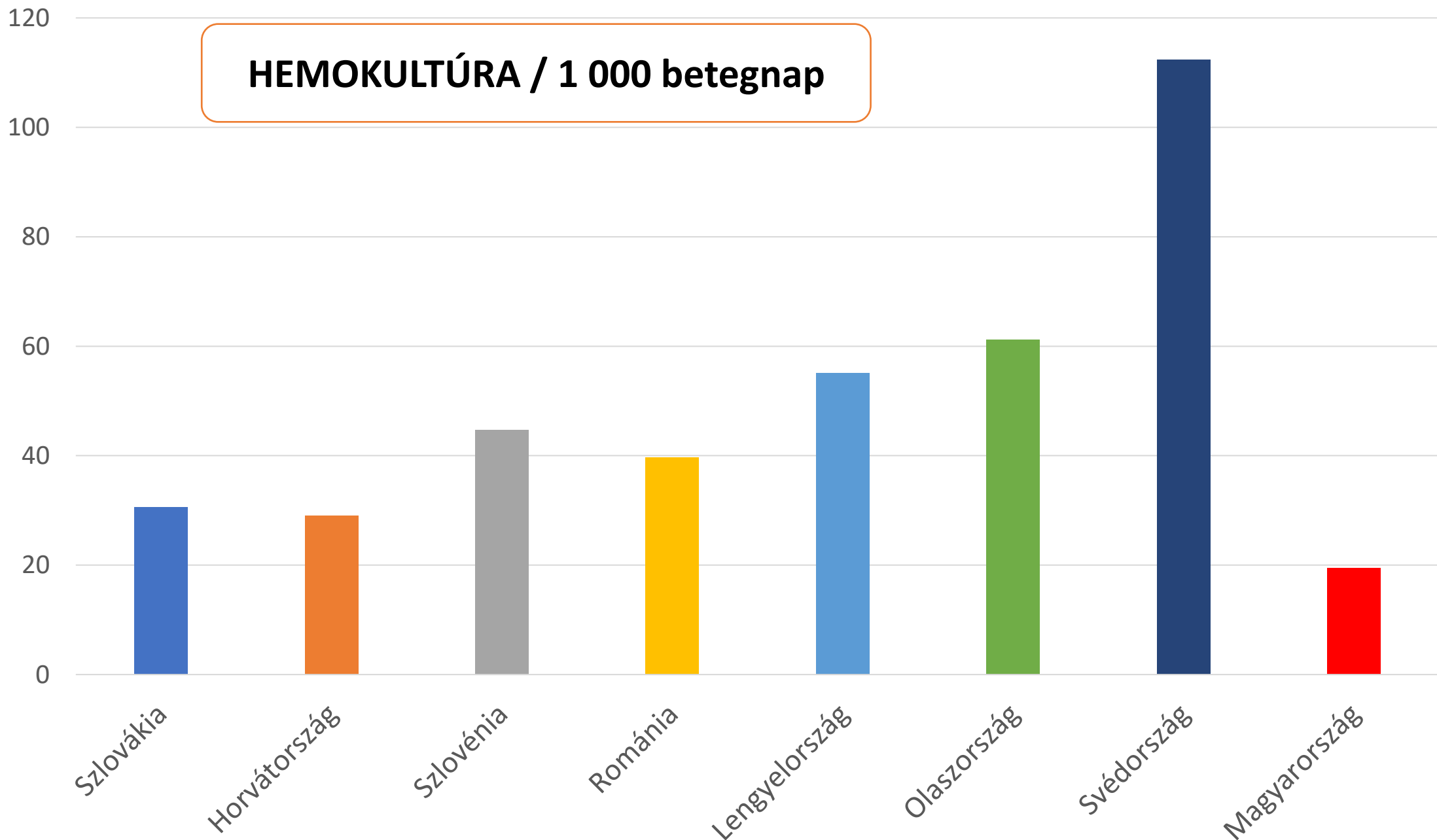
Hazánkban

- Számottevő helyi különbségek a diagnosztikus feltételekben (vizsgálati lehetőségek, távolság, kommunikáció)
- Helyi és referencialaborok
- Diagnosztikus minimumok hiánya vagy figyelmen kívül hagyása

FONTOS ÁBRÁK JÖNNEK



HEMOKULTÚRA / 1 000 betegnap



Unveiling the Hungarian landscape of laboratory and clinical management capacities for invasive fungal infections: navigating the frontlines against fungal menaces

Renátó Kovács, László Majoros, Jannik Stemler, Oliver Andreas Cornely and Jon Salmanton-García 

Ther Adv Infect Dis

2023, Vol. 10: 1–11

DOI: 10.1177/
20499361231219315

© The Author(s), 2023.
Article reuse guidelines:
[sagepub.com/journals-
permissions](https://sagepub.com/journals-permissions)

	<i>n</i>	%
	17	100.0
Patients at care		
COVID-19	17	100.0
Diabetes mellitus	16	94.1
Hematology	13	76.5
HIV/AIDS	5	29.4
ICU: Adults	17	100.0
ICU: Neonatal	10	58.8
Oncology	13	76.5
Parenteral nutrition	14	82.4
Respiratory/Other intermediate ICU	15	88.2
Solid organ transplantation	5	29.4
Stem cell transplantation	6	35.3

Antigen detection	12	70.6
Aspergillus overall	11	64.7
<i>Aspergillus galactomannan</i> (ELISA)	10	58.8
<i>Aspergillus galactomannan</i> (LFA)	6	35.3
<i>Aspergillus galactomannan</i> (LFD)	4	23.5
Candida antigen	6	35.3
Cryptococcus overall	10	58.8
Cryptococcus (LAT)	7	41.2
Cryptococcus (LFA)	6	35.3
Histoplasma	4	23.5
Beta-glucan	9	52.9

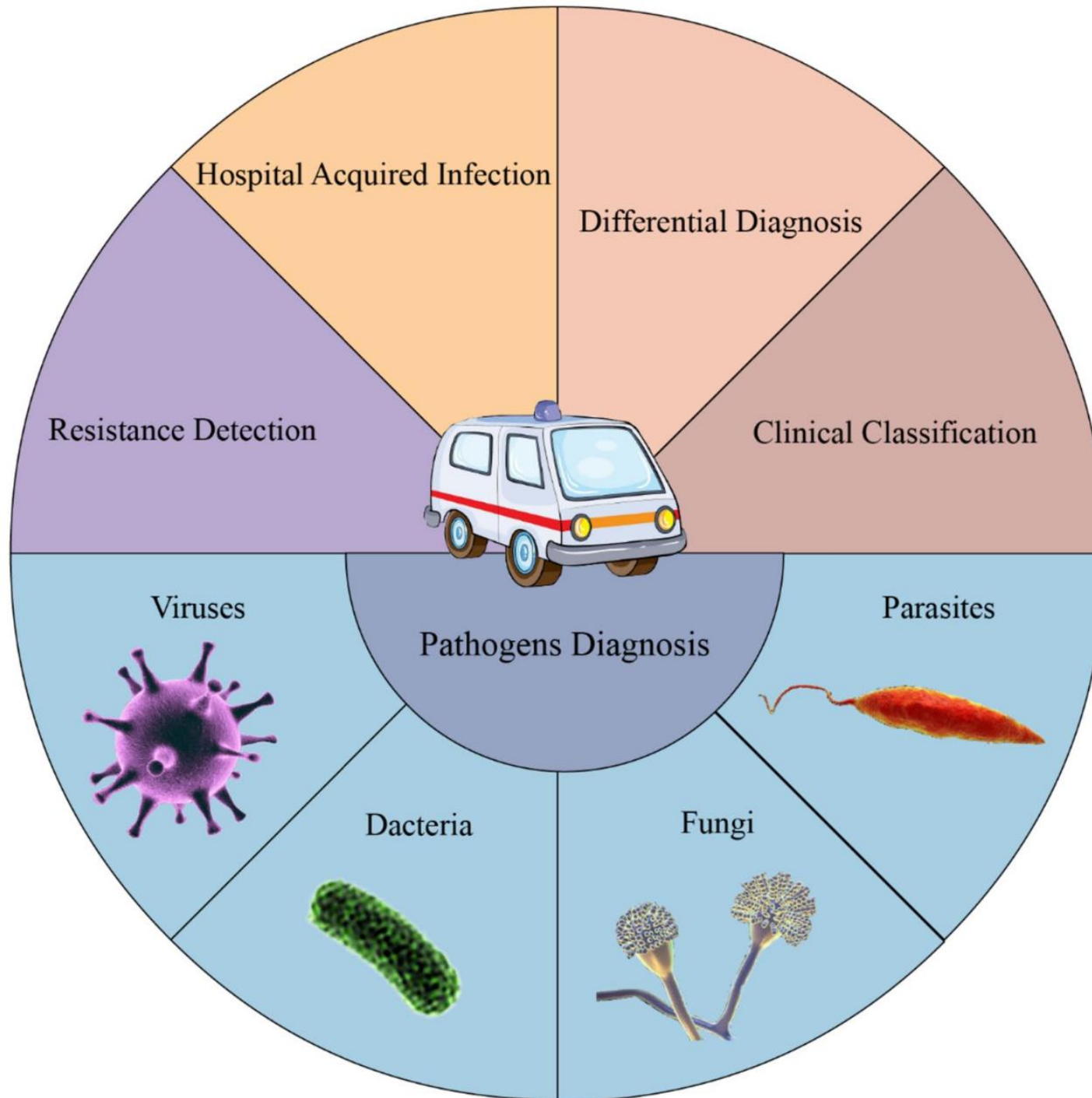
	<i>n</i>	%
	17	100.0
Patients at care		
COVID-19	17	100.0
Diabetes mellitus	16	94.1
Hematology	13	76.5
HIV/AIDS	5	29.4
ICU: Adults	17	100.0
ICU: Neonatal	10	58.8
Oncology	13	76.5
Parenteral nutrition	14	82.4
Respiratory/Other intermediate ICU	15	88.2
Solid organ transplantation	5	29.4
Stem cell transplantation	6	35.3

Molecular tests	10	58.8
<i>Aspergillus</i> PCR	9	52.9
<i>Candida</i> PCR	5	29.4
<i>Pneumocystis jirovecii</i> PCR	7	41.2
Mucorales PCR	6	35.3

A Review of

Luyao Shi¹ · Tingt

Received: 22 August 2023
© The Author(s) 2023



nancy



[8] Oxford Nanopore Technologies introduced the MinION portable sequencing device, which uses nanopore sequencing technology and is able to sequence the entire bacterial genome in a single run.

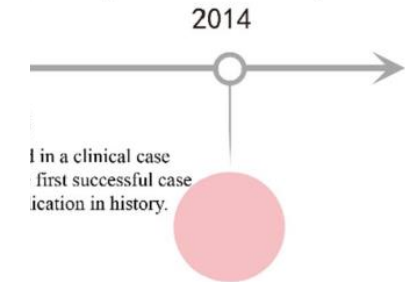


Table 1 Pathogen detection rate of different detection methods

Traditional method ^a	mNGS ^b	Ratio ^c	Treatment yield ^d	Reference ^e
NA	76.2% (112/147)	NA	27.9% (41/147)	[55]
34.5% (19/55)	87.3% (48/55)	2.5	7.3%–30.9%	[56]
87.0% (67/77)	97.4% (75/77)	1.1	NA	[57]
1.0%	24.0%	24.0	NA	[58]
30.8% (4/13)	100.0% (13/13)	3.2	NA	[45]
25.0% (48/192)	80.2% (154/192)	3.2	52.2% (24/102)	[51]
14.0% (14/98)	99.0% (97/98)	7.1	NA	[59]
12.5% (12/96)	88.5% (85/96)	7.1	72.9% (62/85)	[60]
7.1% (5/70)	92.3% (66/70)	12.9	78.6% (55/70)	[61]

^aThe pathogen diagnosis rate of traditional methods

^bThe pathogen diagnosis rate after using mNGS

^cThe ratio of the diagnosis rate of the two diagnostic methods (mNGS/traditional method)

^dThe therapeutic response rate after adjusting the therapeutic drugs according to the mNGS results

^eThe references; mNGS: metagenomic next generation sequencing



AMERICAN
SOCIETY FOR
MICROBIOLOGY

Journal of
Clinical Microbiology®

BACTERIOLOGY



Plasma Microbial Cell-Free DNA Sequencing from over 15,000 Patients Identified a Broad Spectrum of Pathogens

 Sarah Y. Park,^a Eliza J Chang,^a Nathan Ledebor,^b Kevin Messacar,^c Martin S. Lindner,^a Shivkumar Venkatasubrahmanyam,^a Judith C. Wilber,^a Marla Lay Vaughn,^a Sivan Bercovici,^a Bradley A. Perkins,^a  Frederick S. Nolte^a

^aKarius, Redwood City, California, USA

^bMedical College of Wisconsin, Milwaukee, Wisconsin, USA

^cUniversity of Colorado, Children's Hospital Colorado, Aurora, Colorado, USA

J Clin Microbiol. 2023 Aug 23;61(8):e0185522.

KIKBŐL

TABLE 2 ICD-10 codes by principal diagnosis type for those patients with ICD-10 codes indicated on Karius TRFs ($n = 4,423$) from April 2018 to September 2021^a

Principal diagnosis type (ICD-10-CM chapter)	Total	IC	Fever	Sepsis
(Unmappable)	68			
Conditions not elsewhere classified	1,437		722	
Respiratory system diseases	800			
Neoplasms	580	288		
Infectious/parasitic diseases	543	47		231
Blood diseases	485	320		
Circulatory system diseases	416			
Factors influencing health status and contact with health services	290	140		
Musculoskeletal system diseases	259	9		
Nervous system diseases	242			
Digestive system diseases	162	21		
Skin diseases	111			
Genitourinary system diseases	101	15		
Endocrine/metabolic diseases	91	4		
Injury, poisoning, external causes	83	25		
Congenital malformations	76			
Codes for special purposes	20			
Eye/adnexa diseases	16			
Mental/behavioral disorders	13			
Ear/mastoid diseases	7			
Pregnancy/childbirth	7			
External causes of morbidity	3			
Total no. of patients by diagnosis chapter	5,810	869	722	231

^aTRF, test report form; IC, immunocompromised. Fever, any ICD-10 starting with "R50"; sepsis, any ICD-10 starting with "A41"; IC, any ICD-10 annotated as immunocompromised from the Agency for Healthcare Research and Quality (AHRQ) code list. Each TRF could contain up to two ICD-10 codes, and each patient had between 1 and 5 unique ICD-10 codes. For the study period, there were 15,165 patients with a positive or negative report (18,690 reports).

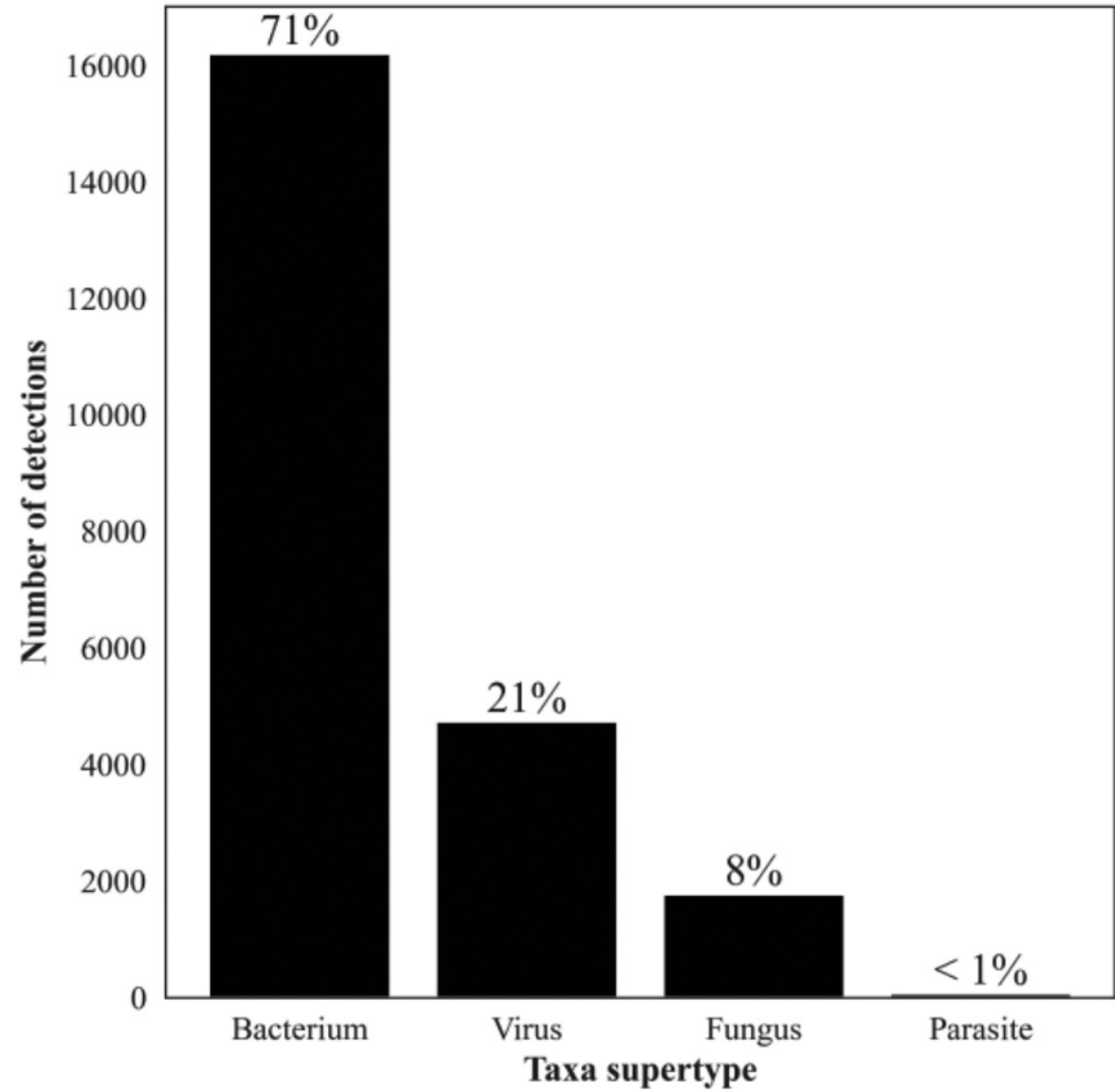


FIG 2 Number of detections by the Karius Test of the different supergroups of taxa from April 2018 to September 2021. $n = 22,792$: bacteria, 16,221; viruses, 4,737; fungi, 1,758; and parasites, 70. Percentages reflect the proportion of total number of detections spanning 701 microbial taxa.

HÁNY- FÉLÉT

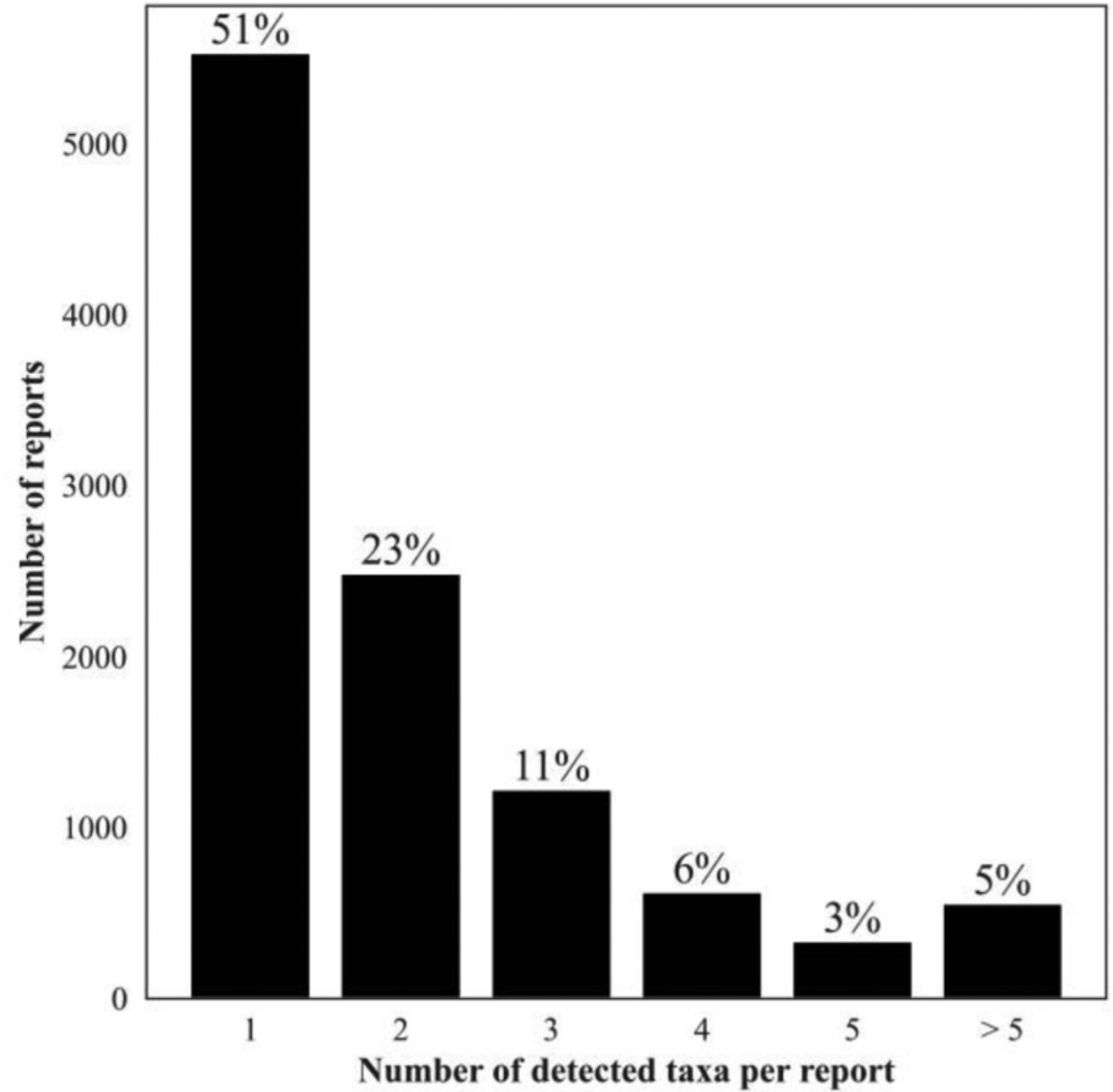





FIG 3 Number of detected taxa counts per report for all positive reports, April 2018 to September 2021. Percentages reflect the proportion of all positive reports ($n = 10,752$).





Review

A decade of clinical microbiology: top 10 advances in 10 years: what every infection preventionist and antimicrobial steward should know

Tulip A. Jhaveri MBBS¹ , Zoe Freeman Weiss MD^{2,3}, Marisa L. Winkler MD, PhD⁴ , Alexander D. Pyden MD^{5,6} ,
Sankha S. Basu MD, PhD² and Nicole D. Pecora MD, PhD⁷

¹Division of Infectious Diseases, University of Mississippi Medical Center, Jackson, MS, USA, ²Division of Pathology and Laboratory Medicine, Tufts Medical Center, Boston, MA, USA, ³Division of Geographic Medicine & Infectious Disease, Tufts Medical Center, Boston, MA, USA, ⁴Division of Infectious Diseases, Emory University School of Medicine, Atlanta, GA, USA, ⁵Division of Pathology and Laboratory Medicine, Lahey Hospital and Medical Center, Burlington, MA, USA, ⁶Department of Anatomic and Clinical Pathology, Tufts University School of Medicine, Boston, MA, USA and ⁷Department of Pathology, Brigham and Women's Hospital, Boston, MA, USA

Table 1. Overview of the top ten innovations in clinical microbiology over the past decade, highlighting their applications, key benefits, and associated challenges

Innovation area	Applications	Key benefits	Challenges/Limitations
PRE-ANALITIKAI FÁZIS: diagnosztikus stewardship (mit mikor mivel érdemes tesztelni?)			
POSZT-ANALITIKAI FÁZIS: mit mikor kivel érdemes közölni?			
		Uniform adherence to stewardship best practices and guidelines	decisions at the expense of patient safety or quality

REVIEW



Machine learning and artificial intelligence for the diagnosis of infectious diseases in immunocompromised patients

Nam K Tran^a, Cileah Kretsch^a, Clayton LaValley^a and Hooman H Rashidi^b

Take-home 1

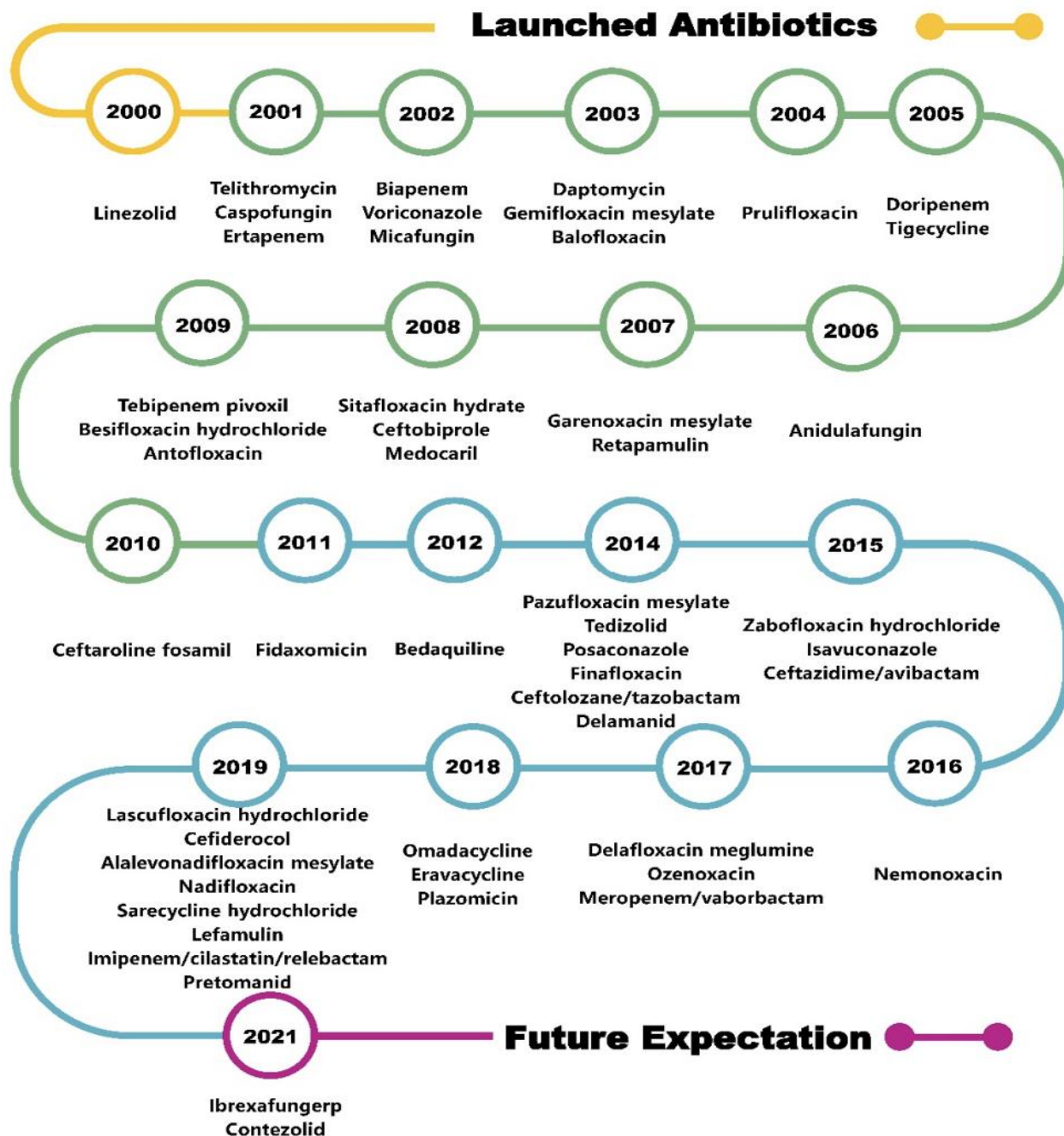
- Az infektológiai diagnosztika fejlődési pályája **hasonló az onkohematológiai módszerekéhez.**
- A molekuláris tesztek sokat adhatnak hozzá a hagyományos diagnosztika teljesítőképességéhez, de valószínűleg **sohasem fogják teljesen kiváltani** azt.
- A diagnosztikus algoritmusok létrehozása és alkalmazása alapvető az **észszerű és költséghatékony** munkához (diagnosztikus stewardship).
- A hazai gyakorlatban egyidejűleg jelen van a **ki nem aknázott hagyományos eszköztár és a high-tech diagnosztikus paletta.**

A collection of various medical supplies including pills, capsules, syringes, and bottles on a white surface. The word "TERÁPIA" is overlaid in a white rounded rectangle with a blue border.

TERÁPIA



Harc a rezisztens baktériumokkal



Linezolid
 Ertapenem
 Tigecyclin
 Ceftarolin
 Fidaxomicin
 Ceftolozan-tazobaktám
 Ceftazidim-avibaktám
 Meropenem-vaborbaktám
 Eravaciklin
 Cefiderokol
 Imipenem-relebaktám

Figure 1. Timeline of antibiotics launched in the last two decades.

Agent	KPC-producer	NDM-producer	OXA-48-like-producer	Carbapenem-resistant <i>Pseudomonas aeruginosa</i>	Carbapenem-resistant <i>Acinetobacter baumannii</i>	<i>Stenotrophomonas maltophilia</i>
Aztreonam-avibactam	Green	Green	Green	Yellow	Red	Green
Cefiderocol	Green	Green	Green	Green	Green	Green
Ceftazidime-avibactam ¹	Green	Red	Green	Yellow	Red	Red
Ceftolozane-tazobactam ¹	Red	Red	Red	Yellow	Red	Yellow
Eravacycline ^{1,2}	Green	Green	Green	Red	Green	Green
Fosfomycin (intravenous)	Yellow	Yellow	Yellow	Yellow	Red	Red
Imipenem-relebactam ³	Green	Red	Yellow	Green	Red	Red
Meropenem-vaborbactam ¹	Green	Red	Red	Red	Red	Red
Plazomicin ^{1,4}	Green	Yellow	Green	Yellow	Red	Red
Polymyxin B ^{1,5} or Colistin ^{1,5}	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow
Tigecycline ^{1,2}	Green	Green	Green	Red	Green	Green

FONTOS ÁBRA JÖN

SZIDEROFÓR CEFALOSPORIN

CEFIDEROCOL

Fetroja®

FETCROJA

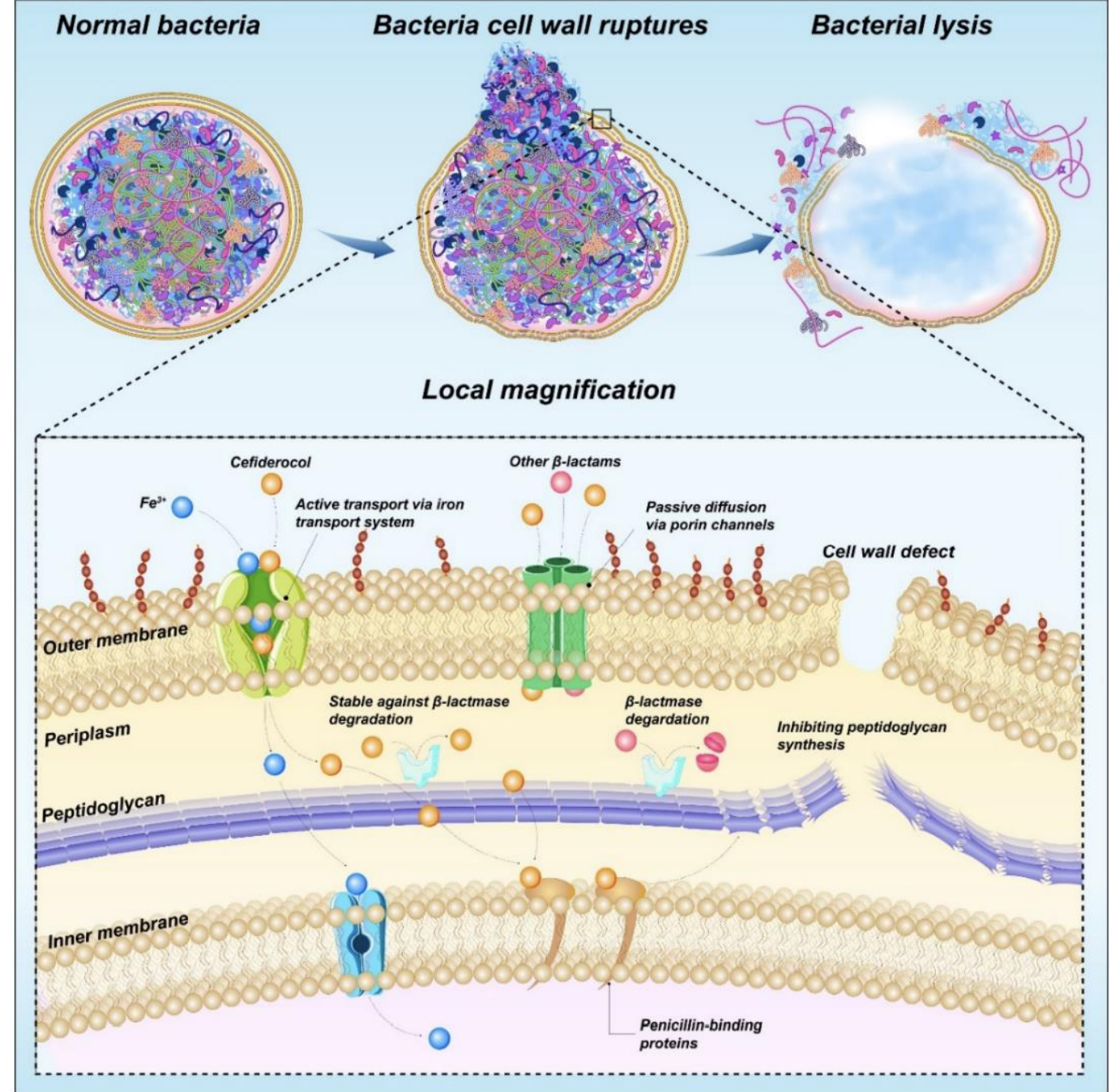



Figure 13. Mechanism of action of cefiderocol.

Nyitott kérdések

- Egyes probléma kórokozók ellen továbbra is kevés a hatékony vegyület
- *In vitro* eredmények és klinikai vizsgálatok
- Empirikus vagy célzott alkalmazás?
- Rezisztenciavizsgálatok és interpretálásuk
- Hozzáférhetőség

The image features a stack of books on the left side, with their pages creating a rhythmic pattern of light and dark lines. A thick, bright yellow diagonal line runs from the top left towards the bottom right, crossing over the books. The background is a solid blue color with a subtle, repeating geometric pattern of interlocking shapes. In the upper right quadrant, the text 'Treatment guidelines' is displayed in a black, italicized serif font, enclosed within a semi-transparent grey rectangular box.

*Treatment
guidelines*

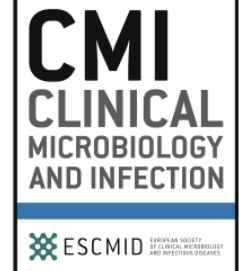


ELSEVIER

Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com



Guidelines

European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines for the treatment of infections caused by multidrug-resistant Gram-negative bacilli (endorsed by European society of intensive care medicine)

Mical Paul ^{1, 2, §}, Elena Carrara ^{3, §}, Pilar Retamar ^{4, 5}, Thomas Tängdén ⁶, Roni Bitterman ^{1, 2}, Robert A. Bonomo ^{7, 8, 9}, Jan de Waele ¹⁰, George L. Daikos ¹¹, Murat Akova ¹², Stephan Harbarth ¹³, Celine Pulcini ^{14, 15}, José Garnacho-Montero ¹⁶, Katja Seme ¹⁷, Mario Tumbarello ¹⁸, Paul Christoffer Lindemann ¹⁹, Sumanth Gandra ²⁰, Yunsong Yu ^{21, 22, 23}, Matteo Bassetti ^{24, 25}, Johan W. Mouton ^{26, †}, Evelina Tacconelli ^{3, 27, 28, *, §}, Jesús Rodríguez-Baño ^{4, 5, §}

<https://doi.org/10.1093/cid/ciae403>

Clinical Infectious Diseases

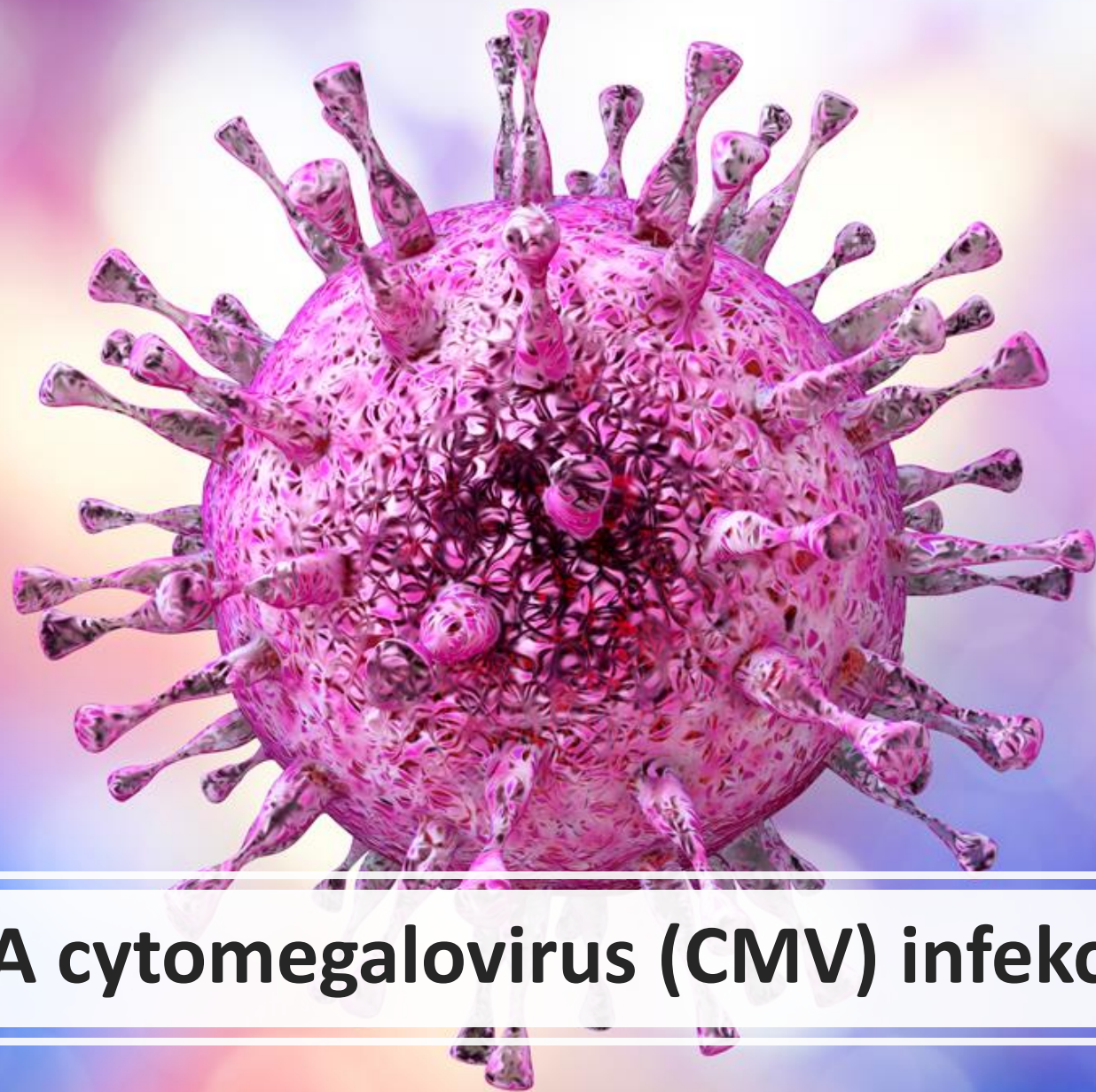
IDSA GUIDELINES



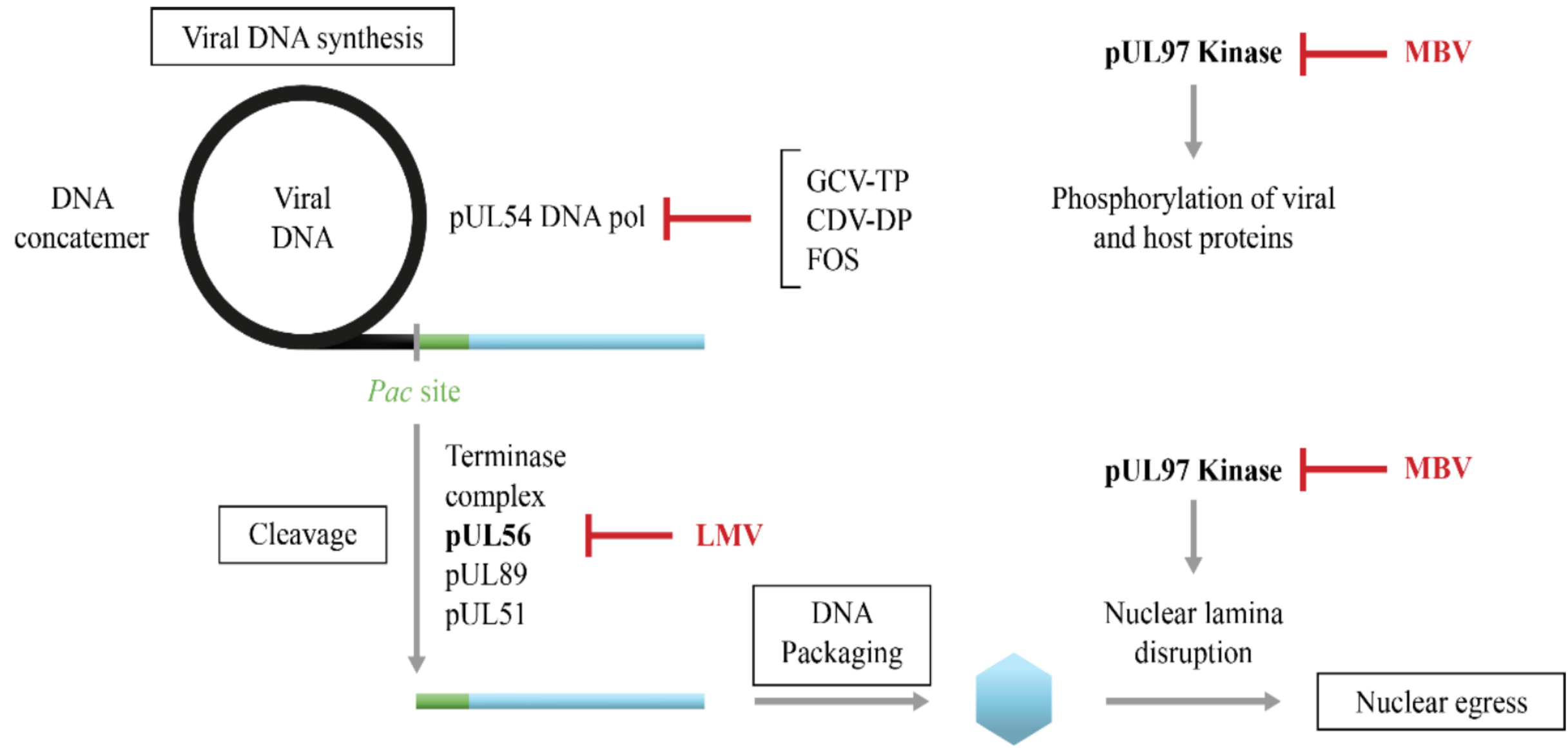
Infectious Diseases Society of America 2024 Guidance on the Treatment of Antimicrobial-Resistant Gram-Negative Infections

Pranita D. Tamma,^{1,✉} Emily L. Heil,² Julie Ann Justo,³ Amy J. Mathers,⁴ Michael J. Satlin,⁵ and Robert A. Bonomo⁶

¹Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA; ²Department of Practice, Sciences, and Health-Outcomes Research, University of Maryland School of Pharmacy, Baltimore, Maryland, USA; ³Department of Pharmacy, Dartmouth Hitchcock Medical Center, Lebanon, New Hampshire, USA; ⁴Departments of Medicine and Pathology, University of Virginia, Charlottesville, Virginia, USA; ⁵Department of Medicine, Weill Cornell Medicine, New York, New York, USA; and ⁶Medical Service and Center for Antimicrobial Resistance and Epidemiology, Louis Stokes Cleveland Veterans Affairs Medical Center, University Hospitals Cleveland Medical Center and Departments of Medicine, Pharmacology, Molecular Biology, and



A cytomegalovirus (CMV) infekció megelőzése és kezelése



GCV= ganciclovir, FOS= foscarnet, LMV= letermovir, MBV= maribavir

Efficacy and safety of extended duration letermovir prophylaxis in recipients of haematopoietic stem-cell transplantation at risk of cytomegalovirus infection: a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial

Domenico Russo, Michael Schmitt, Sylvain Pilorge, Matthias Stelljes, Toshiro Kawakita, Valerie L Teal, Barbara Haber, Charlene Bopp, Sanjeet S Dadwal, Cyrus Badshah**

Summary

Background In a pivotal phase 3 trial of cytomegalovirus prophylaxis with letermovir for up to 100 days after allogeneic haematopoietic stem-cell transplantation (HSCT), 12% of participants developed clinically significant cytomegalovirus infection after letermovir was discontinued. We aimed to evaluate the efficacy and safety of extending the duration of letermovir prophylaxis for clinically significant cytomegalovirus infection from 100 days to 200 days following HSCT.



Lancet Haematol 2024;
11: e127–35

Published Online
December 21, 2023
[https://doi.org/10.1016/
S2352-3026\(23\)00344-7](https://doi.org/10.1016/S2352-3026(23)00344-7)

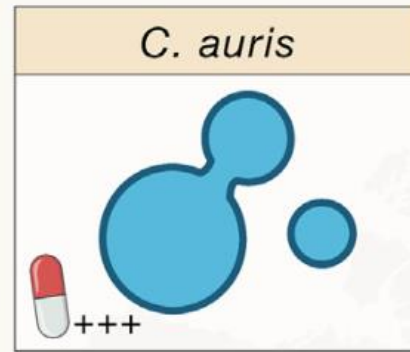
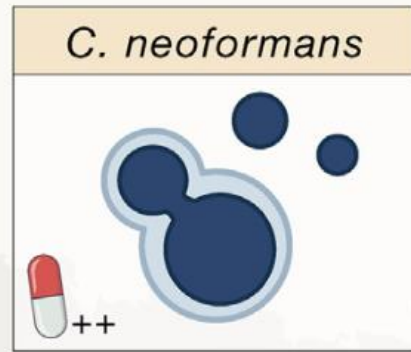
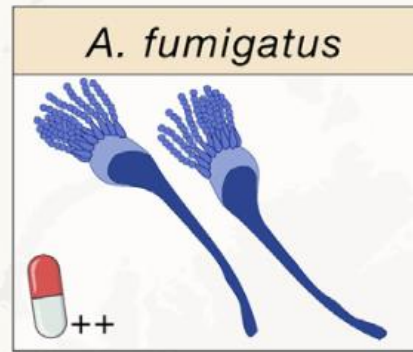
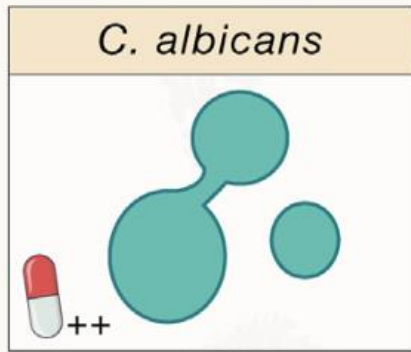


Invazív gombainfekciók ellátása

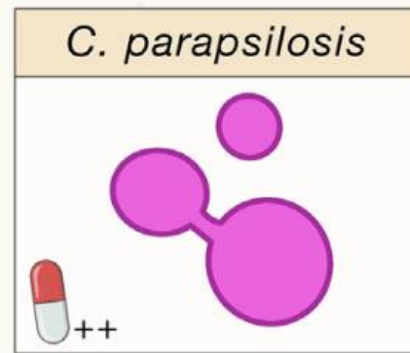
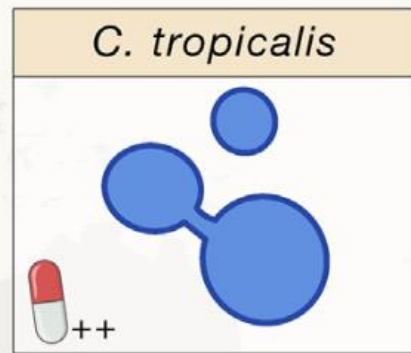
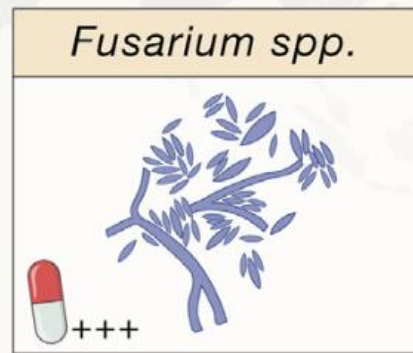
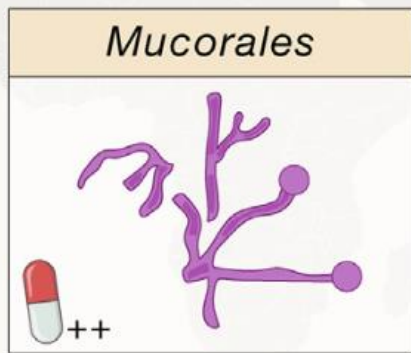
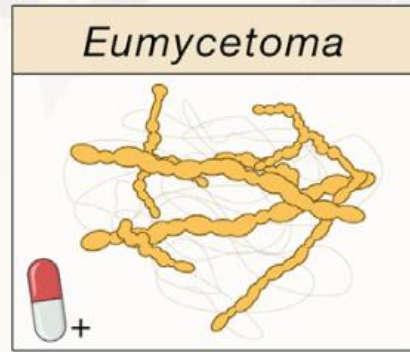
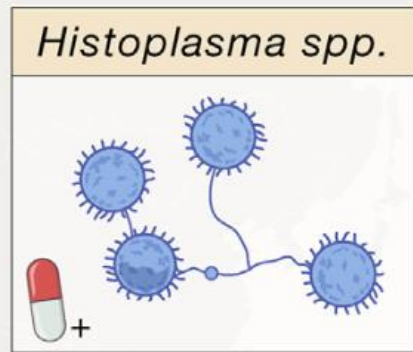
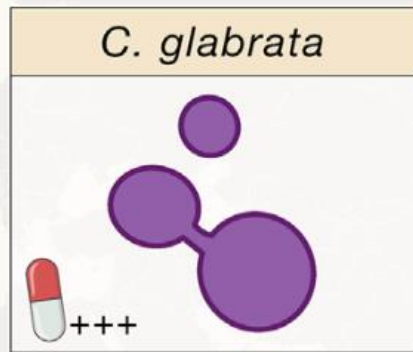
Itt is gondot jelent a rezisztencia

- **Környezeti tényezők**
 - Antifungális vegyületek a környezetben
 - Klimatikus változások (virulencia, rezisztencia)
 - Új speciestek (*C. auris*)
- **Antifungális terápia okozta szerzett rezisztencia**
 - Profilaxis és áttörései infektók
 - Krónikus, relabáló infektó miatt alkalmazott, elhúzódó terápia mellett fellépő rezisztencia
 - Farmakokinetikai és interakciós problémák

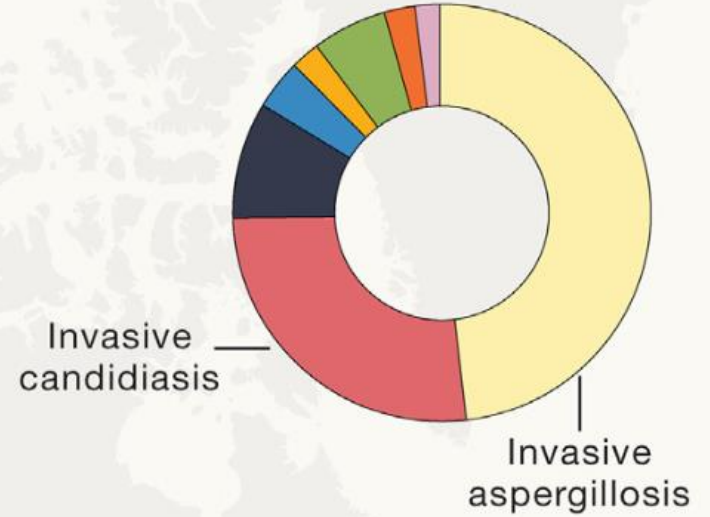
Critical



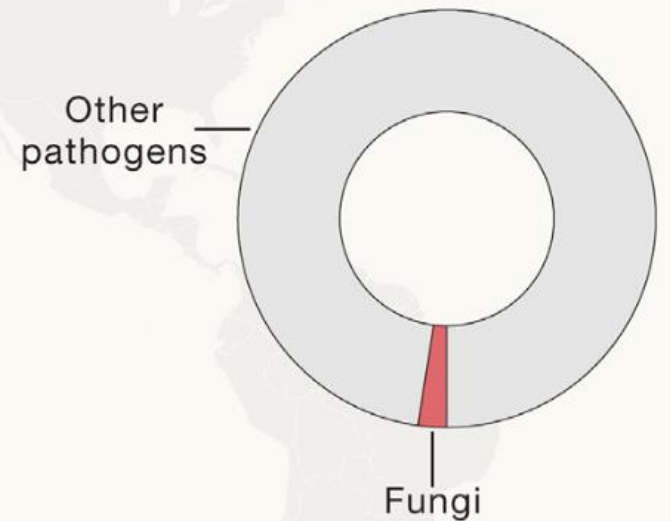
High priority

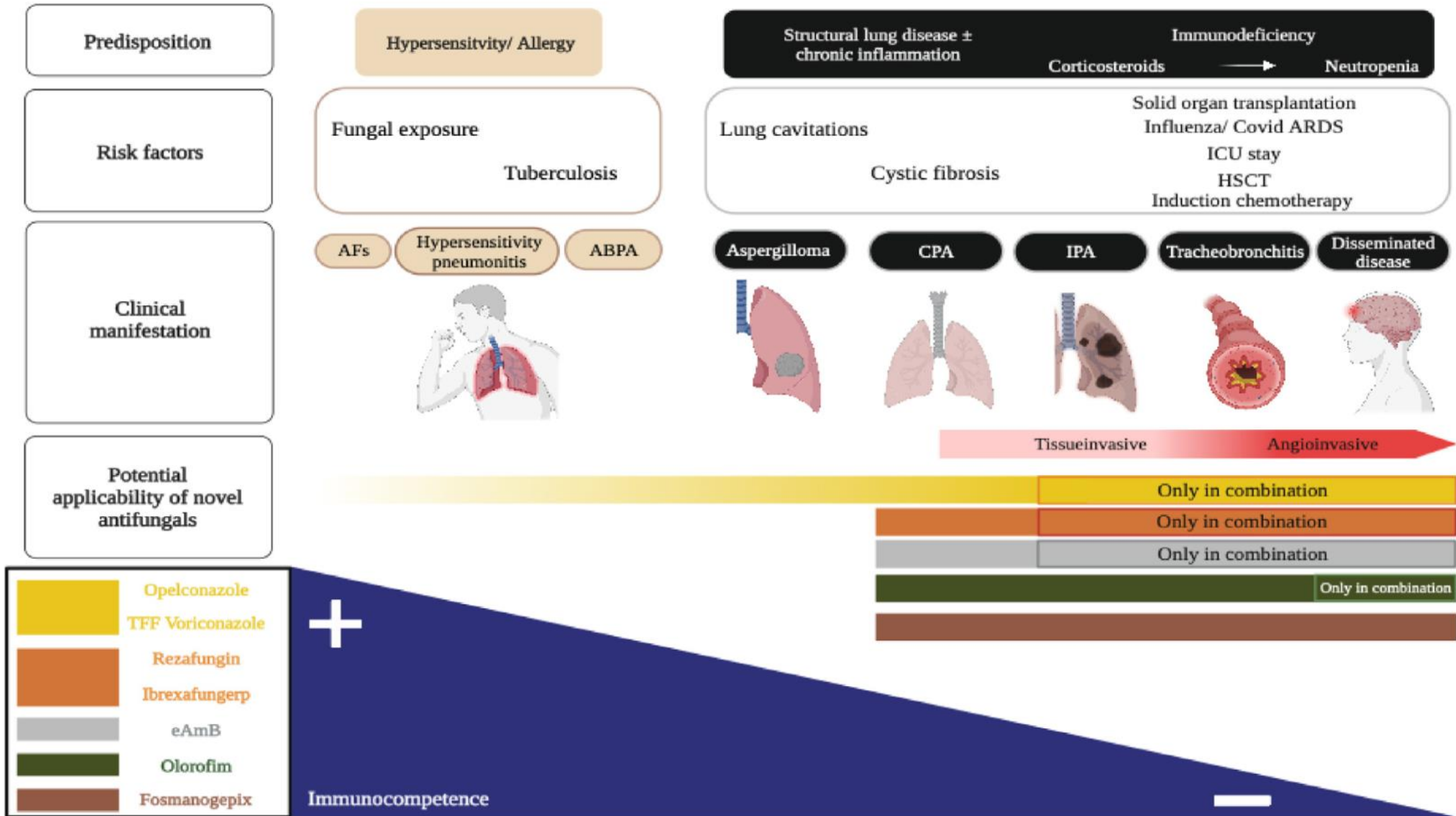


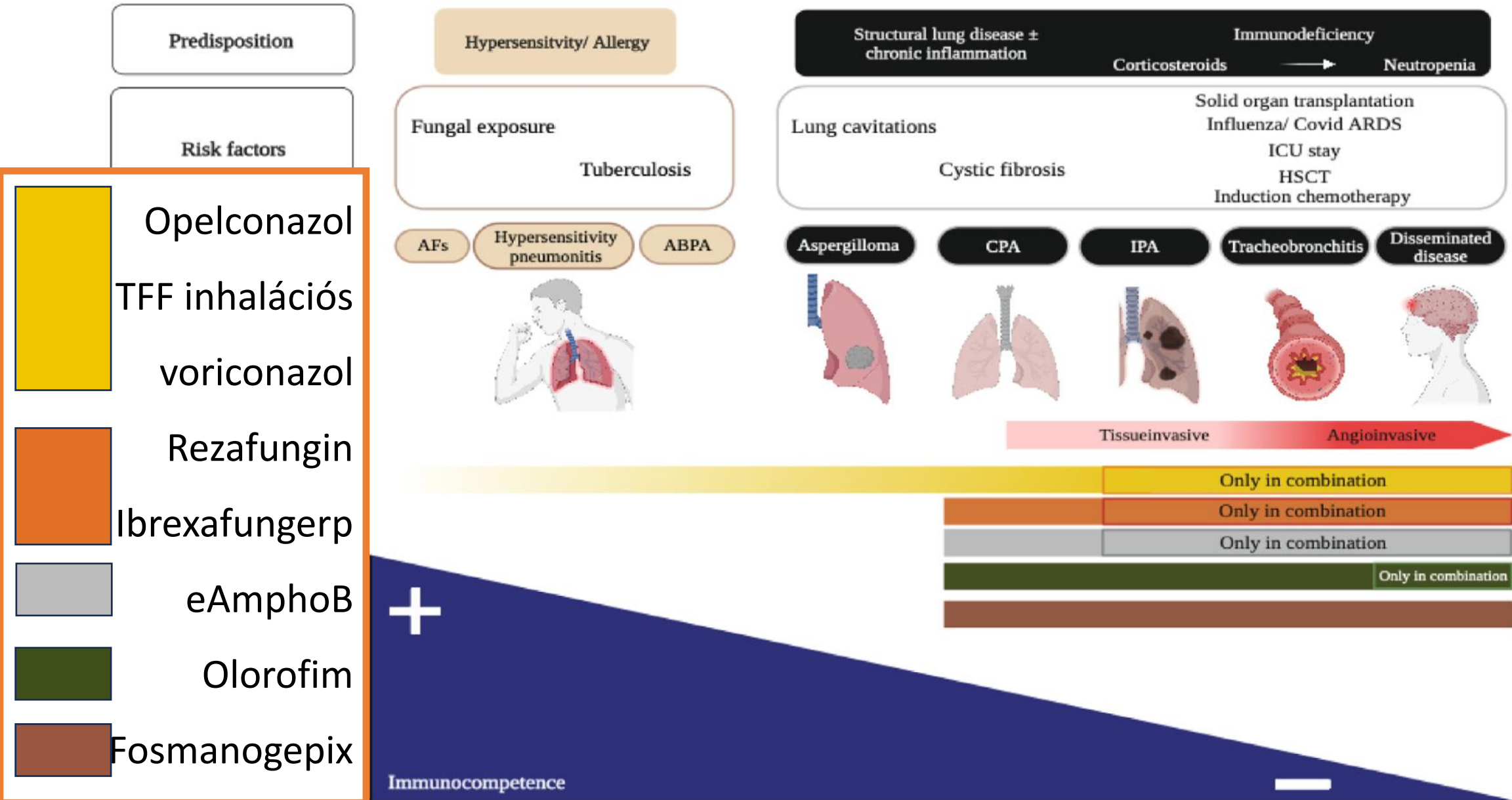
Mortality



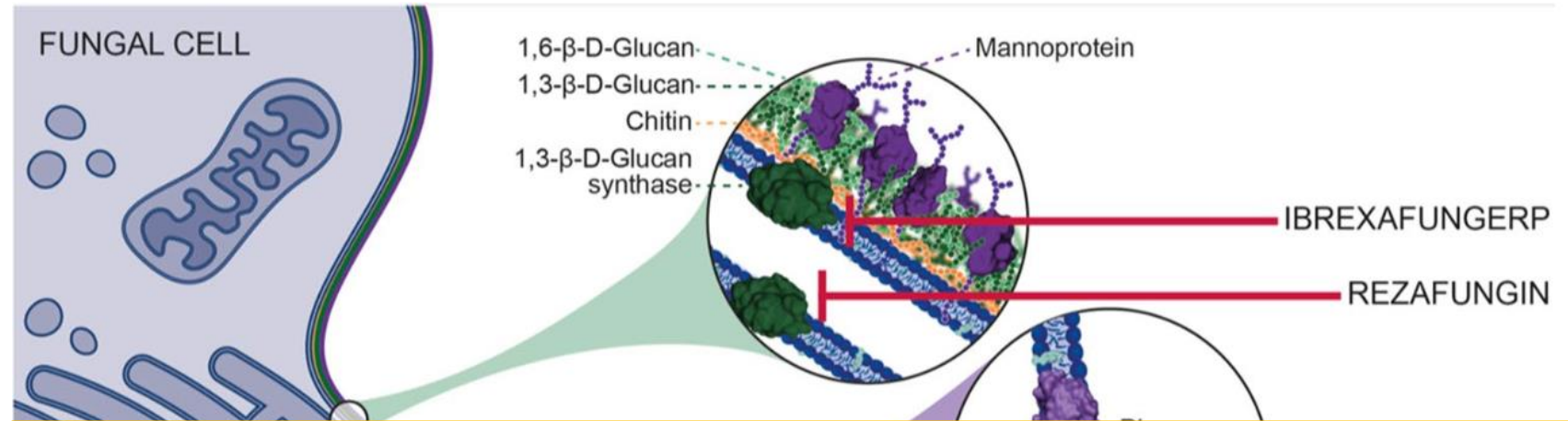
Research funding







Új vegyületek



Fosmanogepix: Gwt1 enzim inhibitor






Ibrexafungerp: triterpenoid glukánszintézis inhibitor


Olorofim: dihydro-orotát dehidrogenáz inhibitor

Opelconazol: triazol

Rezafungin: echinocandin, glukánszintézis inhibitor

Pyrimidine synthesis

Antifungal agents	Fosmanogepix	Ibrexafungerp	Olorofim	Opelconazole	Rezafungin
Pathogens					
	<i>Aspergillus calidoustus</i>	Green	Green	Green	Green
	<i>Aspergillus fumigatus</i>	Green	Green	Green	Green
	Azole-resistant <i>A. fumigatus</i>	Green	Green	Green	Red
	<i>Aspergillus flavus</i>	Green	Green	Green	Green
	<i>Aspergillus lentulus</i>	Green	Green	Green	Green
	<i>Aspergillus nidulans</i>	Green	Green	Green	Green
	<i>Aspergillus niger</i>	Green	Green	Green	Red
	<i>Aspergillus terreus</i>	Green	Green	Green	Green
	<i>Aspergillus tubingensis</i>	Green	Green	Green	Green
	<i>Cunninghamella</i>	Orange	Red	Red	Green
	<i>Lichtheimia</i>	Orange	Red	Red	Green
	<i>Mucor</i>	Orange	Red	Red	Green
	<i>Rhizopus</i>	Orange	Red	Red	Green
	<i>Fusarium spp.</i>	Green	Red	Orange	Green
	<i>Alternaria alternata</i>	Orange	Green	Red	Green
	<i>Cladosporium spp.</i>	Green	Green	Green	Green
	<i>Paecilomyces variotii</i>	Green	Orange	Green	Green
	<i>Purpureocillium lilacinum</i>	Green	Red	Orange	Green
	<i>Scopulariopsis spp.</i>	Green	Red	Green	Green
	<i>Rasamsonia spp.</i>	Green	Green	Green	Green
	<i>Scedosporium spp.</i>	Green	Orange	Green	Green
	<i>Lomentospora prolificans</i>	Green	Orange	Green	Green

	<i>Candida albicans</i>					
	<i>Candida auris</i>					
	<i>Candida dubliniensis</i>					
	<i>Candida glabrata</i>					
	<i>Candida krusei</i>					
	<i>Candida lusitanae</i>					
	<i>Candida parapsilosis</i>					
	<i>Candida tropicalis</i>					


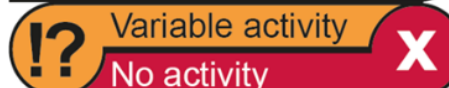
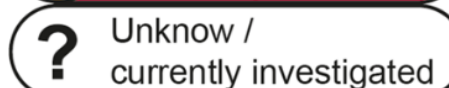

	<i>Cryptococcus gattii</i>					
	<i>Cryptococcus neoformans</i>					

	<i>Trichosporon asahii</i>					
	<i>Exophiala dermatitidis</i>					
	<i>Malassezia furfur</i>					

	<i>Pneumocystis jirovecii</i>					
---	-------------------------------	--	--	--	--	--

	<i>Blastomyces dermatitidis</i>					
	<i>Coccidioides immitis</i>					
	<i>Histoplasma capsulatum</i>					
	<i>Fonsecaea pedrosoi</i>					
	<i>Madurella mycetomatis</i>					
	<i>Talaromyces marneffeii</i>					
	<i>Phialophora verrucosa</i>					

Legend

-  Potent activity
-  Variable activity
-  No activity
-  Unknow / currently investigated

Antifungal agents	Fosmanogepix	Ibrexafungerp	Olorofim	Opelconazole	Rezafungin
-------------------	--------------	---------------	----------	--------------	------------

Megoldásra vár

- Jobb point-of-care diagnosztika
- Antifungális stewardship
- Globális adatgyűjtés
- Antifungális szerek
 - A jelen szereinek hatékonyabb alkalmazása
 - Hozzáférés
 - Új szerek
- Virulencia-ellenes terápia
- Antifungális vakcinák és antifungális immunitást befolyásoló szerek
- Jobban tervezett klinikai vizsgálatok

Take-home 2

- A multirezisztens baktériumok okozta kórházi fertőzések jelentőségét nem lehet eléggé hangsúlyozni.
- A hatékony és biztonságos antibiotikum választás speciális (többirányú) szakértelmet igényel.
- Allogén HSCT-ben a letermovir profilaxis áttörést jelent.
- Új támadáspontú gomballenes szerek a küszöbön.

Q & A

The image features the text "Q & A" rendered in a bold, three-dimensional, red font. The letters are thick and have a slight shadow cast behind them on the surface they are resting on. The background is a smooth, light gray gradient that transitions from a darker shade on the left to a lighter shade on the right. The overall composition is clean and minimalist.