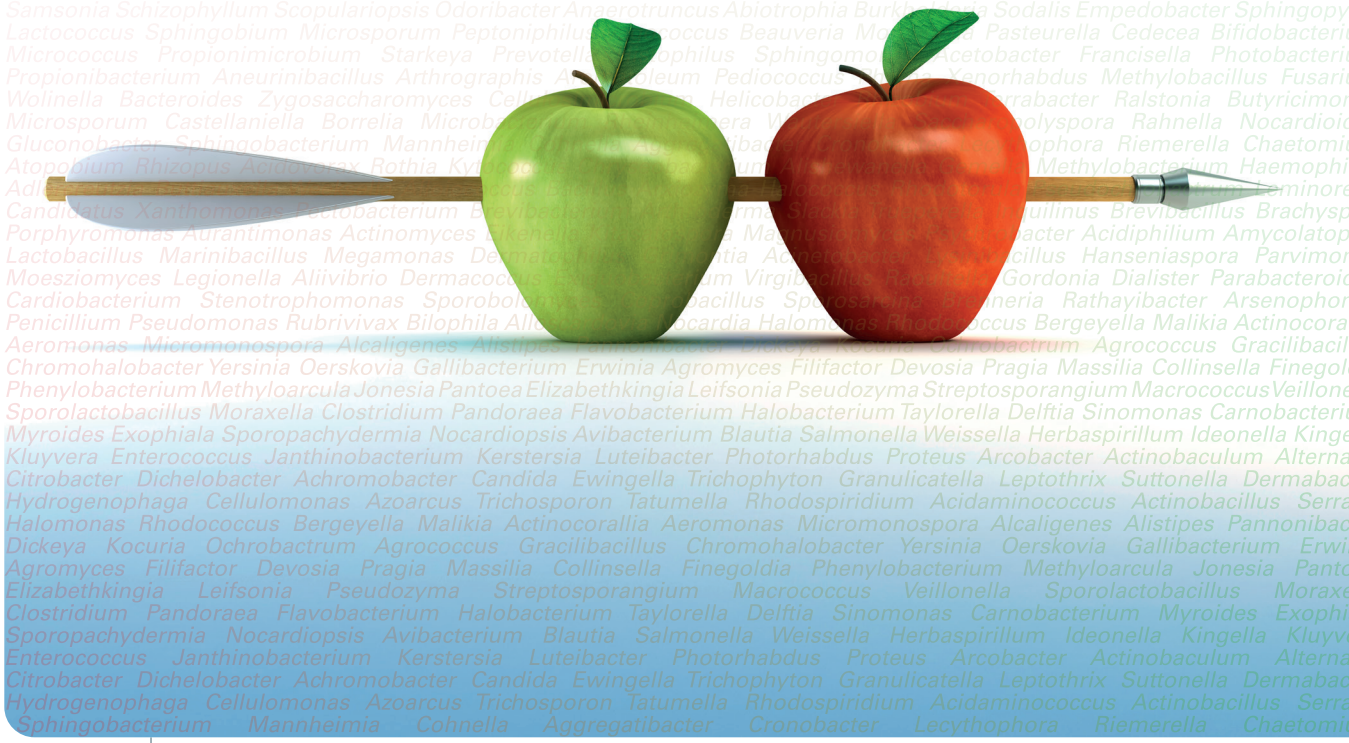
IVD



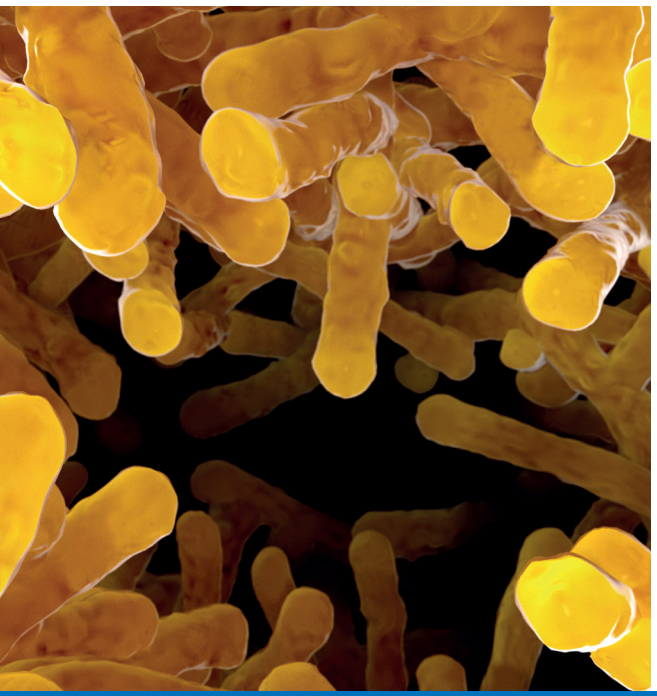
MBT HT Subtyping IVD Module

Changing Microbiology

MALDI-TOF

Innovation with Integrity

Fast Microorganism Identification Combined with Instant Typing



Over the past decade, the implementation of Bruker's MALDI Biotyper® in many microbiology labs worldwide has entirely changed microorganism identification. Its high discriminatory power permits the identification of thousands of different species, but some species are still difficult to differentiate. Bruker has therefore developed the MBT HT Subtyping IVD Module, allowing for automated differentiation of some species which are typically very hard to distinguish.

And there's more! The potential of MALDI-TOF mass spectrometry reaches beyond species identification; the MBT HT Subtyping IVD Module combines the identification of important pathogens with subsequent detection of specific resistance markers in one automated workflow.

The Principle

A prerequisite for the automated typing process is a high confidence identification of the bacterium in the MALDI Biotyper IVD workflow. For species differentiation, the MBT HT Subtyping IVD Module then looks for decisive peaks in the identified mass spectrum, or triggers a sophisticated additional algorithm. For detection of specific resistance markers, the software searches for peaks associated with proteins related to antibiotic resistance and, if present, reports the respective bacterium as presumptive resistant.

Applications of the MBT HT Subtyping IVD Module

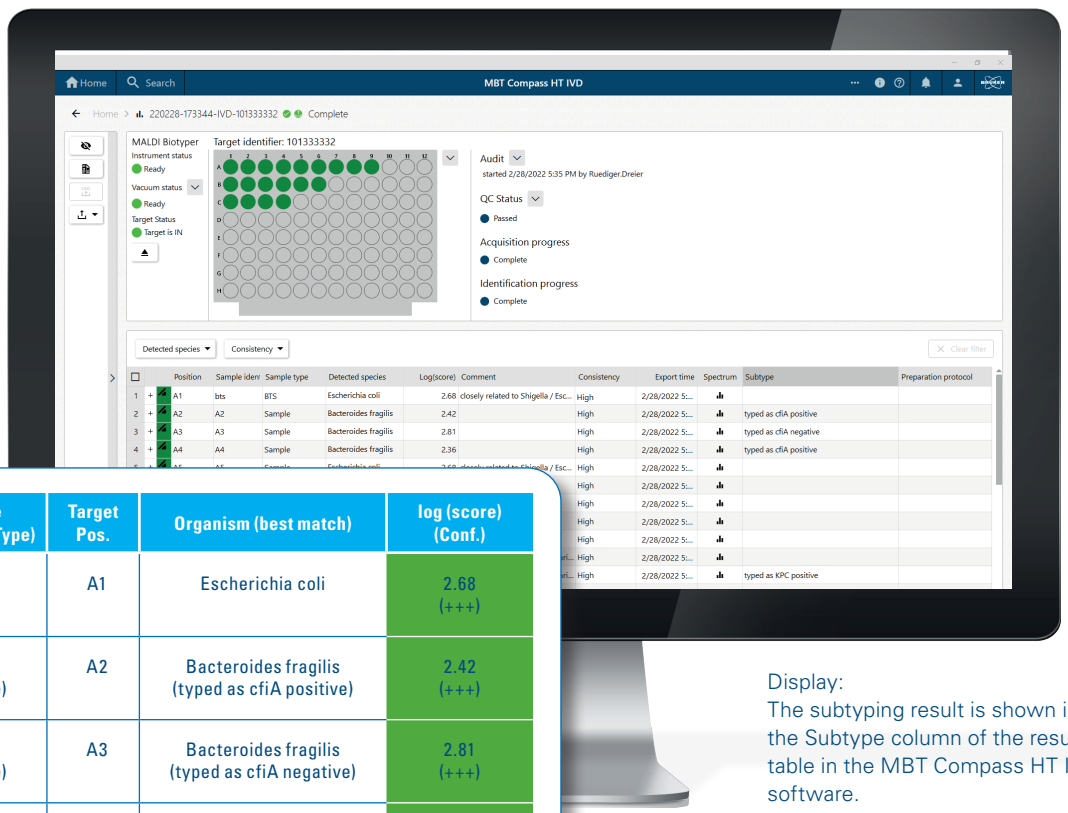
- Detection of KPC-producing *Klebsiella pneumoniae* and *Escherichia coli*
- *Bacteroides fragilis cfiA* subtyping
- Differentiation of *Mycobacterium chimaera* from *Mycobacterium intracellulare*
- Coming soon: differentiation of *Streptococcus pneumoniae, S. mitis_oralis* and *S. pseudopneumoniae*

Seamless and Fast Workflow No Additional Work – A Clear Report

Besides the usual sample preparation for routine microbial identification by the IVD MALDI Biotyper, no additional work needs to be done to benefit from the MBT HT Subtyping IVD Module, no special kits are needed. After high confidence identification of the bacterium in the MALDI Biotyper IVD workflow, the MBT HT Subtyping IVD Module automatically triggers additional algorithms and shows the typing results in both the MBT Compass HT IVD software and in the report.

Seamless workflow
- Routine identification by MALDI Biotyper is performed
- Only if successful, typing is executed automatically
- No additional steps are required

- For KPC positive samples, the result identifier "typed as KPC positive" is displayed. If no characteristic peak has been detected, no typing result is mentioned.
- For *B. fragilis*, the subtyping result is reported as "typed as *cfiA* positive" or "typed as *cfiA* negative".
- For the Mycobacterium_chimaera_intracellulare_group, the result identifier "typed as *M. intracellulare*" or "typed as *M. chimaera*" is displayed.
- Coming soon: For *Streptococcus pneumoniae/ pseudopneumoniae/ mitis_oralis,* the result identifier typed as *S. mitis_oralis* or *S. pneumoniae* or *S. pseudopneumoniae* is displayed.
- Nothing is stated if the subtyping algorithm result is not reliable.



Sample identifier (Type)	Target Pos.	Organism (best match)	log (score) (Conf.)
BTS (BTS)	A1	Escherichia coli	2.68 (+++)
A2 (Sample)	A2	Bacteroides fragilis (typed as cfiA positive)	2.42 (+++)
A3 (Sample)	A3	Bacteroides fragilis (typed as cfiA negative)	2.81 (+++)
A4 (Sample)	A4	Bacteroides fragilis (typed as cfiA positive)	2.36 (+++)

Display:
The subtyping result is shown in the Subtype column of the result table in the MBT Compass HT IVD software.

Report:
Identification results with subtyping results below the species name in the Organism (best match) column.

An Aid to Diagnosis: Instant Resistance Marker Detection with MALDI Biotyper

Antibiotic resistant bacteria are on the rise and are a major global public health threat. Effective prevention and control are therefore of high importance to reduce the risk of infections associated with antibiotic resistant microorganisms. The MBT HT Subtyping IVD Module enables fast detection of specific resistance markers in an automated workflow, hence providing an aid to diagnosis.

Detection of KPC-producing *Klebsiella pneumoniae* and *Escherichia coli*

A significant increase of carbapenem resistant *K. pneumoniae* (CRKP) is observed in many countries worldwide, which is a major concern as infections result in high rates of morbidity and mortality.
The most important mechanism of resistance by CRKP is the production of the *K. pneumoniae* carbapenemase enzyme (KPC), encoded by the bla_{KPC} gene. This plasmid based resistance can easily be exchanged between bacteria by horizontal gene transfer, making it even more dangerous in healthcare settings.

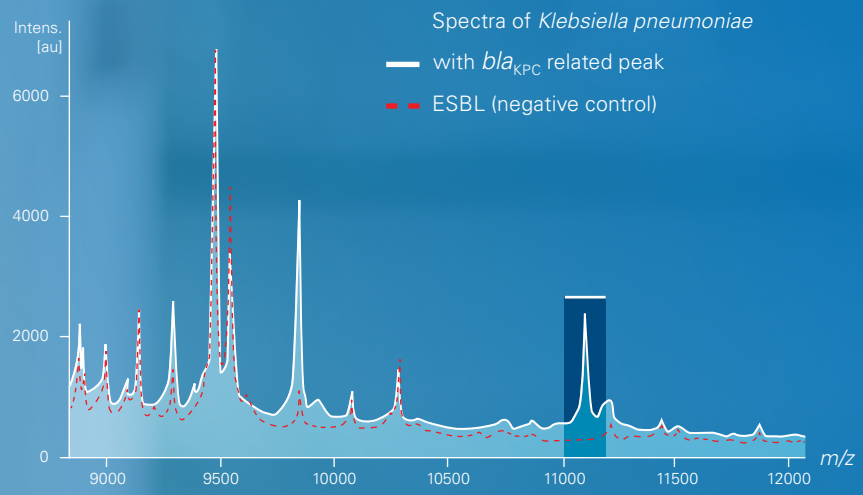
This mechanism and the fact that CRKP resistance could spread rapidly between patients - if not detected in time - demand efficient identification methods for laboratory testing, active surveillance and screening of patients.

Lau *et al.* (2014) discovered a peak in MALDI-TOF mass spectra of KPC-producing *K. pneumoniae*, related to the plasmid carrying bla_{KPC}. This specific peak at 11,109 m/z is clearly detectable in bacterial MALDI-TOF mass spectra.

Prerequisite for the automated detection process with the IVD MALDI Biotyper is the successful identification of the bacterium, i.e. the log(score) ID value must be ≥ 2.0. The MBT HT Subtyping IVD Module then looks for the bla_{KPC} related peak in the sample spectrum. And, if present, the software will report this sample as a KPC positive one.
If no characteristic peak has been detected, nothing is mentioned.

Anna F. Lau *et al.*, Journal of Clinical Microbiology 2014:52(8):2804-2812. https://doi.org/10.1128/JCM.00694-14
Yung-Ho Youn et al., Journal of Clinical Microbiology 2016:54(1):35-42. https://doi.org/10.1128/JCM.01643-15

KPC detection of *K. pneumoniae* and *E. coli* includes only strains with a bla_{KPC} pKpQIL plasmid. If another resistance mechanism is present, it will not be identified by the MBT HT Subtyping IVD Module. Also, if the gene expression rate is low, there will be no characteristic peak and no KPC subtyping alert. Cultivation media and conditions might suppress or induce a signal at m/z 11,109 which is not related to a KPC resistance. Therefore, Columbia Agar with 5% sheep blood agar must be used for cultivation of *K. pneumoniae* and *E. coli*.



Bacteroides fragilis cfiA Subtyping

B. fragilis is the most frequently isolated anaerobic pathogen. Carbapenem resistance in *B. fragilis* is frequently associated with presence of the *cfiA* gene, encoding for a metallo-beta-lactamase conferring resistance to nearly all ß-lactam antibiotics. As a result, infections with *B. fragilis cfiA* positive strains are difficult to treat.

After successful identification, the MBT HT Subtyping IVD Module looks for specific peaks associated with respectively *cfiA* positive and *cfiA* negative *B. fragilis* strains. The best match for the respective sample will be reported as a *cfiA* positive or *cfiA* negative strain. Nothing is stated when the subtyping algorithm result is not reliable.

Ingrid Wybo et al., Journal of Clinical Microbiology 2011:49(5):1961-1964. https://doi.org/10.1128/JCM.02321-10
Elisabeth Nagy et al., Journal of Medical Microbiology 2011:60(11):1584-1590. https://doi.org/10.1099/jmm.0.031336-0

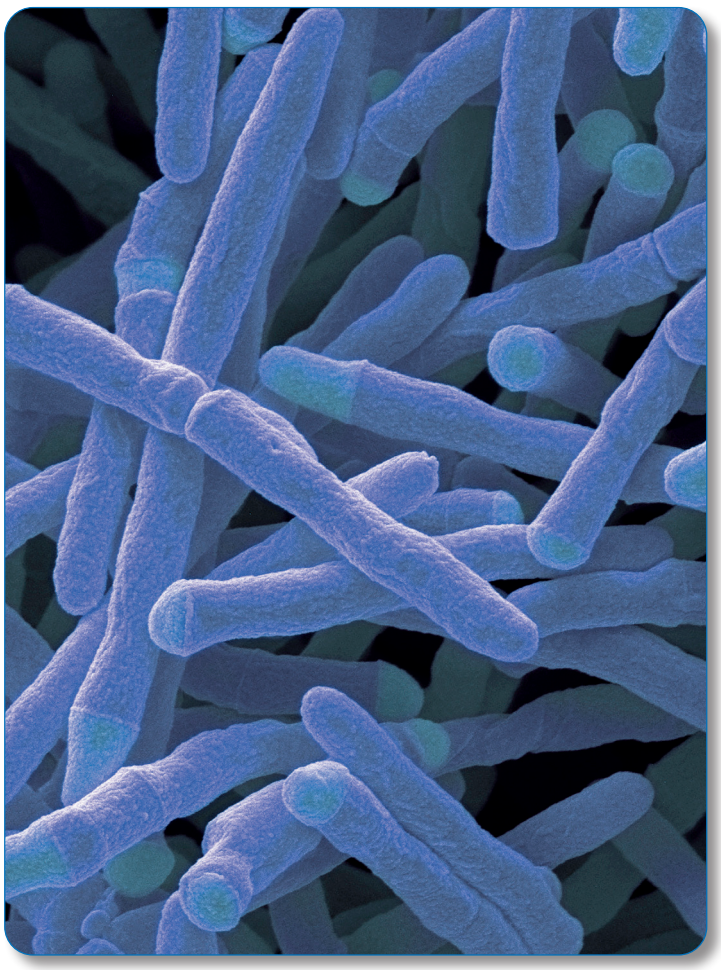
An Early Warning System

The MBT HT Subtyping IVD Module quickly detects bla_{KPC} expressing *K. pneumoniae* and *E. coli*, and *cfiA* positive/negative *B. fragilis* strains. Please note that negative results do not necessarily mean that these strains are susceptible but will require additional confirmation methods.

The final identification results must be assessed by a trained professional experienced in clinical microbiology.

Accurate Differentiation of *Mycobacterium chimaera* from *Mycobacterium intracellulare*

Mycobacterium chimaera very rarely causes infections in humans, but there have been reports about contamination of medical equipment used in heart surgery.
There was a risk that heater-cooler units used in open-heart surgery were contaminated with *M. chimaera* and that exposure of patients to these units in the operating theatre could lead to infections appearing months to years after surgery. Most reported infections were those of prosthetic valves or vascular grafts.



Routine identification using MALDI-TOF mass spectrometry is restricted to the identification of the *M. chimaera / intracellulare* complex because mass spectra of both species are very similar. Conventional identification methods suffer from the same limitation.

After successful identification of the *M. chimaera / intracellulare* complex by the IVD MALDI Biotyper, application of the MBT HT Subtyping IVD Module allows fast and accurate differentiation of both species by thorough comparison of characteristic mass spectrum peaks, as described by Pranada et al. (2017). This differentiation will support further insights into the pathogenic role of *M. chimaera* and can contribute to epidemiological studies which might improve infection control in future.

Mycobacterium avium / intracellulare complex includes several species and only *M. intracellulare* and *M. chimaera* can be subtyped.
Analysis of clinical samples, for example sputum, without any cultivation step does not form part of the intended use / intended purpose; a cultivation step is required.

Note: Prerequisite for successful identification and differentiation of Mycobacteria is an installed MBT HT Mycobacteria IVD Module.

Arthur B. Pranada et al., Journal of Medical Microbiology 2017:66:670-677. https://dx.doi.org/10.1099/jmm.0.000469

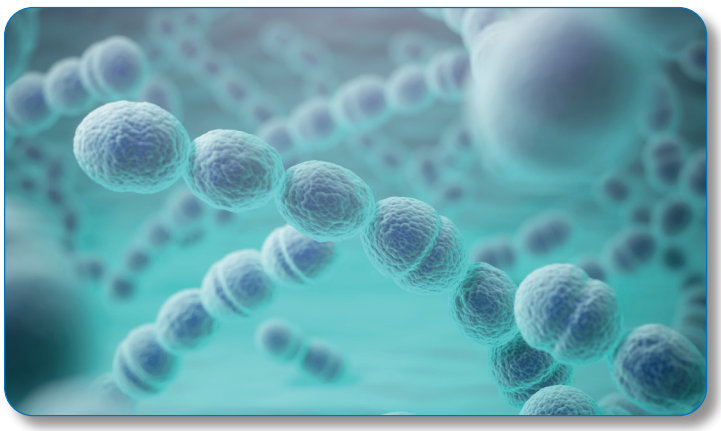
Coming soon

Species Confirmation of *Streptococcus pneumoniae, S. pseudopneumoniae* and *S. mitis_oralis*

Unambiguous species differentiation of "mitis-group streptococci (MGS)" has always been a challenge, even when using state-of-the-art MALDI-TOF mass spectrometry, due to close phenotypic and genotypic similarities within this group. The majority of MGS (*S. mitis* and *S. oralis*) are part of the normal flora and rarely cause severe diseases. On the contrary, *Streptococcus pneumoniae*, also belonging to the MGS, is one of the prominent global pathogens, requiring unequivocal identification. The phenotypically closely related *S. pseudopneumoniae* is regarded as an emerging pathogen causing lower-respiratory-tract infections, while being linked with high rates of antimicrobial resistance, hence its clear-cut confirmation was included as well in the MBT HT Subtyping IVD Module.

This new application of the MBT HT Subtyping IVD Module is based a novel algorithm enabling species confirmation or correction of *S. pneumoniae* and *S. mitis* species group streptococci. After being identified by the MALDI Biotyper as one of the MGS species, a weighed ranking list interpretation is applied to differentiate these species more reliably. Additionally, the species *S. mitis* and *S. oralis* are grouped together in the new library version 2022, to the combination "*Streptococcus mitis_oralis*".

As a result, for *Streptococcus pneumoniae, S. pseudopneumoniae* and *S. mitis_oralis*, the initial species identification based on log(scores) can be confirmed or corrected for a more accurate species identification.



Sample identifier (Type)	Target Pos.	Organism (best match)	log (score) (Conf.)
C1 (Sample)	C1	Streptococcus pneumoniae (typed as Streptococcus pneumoniae)	2.12 (+++)
C2 (Sample)	C2	Streptococcus mitis_oralis (typed as Streptococcus pneumoniae)	2.08 (+++)
C3 (Sample)	C3	Streptococcus mitis_oralis (typed as Streptococcus pneumoniae)	2.25 (+++)
C4 (Sample)	C4	Streptococcus pneumoniae (typed as Streptococcus pneumoniae)	2.13 (+++)
D1 (Sample)	D1	Streptococcus mitis_oralis (typed as Streptococcus pneumoniae)	2.16 (+++)
D2 (Sample)	D2	Streptococcus mitis_oralis (typed as Streptococcus pneumoniae)	2.05 (+++)
BTS (BTS)	H12	Escherichia coli	2.68 (+++)

Report:
Identification results with subtyping results below the species name in the Organism (best match) column.

Inka Harju et al. I, Journal of Clinical Microbiology 2017:55:914–922. https://doi.org/10.1128/JCM.01990-16
Geneviève Garriss et al., MBio 10:e01286-19. https://doi.org/10.1128/mBio.01286-19
Christian Salgård Jensen et al., Diagnostic Microbiology and Infectious Disease 2021:101:115487. https://doi.org/10.1016/j.diagmicrobio.2021.115487

Order Information

Part-No. 1877010
The MBT HT Subtyping IVD Module enables the automated detection of strain specific characteristics.

MBT Compass HT IVD software is a prerequisite for the use of the MBT HT Subtyping IVD Module.

Differentiation of *Mycobacterium chimaera* from *M. intracellulare* needs an installed MBT HT Mycobacteria IVD Module.

Please contact your local representative for availability in your country.
Not for sale in the USA.

CE IVD

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