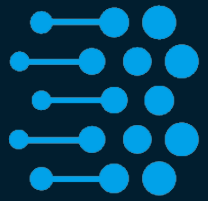


BiomeDx

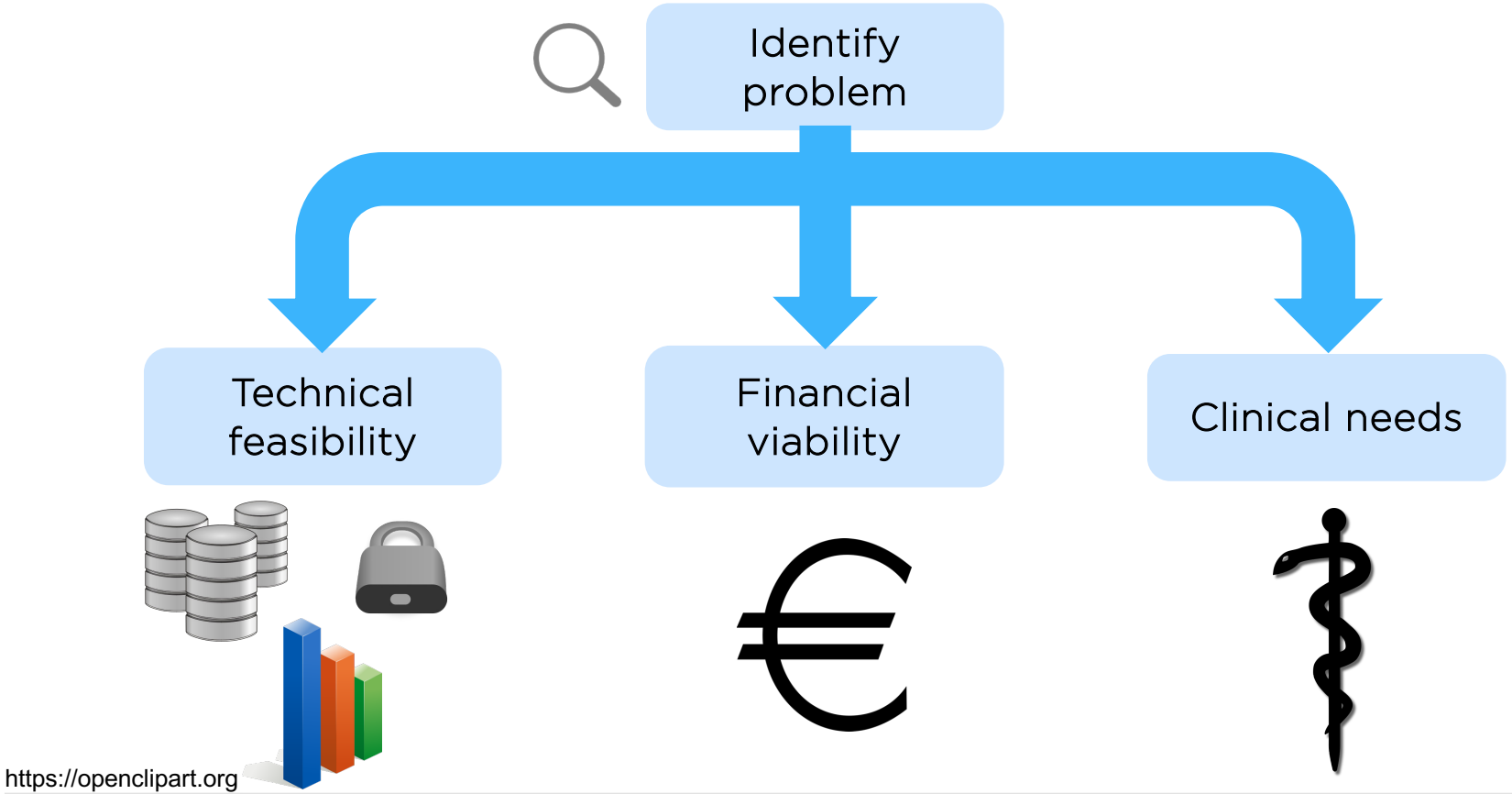
Building microbiome based diagnostic tools a journey from raw data to final product

Christian Jansen MSc MSc

Overview

1. Background
2. Biomarker development
3. BiomeOne validation study results
4. BiomeOne CE-IVD medical product

1. Background



1. Microbiome Oncology Cycle

BiomeDx

Medically certified available
(CE-IVD)

BiomeOne®
for therapy management

Early detection

Donor selection

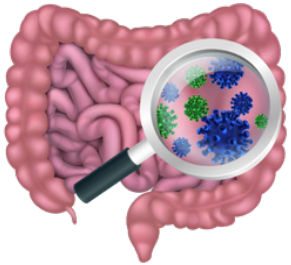
Microbiome Oncology Cycle

BiomeCRC
for prevention

RUO available

BiomeFMT
for treatment

Under development

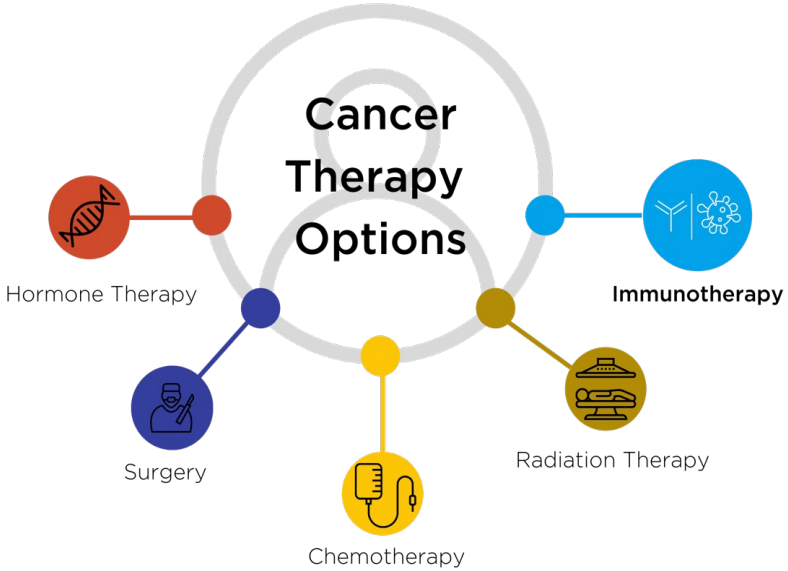


Therapy

Prevention

1. Cancer therapy options

Immunotherapy (ICI) is the rising therapy option for cancer



30 % of patients respond to immunotherapy (ICI)

70%

of cancer patients are non-responders or suffer some severe side effects (irAE)

Reference:
https://www.marketsandmarkets.com/

2. BiomeOne biomarker development

Dataset

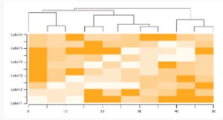
Over **10.000 patients worldwide** were used for the biomarker development (20% cancer patients)

Partnered studies + Proprietary data + Public data

Microbiome data

Next-Generation Sequencing

Bioinformatics



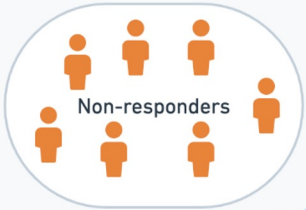
1400 different species identified

Clinical data

- Response
- Immune-related adverse events
- Tumor type
- Gender, country, age, diet

Biomarker identificatio

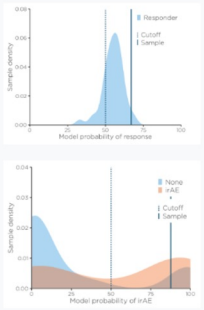
Data analysis



Classification algorithm to distinguish response

Approx. 15 million data points included in the calculation

BiomeOne validation



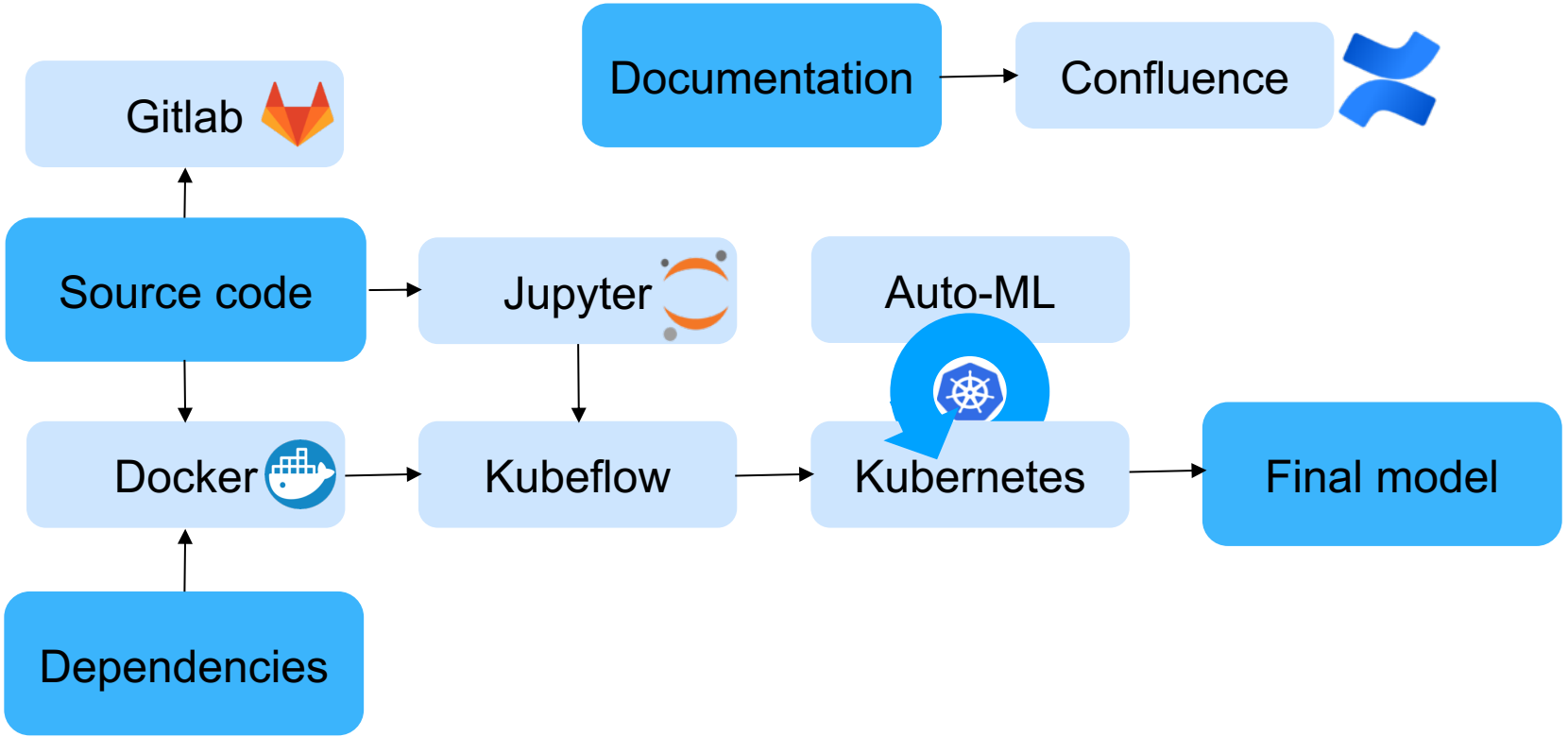
Validation through multi-centric study (5 centres) with **III/IV patients** (melanoma, NSCLC, renal cell carcinoma)

Sensitivity: 81%
+20% compared to current gold standard

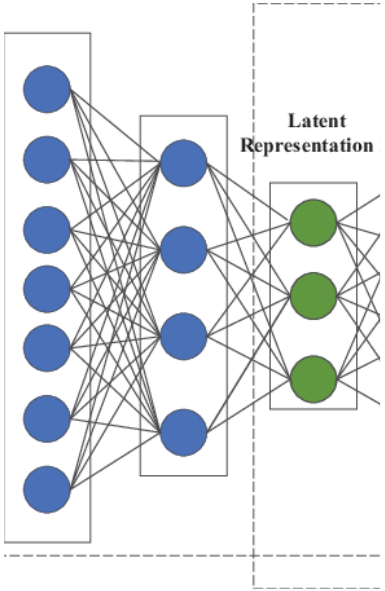
Clinical application
ICI-response prediction
irAE prediction
FMT selection

2. Biomarker development infrastructure

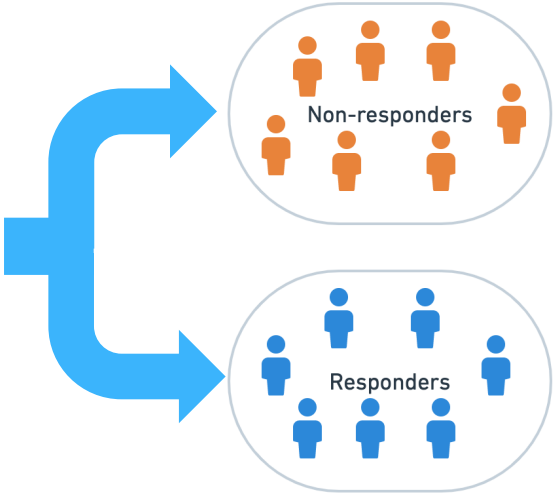
BiomeDx



2. Dimensionality reduction & Final model



+



Training data AE:
Cancer patient datasets
Healthy customer datasets

Training & validation data RF:
Cancer patient datasets
(compressed)

Mac et al 2018 DOI:10.1145/3287921.3287946
Sarica et al 2017 DOI:https://doi.org/10.3389/fnagi.2017.00329

3. Validation results

BiomeDx

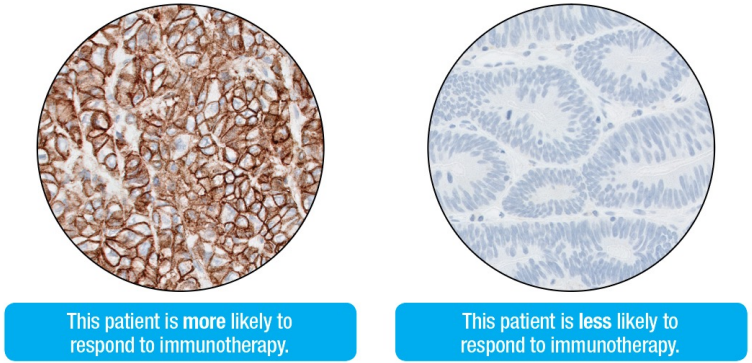
BiomeOne probability for response (high / low)

	Responder CR + PR	**Non-responder** SD + PD	Total
BiomeOne result: High	34 (pass)	10 (fail)	**44**
BiomeOne result: Low	8 (fail)	11 (pass)	**19**
Total	**42**	**21**	**63**

- Sensitivity: = 81%
- Specificity: = 52%
- Positive predictive value (PPV): = 77%
- Negative predictive value (PPN): = 58%

3. Comparison with PD-L1 testing

PD-L1 expression testing via microscopic staining was until now the only available biomarker to predict ICI therapy response



BiomeOne®	PD-L1 Test
+ non-invasive	- invasive tissue sampling
+ scalable	- needs to be evaluated one by one
+ applicable to many indications	- only applicable to some indications
+ can predict irAE (RUO)	- only able to predict response
+ objective result	- human error

https://www.captodayonline.com/scoring-gastric-gej-cancers-pd-l1-expression/

3. Comparison with PD-L1 testing

BiomeDx

Subset of 38 NSCLC patients were tested

	R	NR	
PDL1 +	19	5	24
PDL1 -	9	5	14
	28	10	38

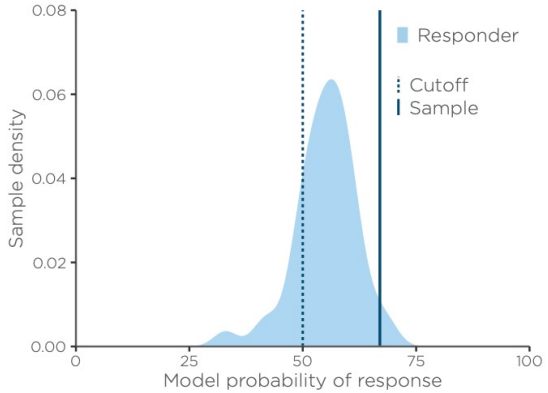
	R	NR	
BiomeOne® +	22	5	27
BiomeOne® -	6	5	11
	28	10	38

PD-L1
Sensitivity: 67.86%
Specificity: 50.00%
PPV: 79.19%
NPV: 35.71%

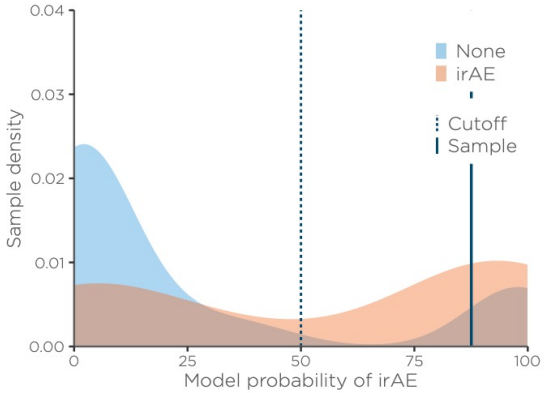
BiomeOne
Sensitivity: 78.57%
Specificity: 50.00%
PPV: 81.48%
NPV: 45.45%

4. The report

Probability of response: high



Probability of irAEs: high



Diversity

5.27

Normal range: 5.62 - 6.42

Bacterial richness

174

Normal range: 202 - 320

Clinical response

The analysis of the intestinal microbiome reveals a high probability (67%) of the occurrence of a response to a checkpoint inhibitor based cancer immunotherapy (CTLA-4, anti-PD-1 or anti-PD-L1).

Please note: The values 0 - 50 % represent a low probability of the occurrence of a response. The values 51 - 100 % represent a high probability of the occurrence of a response.

Enterotype

1

Tolerability (irAEs)

The analysis of the intestinal microbiome reveals a high probability (88%) of the occurrence of immune-related adverse events (irAEs) of any grade during a checkpoint inhibitor based cancer immunotherapy (CTLA-4, anti-PD-1 or anti-PD-L1).

Please note: The values 0 - 50 % represent a low probability of the occurrence of irAEs. The values 51 - 100 % represent a high probability of the occurrence of irAEs.

4. Regulatory and QM challenges

BiomeDx

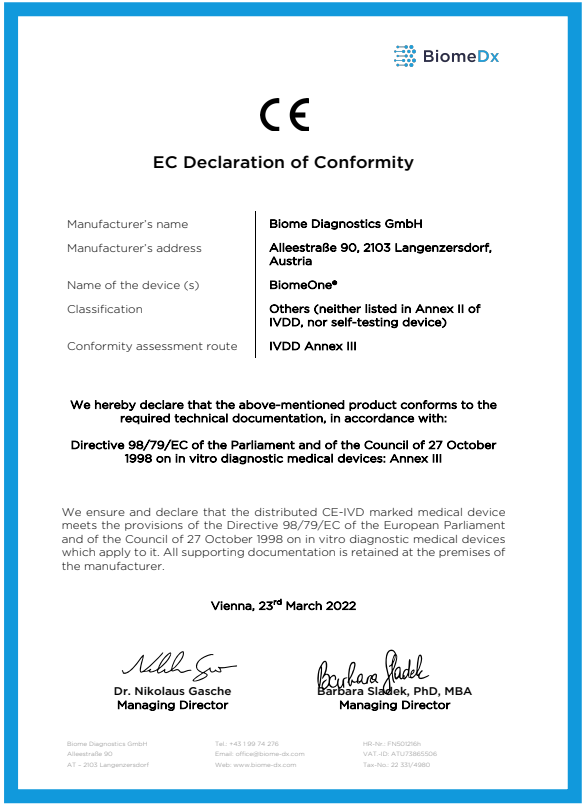
BiomeOne CE-IVD registered medical device

Regulatory Requirements:

- IEC 62304:2006 Software Life Cycle process
- ISO 14971:2019 Risk Management
- ISO 13485:2016 & ISO 9001 eQMS – electronic Quality Management System
- EN 62366_1:2015+A1:2020 Usability Engineering Processes
- MDCG Guidances

New Challenge

CE-IVD registered medical device Registration as IVDR presumably as a class C medical device 2017/746



BiomeDx

CE

EC Declaration of Conformity

Manufacturer's name	Biome Diagnostics GmbH
Manufacturer's address	Alleestraße 90, 2103 Langenzersdorf, Austria
Name of the device (s)	BiomeOne®
Classification	Others (neither listed in Annex II of IVDD, nor self-testing device)
Conformity assessment route	IVDD Annex III

We hereby declare that the above-mentioned product conforms to the required technical documentation, in accordance with:

Directive 98/79/EC of the Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices: Annex III

We ensure and declare that the distributed CE-IVD marked medical device meets the provisions of the Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices which apply to it. All supporting documentation is retained at the premises of the manufacturer.

Vienna, 23rd March 2022

Dr. Nikolaus Gasche
Managing Director

Barbara Sladek, PhD, MBA
Managing Director

Biome Diagnostics GmbH
Alleestraße 90
AT – 2103 Langenzersdorf

Tel.: +43 1 99 74 276
Email: office@biome-dx.com
Web: www.biome-dx.com

HR-Nr.: FN501216h
VAT.-ID: ATU73865506
Tax-No.: 22 331/4980

4. Key takeaways

BiomeDx

Study results

- Results indicate detectable difference between responders and non-responders
- BiomeOne outperforms PD-L1 testing on subset of our study

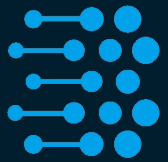
Biomarker (IVD) development

- Has been CE-IVD marked 05/22
- Predicts response (CE-IVD marked)
  - Sensitivity 81%
  - Specificity 52%
- Predicts occurrence of irAE (RUO)

CE IVD

BiomeOne is ready to use

THANK YOU!



BiomeDx

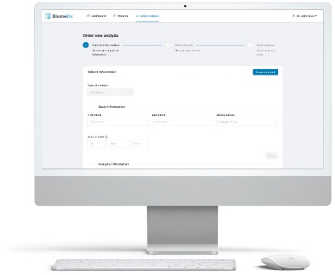
Advancing cancer care through microbiome intelligence

Christian Jansen, MSc MSc
christian.jansen@biome-dx.com
www.biome-dx.com

BiomeOne procedure

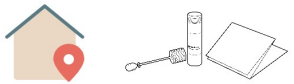
Order

Order **BiomeOne kit** directly via the **BiomeDx Platform**



1 day delivery

Sample taking



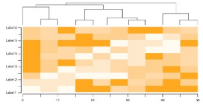
Sample is taken from at-home by the patient

1 day delivery

Laboratory analysis

Next-Generation Sequencing

Bioinformatics



Identify significant bacteria species

Classification algorithm

Response and irAE prediction

BiomeOne model

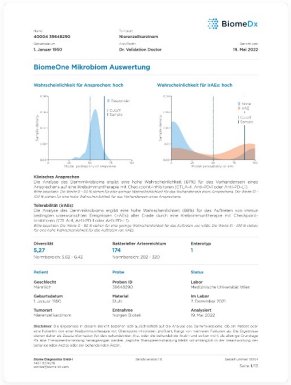
Responder

Non-responder

BiomeOne report

Report generated and returned to the doctor with

- **Probability of response**
- **Probability of irAEs**
- Microbiome results


BiomeDx

BiomeOne Mikrobiom Auswertung

MEDICAL DEVICES QUALITY MANAGEMENT ISO ISO 13485:2016

CERTIFIED ISO 9001:2015 COMPANY

CE IVD