



# Integrating ATCC® Reference Materials into your Molecular Diagnostics Workflows

The Nexus of Bioinformatics with Authenticated Cells, Microorganisms, and Derivatives

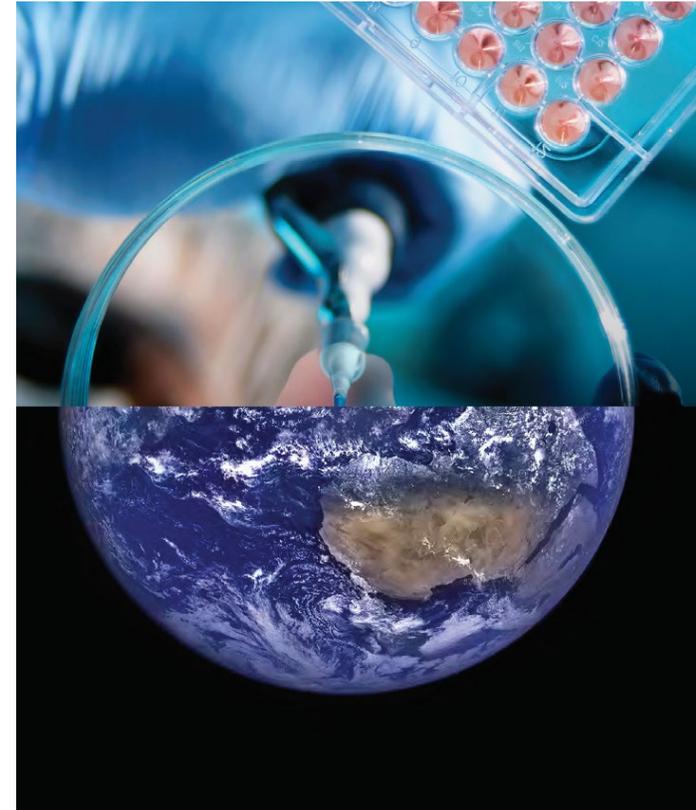
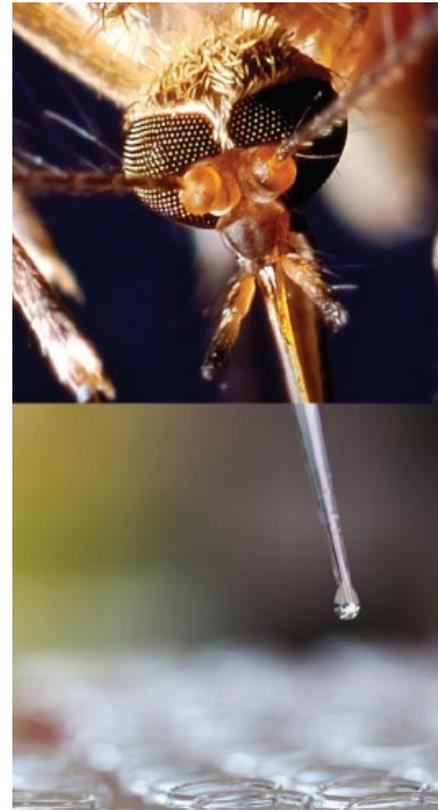
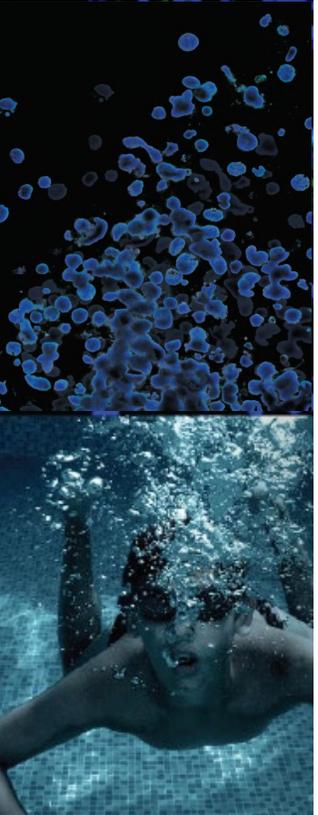
**Victoria Knight-Connoni, PhD**

Head of Content Development & BioNexus *Principal Scientist*, ATCC®

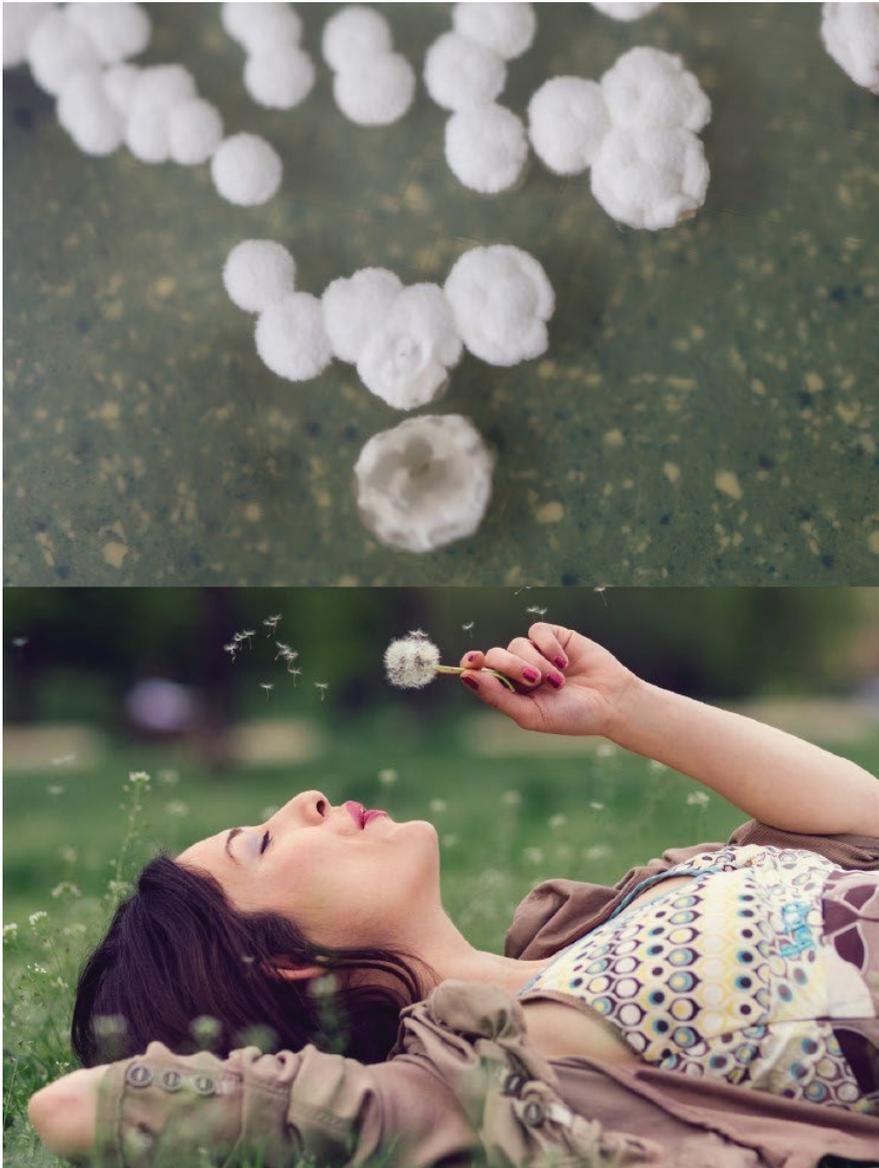
**Fang Tian, PhD**

*Director, Biological Content*, ATCC®

Credible Leads to Incredible™



# Outline



- Introduction
- ATCC®'s collection of biological resources
- Integrating ATCC® biological materials into microbial molecular diagnostics workflows
- Integrating ATCC® biological materials into oncology molecular diagnostics workflows
- Summary
- Questions?

# ATCC® – Life science innovations that touch people

- Founded in 1925 - we have been supplying scientists with essential scientific resources, services, and standards for nearly a century
- ATCC® is ISO 9001 and ISO 13485 certified and ISO/IEC 17025 and ISO 17034 accredited
- Leading global supplier of authenticated cell models and viral and microbial standards
- An innovative R&D company that provides better models
  - Gene editing, microbiome, NGS, primary cells, and advanced cell models
- Services provider
  - Customer base in diagnostics, drug discovery, and applied markets; cGMP and Biorepository Services
- Patent repository consists of >90% of all USA bio-patents



Established partner to global researchers and scientists



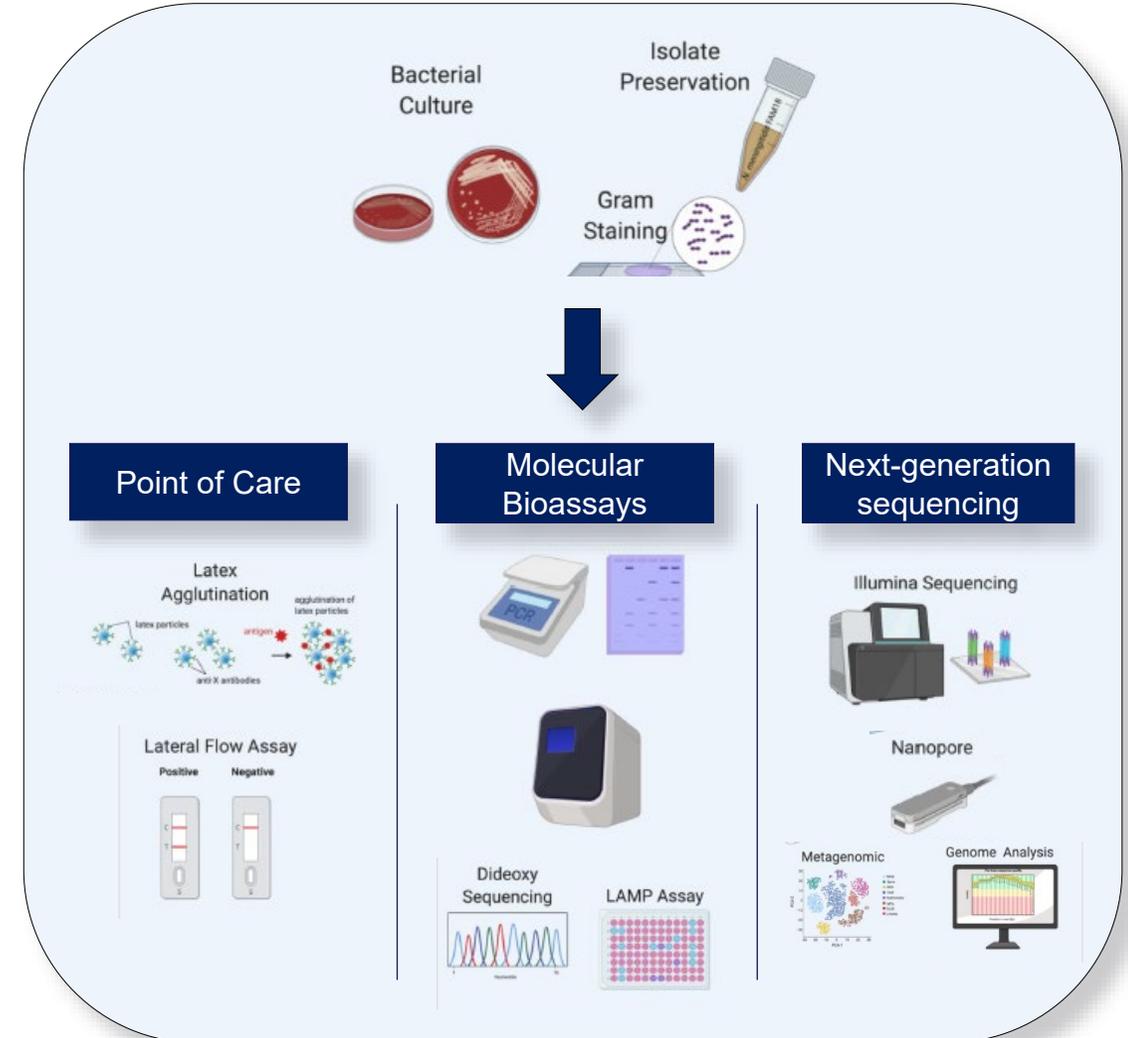


# Integrating ATCC<sup>®</sup> Biological Materials into Microbial Molecular Diagnostics Workflows

# Current state of molecular diagnostics for infectious disease

Shift from culture-based methods to rapid high-throughput molecular based assays

Point of care testing	
↑ No need to culture	↓ Less sensitive
↑ Cheap and easy to perform at bedside	↓ Absent calibrations and/or quality control
↑ Rapid results	
Molecular bioassays	
↑ No need to have viable pathogen	↓ Requires specialized equipment and expertise
↑ Sensitive and species specific	↓ Can be cost prohibitive
Next-generation sequencing	
↑ Allows full characterization of pathogen	↓ Requires specialized equipment and expertise
	↓ Can be cost prohibitive
	↓ Longer turnaround time

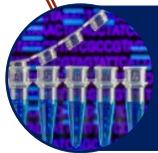


Adapted from Diallo K, et al. EBioMedicine 65: 103274, 2021. PubMed: 33721818

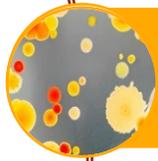
# Challenges in molecular diagnostics



Ability to detect emerging agents and variants as new variants and pathogens are always emerging



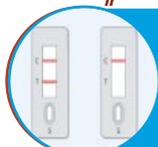
Tests that provide actionable results by identifying the presence or absence of pathogens



Speed to answer → balance of large and small panels



Development timeline and ROI



Trend to decentralize assays and move to POCT

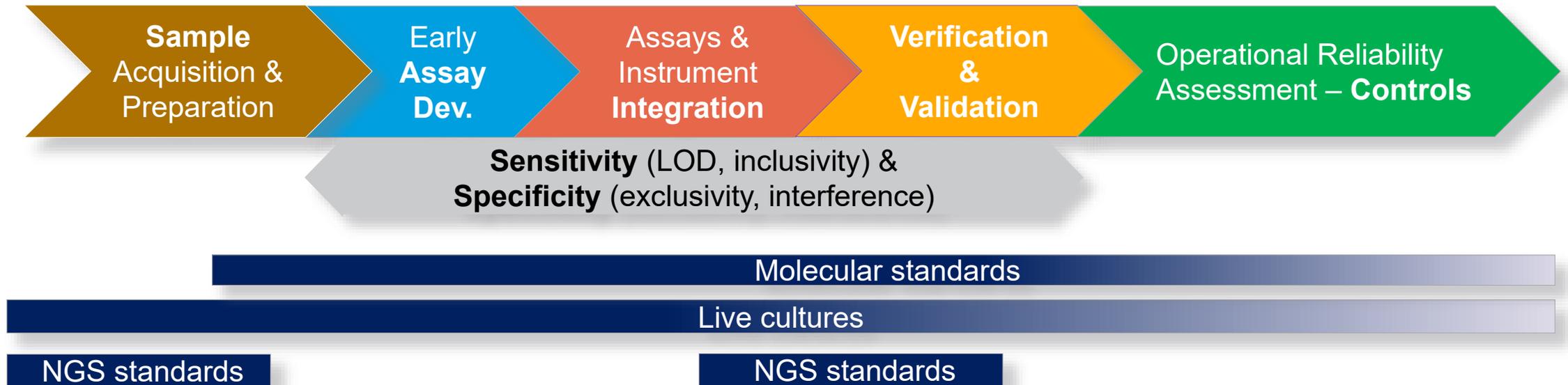


Affordability, availability, coverage

Access to comprehensive repositories of authenticated biomaterials and standards

# Materials needed for LDT or IVD technology development

*Molecular diagnostics development*



- Each stage of the development pipeline requires different materials for testing and assay validation
- Access to complementary materials allows for rapid development of assays

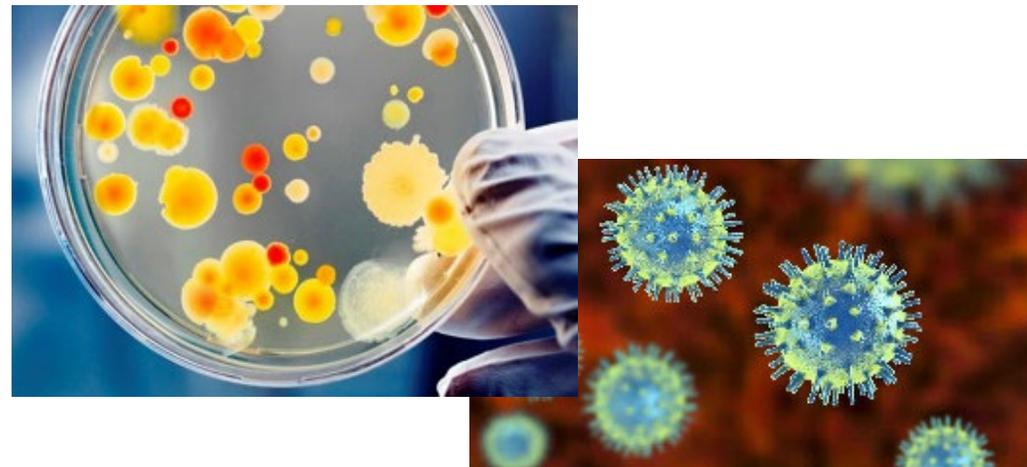
# Reliable biomaterials should be used as controls

## Types of materials to choose:

Reference Material	Benefit	Disadvantage
Live microbes	Sustainable source, maintains complexity of the intact microorganism, provides entire genome	Difficulty accessing materials, biosafety
Inactivated materials	Ability to access to pathogens in BSL 1 labs	Cells may no longer perform as live microbe
Genomic DNA/RNA	Ease of access, safe to use	May not mimic live microbe
Synthetic oligonucleotides	Easy to design and synthesize, allows access to non-culturable materials	May not resemble complexity of the whole genome

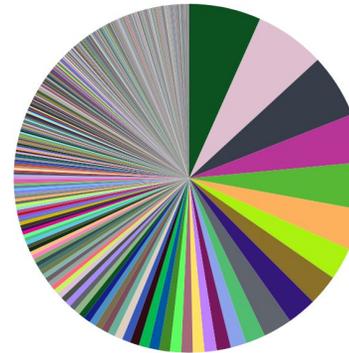
## Other things to consider:

- Use fully authenticated materials
- Avoid contamination or misidentification

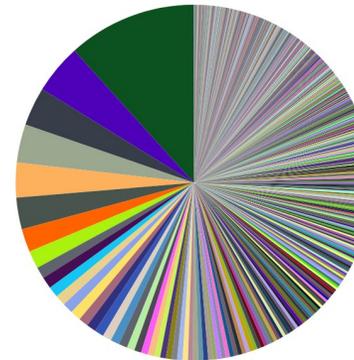


# ATCC®'s comprehensive collection of microbes

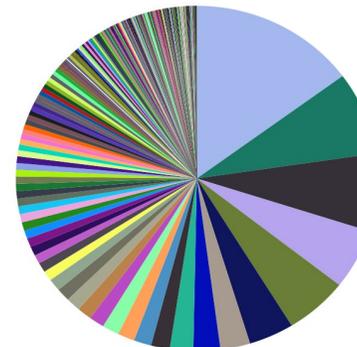
- Comprehensive microbial collection with enhanced authentication
  - 70,000+ bacteria, fungi, viruses, and protozoa
  - Over 1,300 microbial type strains
- Brand recognition
  - Organizations and regulatory agencies specify ATCC® cultures in their standards and guidelines
  - USP, ISO, FDA, CLSI, USDA, ASTM, AOAC, WHO
  - Over 475 reference strains recommended for use in quality control
- ATCC® has live microbes and derivatives, including inactivated materials and nucleic acids
- ATCC® uses a variety of advanced techniques to characterize and authenticate biomaterials—no single method of identification is sufficient



Bacteriology  
1226 genera



Mycology  
1864 genera

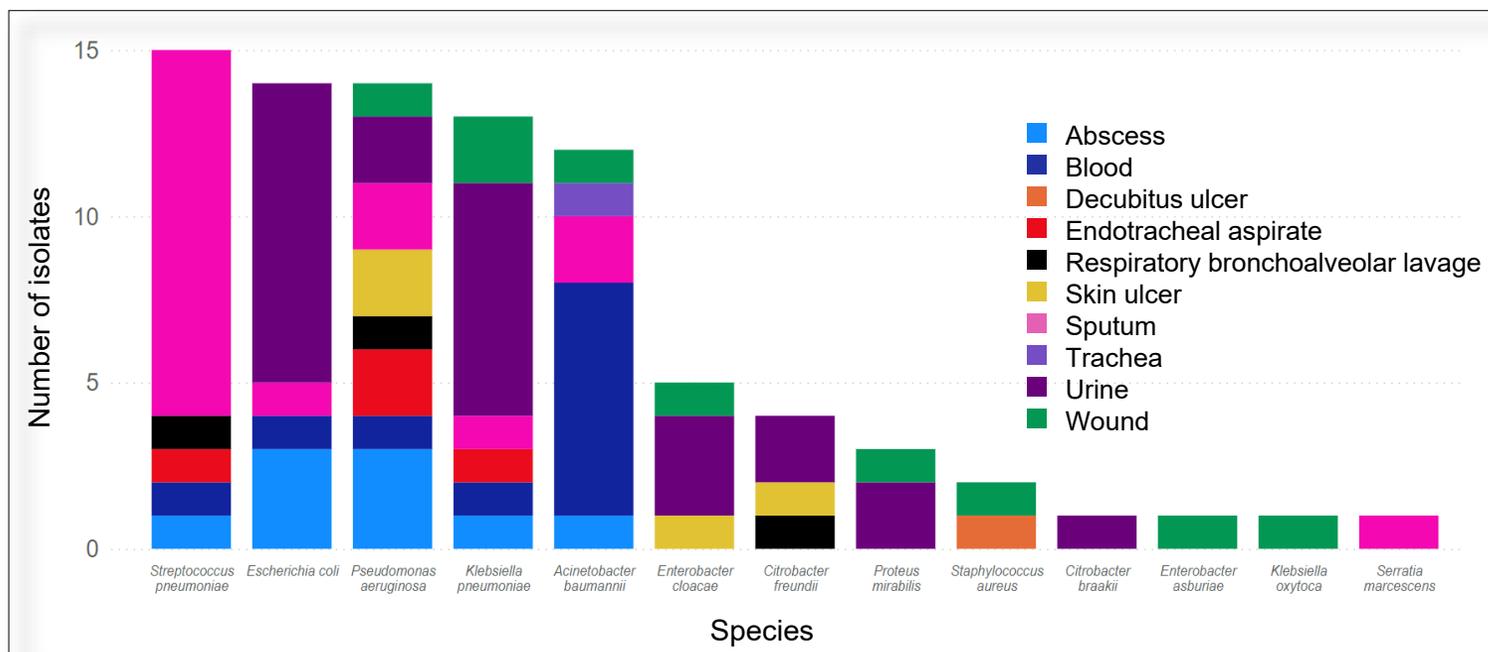


Virology  
200 genera

# ATCC® is a resource for highly characterized clinical isolates

We are building a panel of highly characterized antimicrobial strains. Data includes:

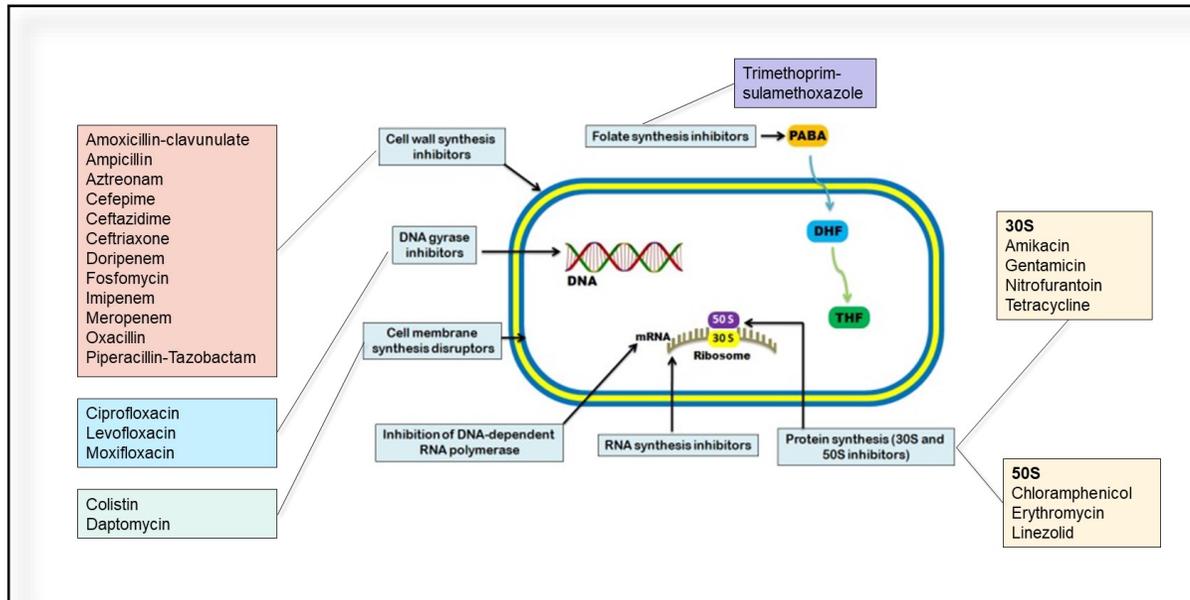
- **Susceptibility data** – minimum inhibitory concentration (MIC) values and susceptibility profiles for targeted drugs
- **Genetic data** – DNA sequence information for antibiotic resistance genes and 16S rRNA genes
- **Source information** – geography, collection date, patient age and gender, and collection site



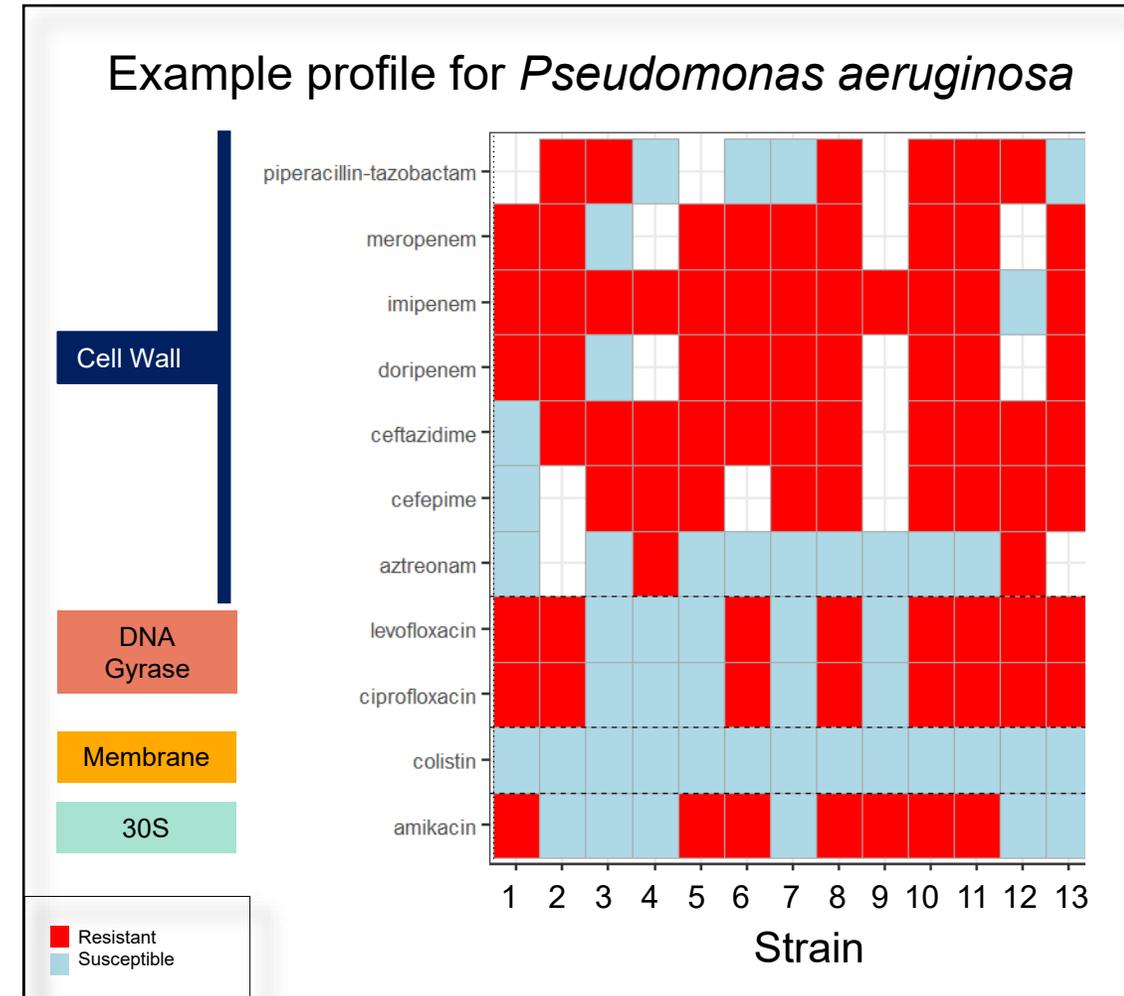
Species	Number of isolates
<i>Acinetobacter baumannii</i>	13
<i>Citrobacter braakii</i>	1
<i>Citrobacter freundii</i>	4
<i>Enterobacter asburiae</i>	1
<i>Enterobacter cloacae</i>	5
<i>Escherichia coli</i>	17
<i>Klebsiella oxytoca</i>	1
<i>Klebsiella pneumoniae</i>	16
<i>Proteus mirabilis</i>	3
<i>Pseudomonas aeruginosa</i>	16
<i>Serratia marcescens</i>	1
<i>Staphylococcus aureus</i>	2
<i>Streptococcus pneumoniae</i>	15

# Highly characterized clinical isolates – authentication

- The clinical isolates were screened against a panel of antimicrobial compounds
- Genomes of the strains are available on the **ATCC<sup>®</sup> Genome Portal (genomes.atcc.org)**
- CoA lists the sequence for target genes based upon phenotypic profile



Modified from Uddin TM, et al. J Infect Public Health 14(12): 1750-1766, 2021. PubMed: 34756812



# Challenge: Need for materials to allow for actionable results

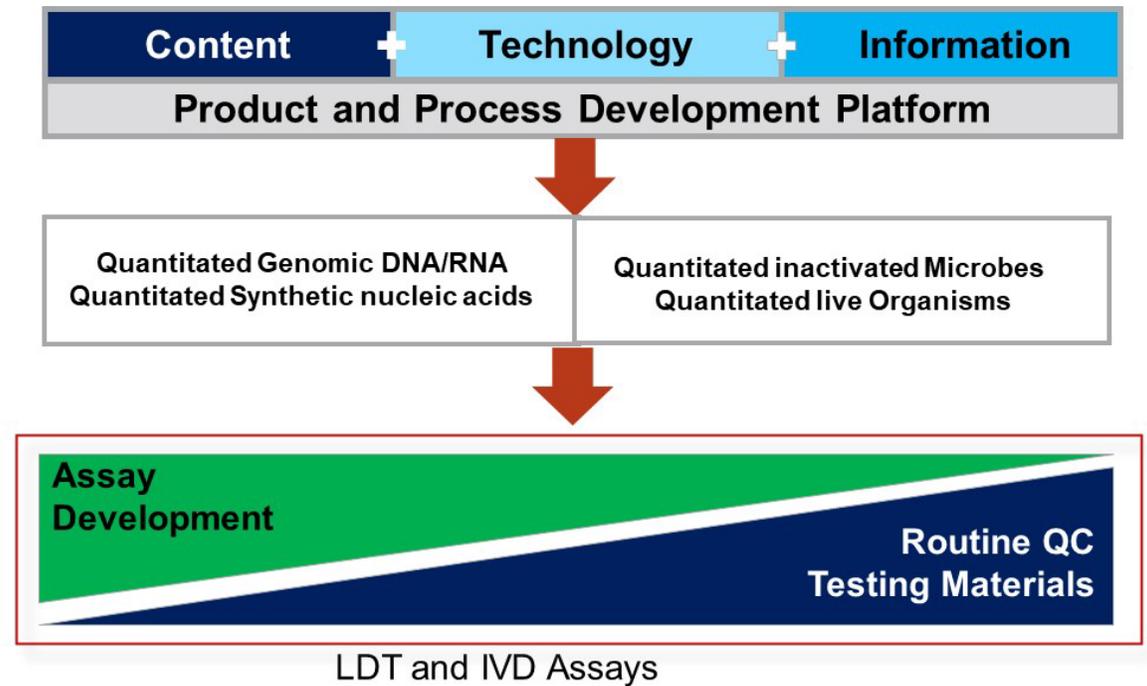
## Agent identification

### Materials for assay development

- What:
  - Large panels of pathogens
  - Genomic and synthetic nucleic acids
  - Inactivated organisms
- Why: Used to determine the limit of detection and the inclusivity and exclusivity of assays

### Materials for routine QC

- What:
  - Small panel of well-authenticated pathogens
  - Positive and negative controls
- Why: Routine testing of assays to demonstrate performance



# ATCC®'s quantified genomic nucleic acids

- ATCC® has a portfolio of quantitated nucleic acid standards

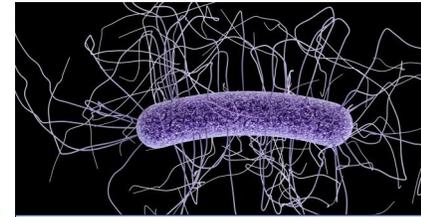
- Blood-borne disease pathogens
- Gastro-intestinal disease pathogens
- Respiratory disease pathogens
- Sexually transmitted disease pathogens
- Vector-borne disease pathogens

- Product requirements:

- Concentration:  $1 \times 10^5 - 1 \times 10^6$  genome copies/ $\mu\text{L}$
- Volume: 100  $\mu\text{L}$ /vial
- Format: Frozen
- Stability: 5 years

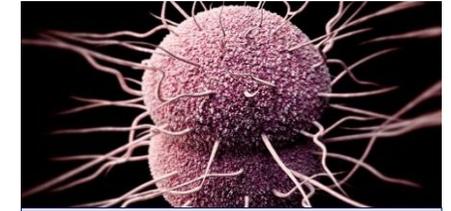
- Authentication

- Identity: Amplicon sequencing
- Integrity: High-molecular-weight DNA by gel electrophoresis



- Astrovirus
- Cyclospora cayetanensis*
- Hepatitis A and E viruses
- Norovirus GI and GII
- Sapovirus
- Mycobacterium avium* subsp. *paratuberculosis*
- Clostridioides difficile*
- Salmonella enterica* subsp. *enterica* serovar Typhimurium
- Cryptosporidium parvum*
- Human Enterovirus 71
- Rotavirus A
- Dientamoeba fragilis*
- Babesia canis*
- Giardia lamblia*
- Murine norovirus
- Legionella pneumophila* subsp. *pneumophila*
- Human enterovirus 71 strain H
- Entamoeba histolytica*
- Escherichia coli*

**Gastro-intestinal  
disease**



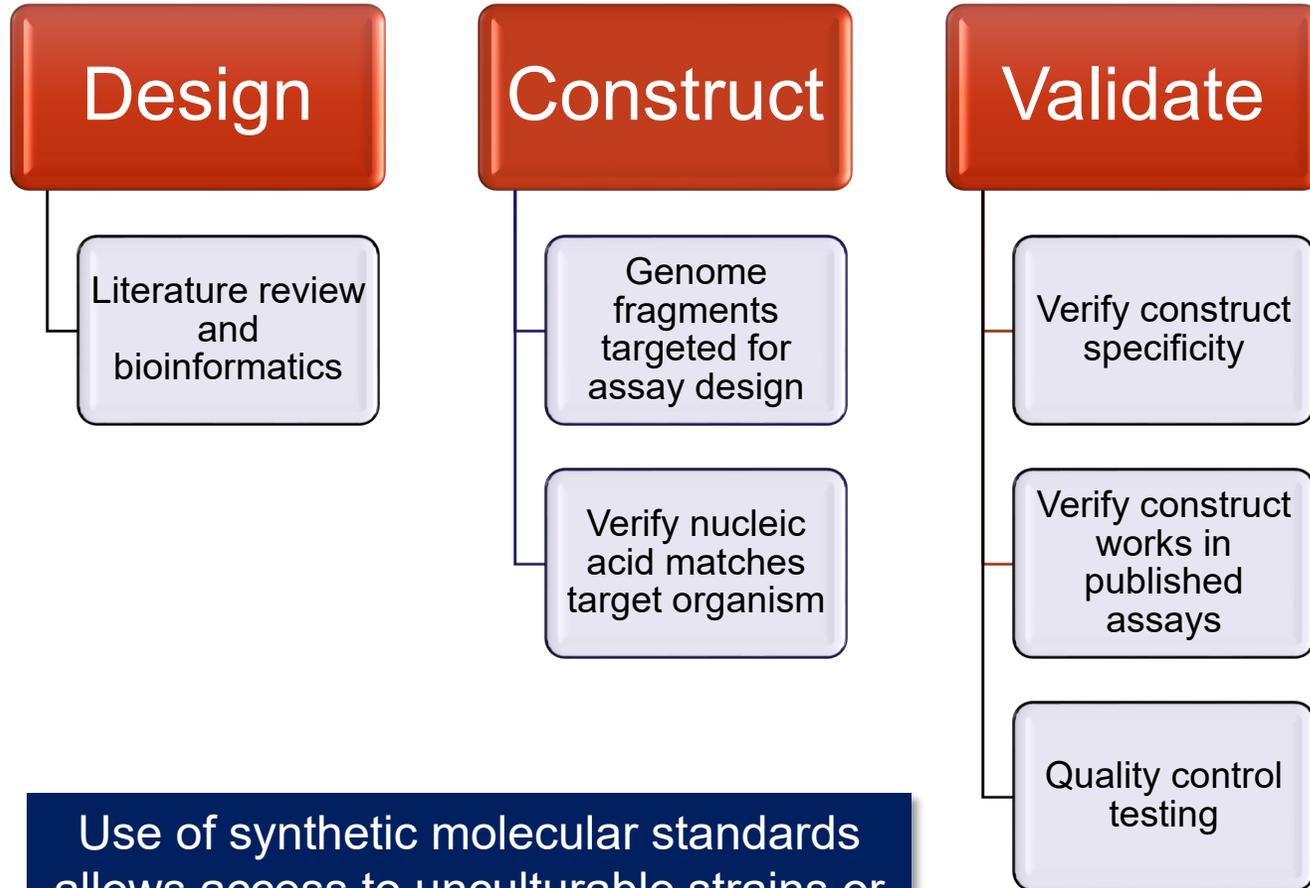
- Neisseria gonorrhoeae*
- Human immunodeficiency virus 1
- Human papillomavirus 16
- Human papillomavirus 18
- Human papillomavirus 31
- Human T-cell leukemia virus 2
- Treponema pallidum*
- Chlamydia trachomatis* LGV I
- Chlamydia trachomatis* LGV II
- Chlamydia trachomatis* LGV III
- Human herpesvirus 1
- Human herpesvirus 2
- Hepatitis B virus
- Human herpesvirus 8
- Human herpesvirus 7
- Human herpesvirus 6
- Mycoplasma genitalium*
- Staphylococcus saprophyticus*
- Haemophilus ducreyi*

**Sexually  
transmitted disease**

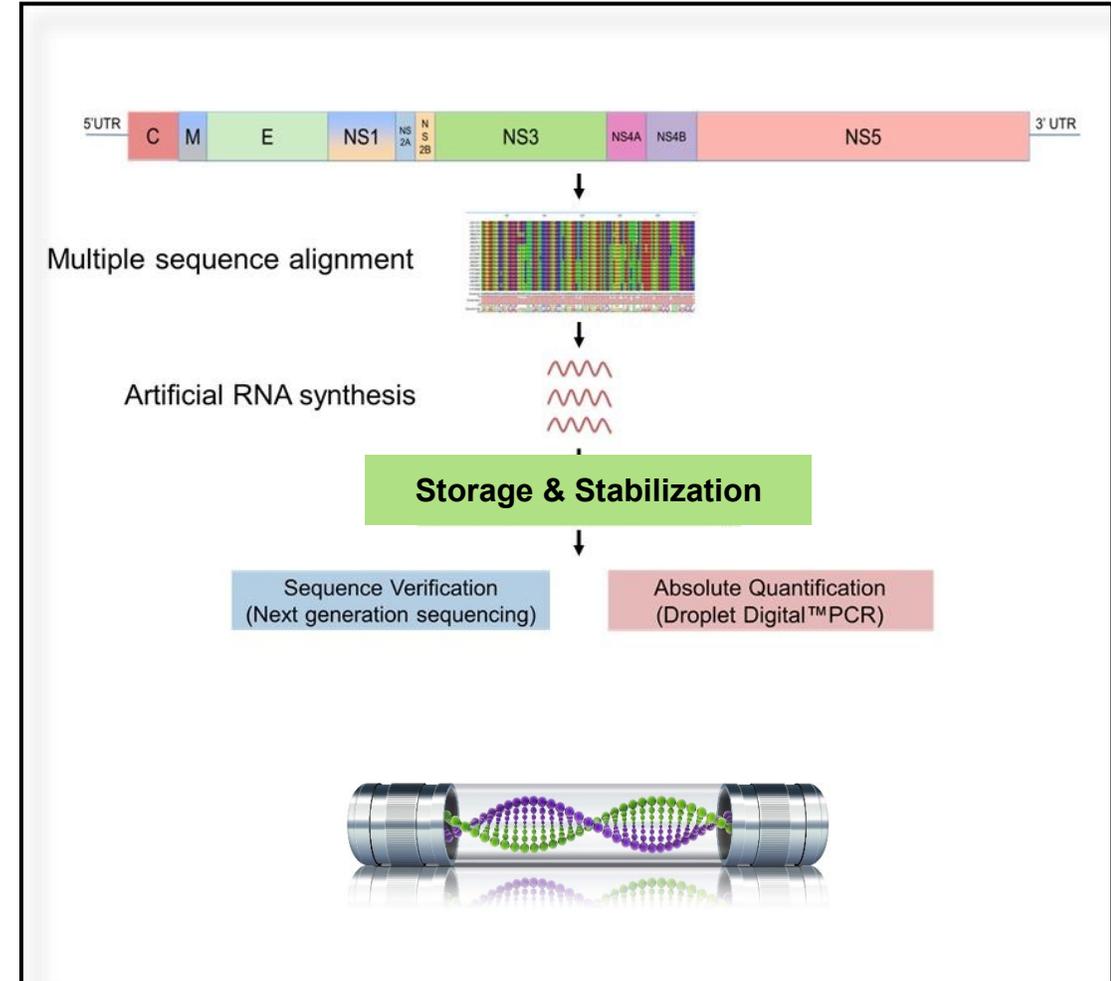
Find out  
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# Synthetic standards allow for access to materials that are unculturable or inaccessible



Use of synthetic molecular standards allows access to unculturable strains or downgrading of BSL level



# ATCC® has a portfolio of synthetic nucleic acid standards

- ATCC® has a panel of synthetic molecular standards
  - 8 Bacteria
  - 1 Fungi
  - 8 Protozoa
  - 50 Viral
- Product requirements:
  - Concentration:  $1 \times 10^5 - 1 \times 10^6$  genome copies/ $\mu\text{L}$
  - Volume: 100  $\mu\text{L}$ /vial
  - Format: Frozen
  - Stability: Accelerated stability for 5 years
- Authentication
  - Identity: NGS to verify synthetic sequence
  - Function: qPCR 3.32 cycles between Cq threshold
  - Integrity: High-molecular-weight DNA by gel electrophoresis

Find out  
More



African swine fever  
Astrovirus  
Avian paramyxovirus  
Boca virus  
BK virus  
Bourbon virus  
Chikungunya  
Dengue virus\*  
Eastern equine encephalitis  
Hepatitis A  
Norovirus\*  
Human metapneumovirus  
Sapovirus  
SARS-CoV2  
HIV\*  
Human Herpes virus\*  
Hepatitis\*  
Human papillomavirus  
Human parechovirus 3  
MERS  
Murine norovirus  
Parvovirus\*  
Powassan virus\*  
St Louis encephalitis  
T-cell leukemia virus  
West Nile virus  
Yellow fever virus  
Zika virus

## Viruses

\* Multiple standards

*Pneumocystis jirovecii*

## Fungi

*Babesia canis*  
*Cryptosporidium hominis*  
*Cyclospora cayetanensis*  
*Dientamoeba fragilis*  
*Giardia lamblia*  
*Plasmodium malariae*  
*Plasmodium vivax*  
*Trypanosoma cruzi*

## Protozoa

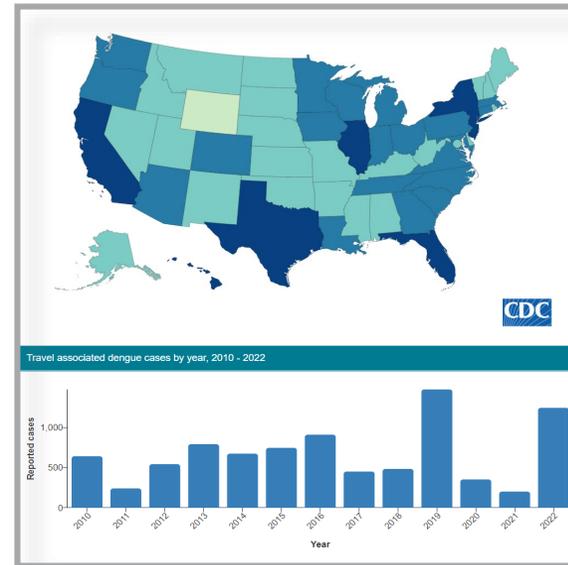
*Chlamydia trachomatis* I  
*Chlamydia trachomatis* II  
*Chlamydia trachomatis* III  
*Treponema pallidum*  
*Coxiella burnetii*  
*Mycoplasma leprae*  
*Mycoplasma genitalium*  
*Ureaplasma urealyticum*

## Bacteria

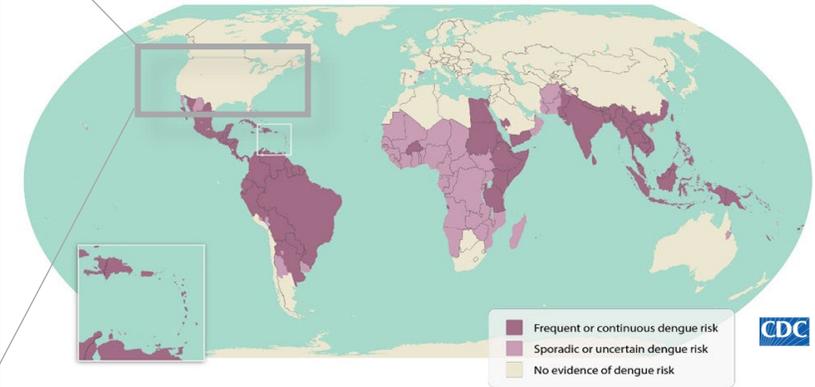


# Case study: Development of a synthetic for Dengue virus

- Viral infection caused by Dengue virus, which is transmitted by *Aedes aegypti* mosquitoes
- Half the world's population now at risk with 100-400 million infections/year
- People can be infected with dengue multiple times



CDC. Dengue - Historic Data (2012-2022). Accessed online <https://www.cdc.gov/dengue/statistics-maps/historic-data.html>



CDC. Dengue - Dengue around the world. Accessed online <https://www.cdc.gov/dengue/areaswithrisk/around-the-world.html>



*Aedes aegypti* mosquitoes spread dengue to people through bites

**REUTERS**

## Dengue will 'take off' in southern Europe, US, Africa this decade, WHO scientist says

Jennifer Rigby  
October 6, 2023 · 3 min read

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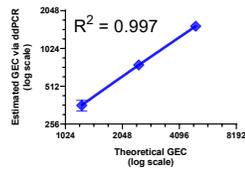
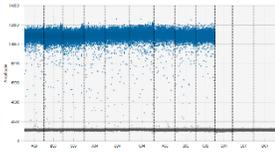
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### Spike in dengue cases due to global warming, warns WHO

# Dengue virus synthetic control development

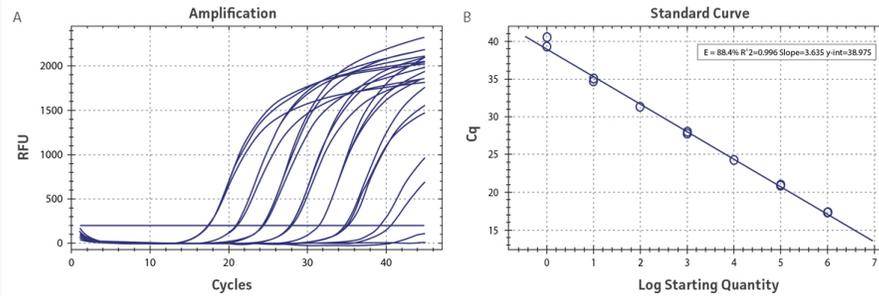
## Product Manufacturing

### Quantification via ddPCR™



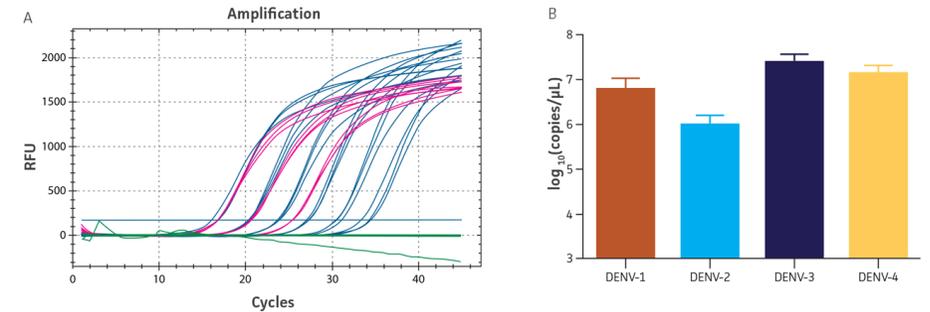
## Product Utility and Performance Assessment

### Assay compatibility



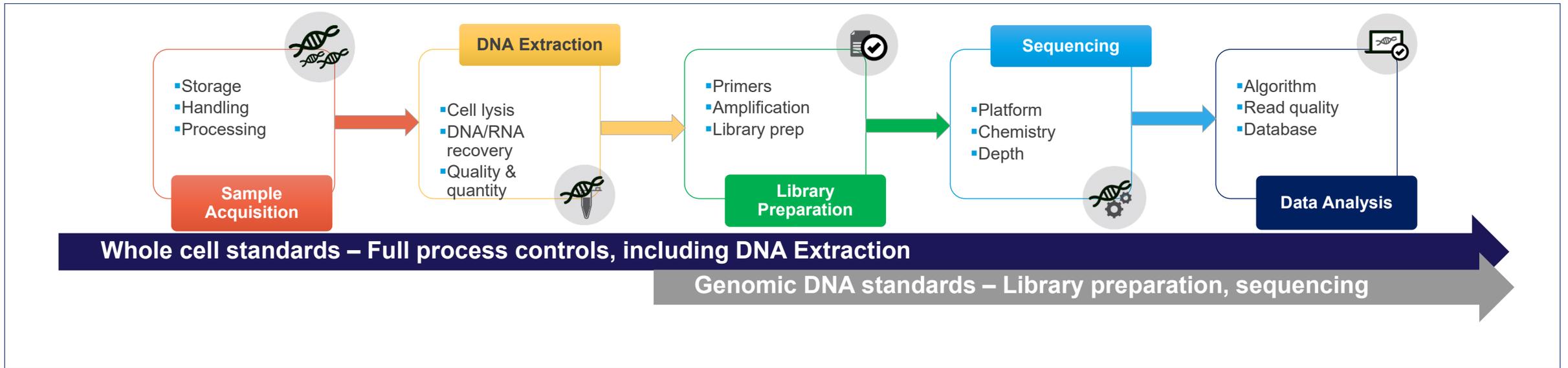
Assays	Feat.	DENV-1	DENV-2	DENV-3	DENV-4
CDC	Slope	-3.2	-3.3	-3.3	-3.6
	R <sup>2</sup>	0.99	1.00	0.99	1.00
Published	Slope	-3.5	-3.5	-3.7	-3.8
	R <sup>2</sup>	0.99	1.00	0.99	1.00

### Dengue virus titration via qPCR using synthetic controls



ATCC® No.	Lineage	Live Virus
VR-3228SD™	<b>DENV-1</b>	TH-S-man (ATCC® VR-1586™)
VR-3229SD™	<b>DENV-2</b>	New Guinea C (NR-84, BEI Resources)
VR-3230SD™	<b>DENV-3</b>	Philippines/H87/1956 (NR-80, BEI Resources)
VR-3231SD™	<b>DENV-4</b>	H241 (ATCC® VR-1257™)

# Next-generation sequencing provides solutions for IVD



## Whole Cell Standards

- Live quantified cultures
- Allow to verify storage and extraction methods



## Genomic DNA Standards

- Extracted genomes/synthetics
- Allow testing of LOD and specificity

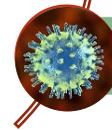
Assay development, optimization, verification, and quality control



**Diversity Panel:** Even and staggered mixtures of whole cells and nucleic acids for assay development and pathogen detection.



**Site specific mixtures:** Oral, skin, vaginal, and gut. 6-12 strain mixture of live and nucleic acids.



**Virome standards:** 6 strain mixture of live and nucleic acids.

Find out More



# Summary

## We offer a range of products to accelerate your microbiology diagnostic assay development & validation projects

- ATCC<sup>®</sup> strains and genomic DNA products offer a robust set of reference standards ideal for the development and validation of molecular assays:
  - Diverse collection of bacterial, fungal and viral cultures
  - Genomic DNA standards are ready-to-use reference materials eliminating additional costs and time required for cell line expansion, DNA extraction, and quantitation.
  - Synthetic standards provide controls for organisms that are difficult to culture or extract
  - NGS standards of whole cell and quantitative DNA from organisms in even and staggered mixtures
- What do **YOU** need?
  - ATCC<sup>®</sup> exists as a resource for scientists/pathologists



# Integrating ATCC<sup>®</sup> Biological Materials into Oncology Molecular Diagnostic Workflows

# Current state of oncology molecular test biomarkers

## Well-established biomarkers

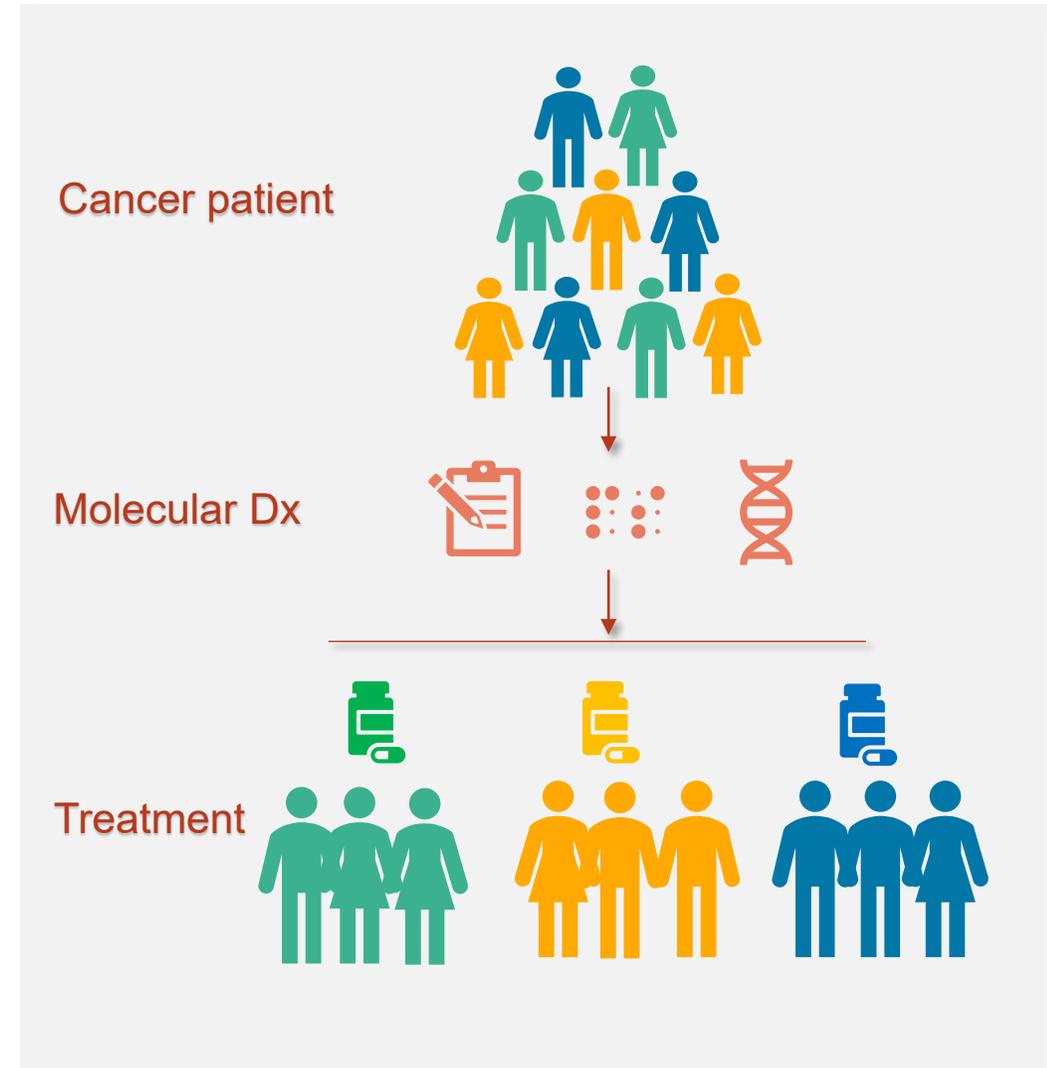
- Approved genetic testing involved a group of genetic tests carried out in patients with specific cancers for a specific therapeutic purpose
- Recommendations from NCCN and FDA
- Biomarker for main cancer types. Examples:
  - Non-small cell lung cancer: ALK, EGFR, ROS1, KRAS, MET, RET
  - Colon and rectal cancers: KRAS/NRAS, BRAF
  - Breast cancer: ER, PR, HER2, BRCA1/2

## Targets of special interest: Immunotherapy

- Programmed death–ligand 1 (PD-L1) expression
- Microsatellite instability and deficient MMR
- Tumor mutation burden—an emerging biomarker

## Other new biomarkers in Research

- NTRK and Entrectinib
- CDK4/CDK6 and Palbociclib
- FGFR and Erdafitinib
- DDR2 and Dasatinib
- MET and Crizotinib
- mTOR and Sapanisertib
- PIK3CA and Taselisib



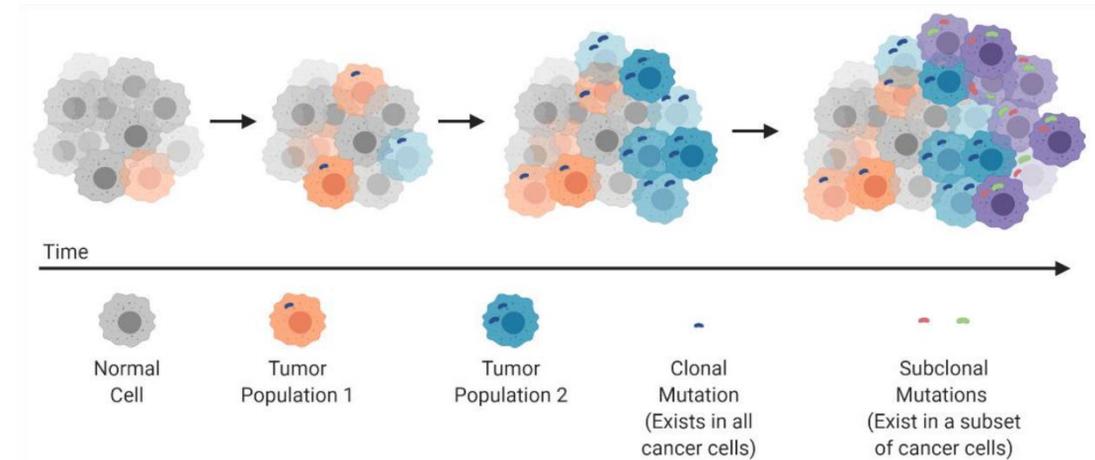
# Challenges in oncology molecular profiling

## ■ Tumor heterogeneity

- Each person's cancer has a unique combination of genetic changes

## ■ Platform heterogeneity

- Various commercial platforms for molecular profiling
- Each test has its own sensitivity and specificity
- Technology is continuously evolving
- Variant calling in NGS data is also evolving



EI- Sayes N, et al. Cancers 13(4): 806, 2021. PubMed: 33671881

Use appropriate controls in your molecular assays to gain confidence in your test results and ensure accuracy and reproducibility of your data

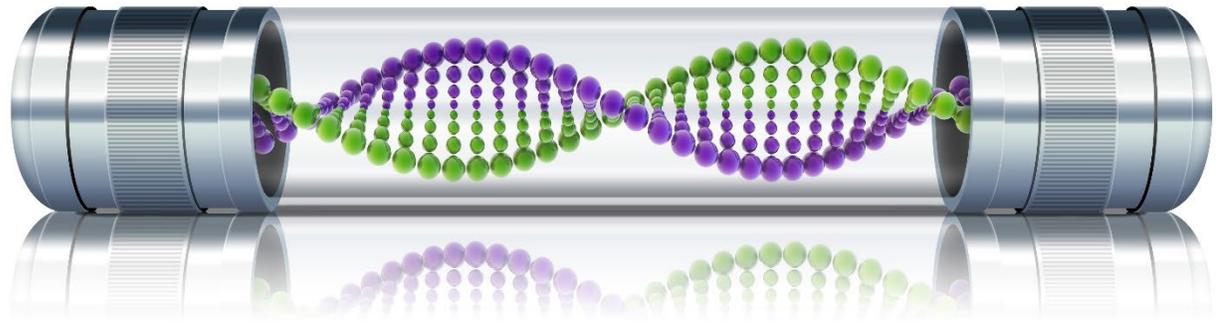
# Use reliable biomaterials as controls

## Types of materials to choose:

Reference Material	Benefit	Disadvantage
Synthetic oligonucleotides	Easy to design and synthesize	Do not resemble complexity of the whole genome
Cell line and cell line genomic DNA	Sustainable source, mimics complexity of the whole genome	Rare mutations are difficult to obtain
Patient biopsy samples	Representative	Not a sustainable source

## Other things to consider:

- Fully authenticated
- Avoid contamination or misidentification
- Characterized genetic alterations
- Stable molecular profiles
- Reproducible results



# Oncology biomarkers in human cancer cell lines

## ATCC® quantified human genomic DNAs

Cell lines from relevant diseases

Quantified biomarker

Mut. allelic freq.

Absolute gene copies

CNV

ATCC® No.	Purified from Cell Line	Disease	Quantified Oncology Bio-marker	Report mutation allelic frequency *	Report absolute gene copies / ng DNA **	Report relative gene copy number **
CRL-1648DQ™	CA46	Burkitt's lymphoma	TP53 R248Q	√	√	√
HTB-30DQ™	SK-BR-3	Breast adenocarcinoma	TP53 p.R175H	√	√	√
HTB-122DQ™	BT-549	Breast ductal carcinoma	TP53 p.R249S	√	√	√
HTB-131DQ™	MDA-MB-453	Breast carcinoma	PIK3CA p.H1047R	√	√	√
CCL-225DQ™	HCT-15	Colon adenocarcinoma	KRAS p.G13D	√	√	√
CCL-227DQ™	SW620	Colon adenocarcinoma	KRAS p.G12V TP53 p.R273H	√	√	√
CCL-231DQ™	SW48	Colon adenocarcinoma	EGFR p.G719S	√	√	√
CL-187DQ™	LS180	Colon adenocarcinoma	KRAS p.G12D	√	√	√
CRL-2158DQ™	LS1034	Colon carcinoma	TP53 p.G245S	√	√	√
CRL-5973DQ™	SNU-5	Stomach undifferentiated adenocarcinoma	MET amplification	–	√	√
CRL-5974DQ™	SNU-16	Stomach undifferentiated adenocarcinoma	MYC amplification	–	√	√
HTB-111DQ™	AN3 CA	Endometrium adenocarcinoma	PTEN p.R130fs	√	√	√
CRL-2868DQ™	HCC827	Lung adenocarcinoma	EGFR p.ELREA746del EGFR amplification	√ –	√	√
CRL-5908DQ™	NCI-H1975	Lung non-small cell carcinoma	EGFR p.T790M; EGFR p.L858R	√	√	√
CRL-2177DQ™	SW 1271	Lung small cell carcinoma	NRAS p.Q61R	√	√	√
CRL-5928DQ™	NCI-H2170	Lung squamous cell carcinoma	HER 2 amplification	–	√	√
CRL-7898DQ™	A101D	Skin malignant melanoma	BRAF p.V600E	√	√	√

## CRM cell lines and DNAs

Stated level of confidence for traceability and values of uncertainty

ATCC® No.	Cell line name	Amino acid change	DNA change
CRM-TIB-161™	HuT 78	WT	WT
CRM-CCL-119™	CCRF-CEM	p.G12D	c.35G>A
CRM-CCL-185™	A549	p.G12S	c.34G>A
CRM-CRL-1420™	MIA PaCa-2	p.G12C	c.34G>T
CRM-HTB-174™	NCI-H441	p.G12V	c.35G>A
CRM-CRL-3211™	PSN1	p.G12R	c.34G>C
CRM-CCL-155™	RPMI 8226	p.G12A	c.35G>C
CRM-HTB-26™	MDA-MB-231	p.G13D	c.38G>A



BRAF, EGFR, ERBB2,  
KRAS, NRAS, MET, MYC,  
PIK3CA, pTEN, TP53

Find out  
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# Batch-specific test results for each production lot

**Example:** ATCC® CRL-5908DQ™ quantitated human gDNA from NCI-H1975 cell line

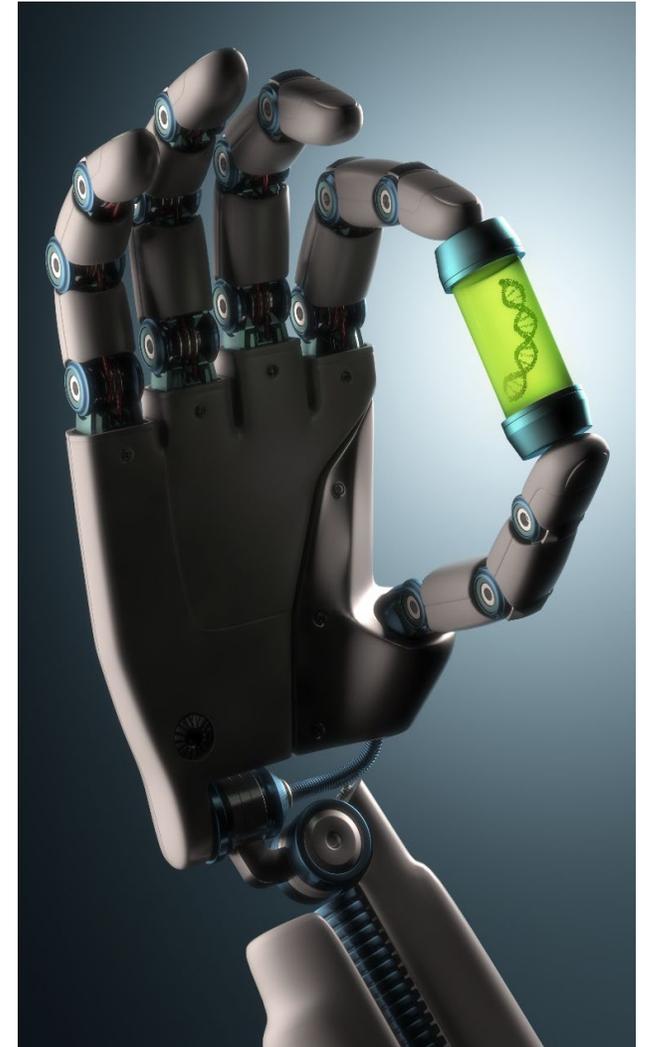
- **Lot:** 64216185
- **Gene:** EGFR
- **Mutation:** EGFR T790M. (Expected DNA change: c.2369C>T.)      Base call: A = 0.0%, C = 33.3%, G = 0.1%, T = 66.6%
- **Mutation:** EGFR L858R. (Expected DNA change: c.2573T>G.)      Base call: A = 0.1%, C = 0.1%, G = 64.2%, T = 35.7%
- **EGFR absolute gene copy number:**  $5.16 \times 10^4$  copies/ $\mu$ L
- **EGFR relative gene copy number (CNV):** 4.7
- **Total DNA amount:** 4.8  $\mu$ g/vial,
- **DNA concentration:** 97 ng/ $\mu$ L
- **Volume per vial:** 49  $\mu$ L/vial

**CoA report result – NGS** (Coverage > 10,000X)

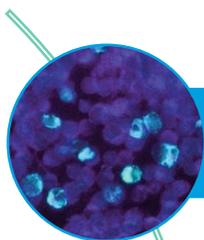
NGS result uncertainty is equal or smaller than  $\pm 5\%$ . The reported uncertainty represents the uncertainty expressed at approximately the 99% confidence level using a coverage factor of k=3.

**CoA report result – ddPCR™** (Average of nine data points)

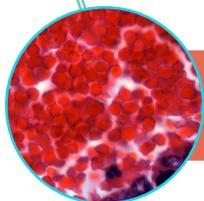
ddPCR™ uncertainty is equal or smaller than  $\pm 25\%$ . The reported uncertainty represents uncertainty expressed at approximately the 99% confidence level using a coverage factor of k=3.



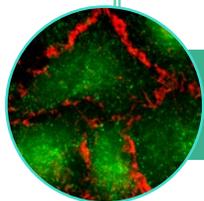
# Tumor/normal matched cell line pairs



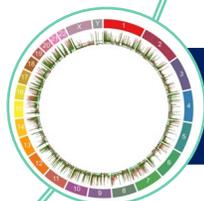
Over 40 pairs of tumor/normal donor matched ATCC® cell lines



Major cancer types: lung, breast, skin, bone cancer



Allows for study on cancer-specific mutations, tumor mutation burden (TMB)



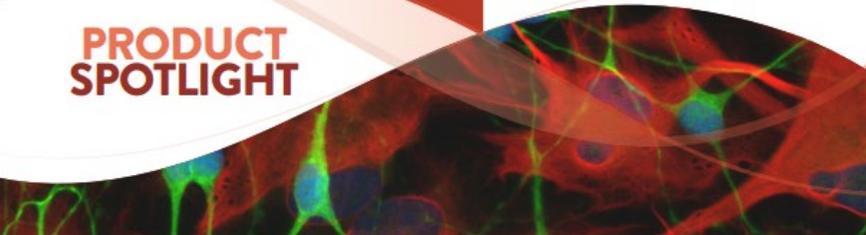
Well-characterized reference cell lines associated with WGS and WES datasets

Find out More





## PRODUCT SPOTLIGHT



### TUMOR/NORMAL MATCHED CELL LINE PAIRS

Tumor-derived cell lines matched to either normal or metastatic cell lines obtained from the same patient provide a valuable resource for cancer studies. The availability of such models allows researchers to analyze cancer-specific mutations, monitor the behavior and chemical sensitivity of tumor lines based on their normal counterparts, and develop drugs or therapies to target specific cancers or cancer mutations.

**Table 1: Tumor and normal cell lines from the same individual**

Cancer type	Tissue source	Name	ATCC® No.	Tissue source	Name	ATCC® No.
<b>Primary site of disease</b>		<b>Normal pairing</b>				
Adenocarcinoma	Lung	NCI-H1395	<a href="#">CRL-5868™</a>	Peripheral Blood	NCI-BL1395	<a href="#">CRL-5957™</a>
Adenocarcinoma	Lung	NCI-H1437	<a href="#">CRL-5872™</a>	Peripheral Blood	NCI-BL1437	<a href="#">CRL-5958™</a>
Adenocarcinoma	Lung	NCI-H2009	<a href="#">CRL-5911™</a>	Peripheral Blood	NCI-BL2009	<a href="#">CRL-5961™</a>
Adenocarcinoma	Lung, lymph node (metastasis)	NCI-H2087	<a href="#">CRL-5922™</a>	Peripheral Blood	NCI-BL2087	<a href="#">CRL-5965™</a>
Adenocarcinoma	Lung, pleural effusion	NCI-H2122	<a href="#">CRL-5985™</a>	Peripheral Blood	NCI-BL2122	<a href="#">CRL-5967™</a>
Basal Cell Carcinoma	Skin	TE 354.T	<a href="#">CRL-7762™</a>	Skin	TE 353.Sk	<a href="#">CRL-7761™</a>
Benign Osteoid Osteoma	Bone	Hs 919.T	<a href="#">CRL-7672™</a>	Skin	Hs 919.Sk	<a href="#">CRL-7671™</a>
Carcinoma	Mammary gland; breast	Hs 605.T	<a href="#">CRL-7365™</a>	Skin	Hs 605.Sk	<a href="#">CRL-7364™</a>
Carcinoma	Mammary gland; breast	Hs 854.T	<a href="#">CRL-7590™</a>	Skin	Hs 854.Sk	<a href="#">CRL-7589™</a>
Ductal Carcinoma	Mammary gland; breast	HCC1008	<a href="#">CRL-2320™</a>	Peripheral Blood	HCC1007.BL	<a href="#">CRL-2319™</a>
Ductal Carcinoma	Mammary gland; breast	HCC1954	<a href="#">CRL-2338™</a>	Peripheral Blood	HCC1954.BL	<a href="#">CRL-2339™</a>
Ductal Carcinoma	Mammary gland; breast	Hs 578T	<a href="#">HTB-126™</a>	Mammary Gland, Breast	Hs 578Bst	<a href="#">HTB-125™</a>
Malignant Melanoma	Skin	COLO 829	<a href="#">CRL-1974™</a>	Peripheral Blood	COLO 829BL	<a href="#">CRL-1980™</a>
Melanoma	Skin	Hs 895.T	<a href="#">CRL-7637™</a>	Skin	Hs 895.Sk	<a href="#">CRL-7636™</a>
Mesothelioma	Lung, pleural effusion	NCI-H2052	<a href="#">CRL-5915™</a>	Peripheral Blood	NCI-BL2052	<a href="#">CRL-5963™</a>
Neuroendocrine Carcinoma	Lung, pleural effusion	NCI-H1770	<a href="#">CRL-5893™</a>	Peripheral Blood	NCI-BL1770	<a href="#">CRL-5960™</a>
Osteosarcoma	Bone	Hs 704.T	<a href="#">CRL-7444™</a>	Skin	Hs 704.Sk	<a href="#">CRL-7443™</a>
Osteosarcoma	Bone	Hs 707(A).T	<a href="#">CRL-7448™</a>	Skin	Hs 707(B).Ep	<a href="#">CRL-7449™</a>
Osteosarcoma	Bone	Hs 888.T	<a href="#">CRL-7622™</a>	Lung	Hs 888.Lu	<a href="#">CCL-211™</a>
Osteosarcoma	Bone	Hs 889.T	<a href="#">CRL-7626™</a>	Skin	Hs 889.Sk	<a href="#">CRL-7625™</a>
Osteosarcoma	Bone	Hs 890.T	<a href="#">CRL-7628™</a>	Skin	Hs 890.Sk	<a href="#">CRL-7627™</a>
Pagetoid Sarcoma	Skin	Hs 925.T	<a href="#">CRL-7677™</a>	Skin	Hs 925.Sk	<a href="#">CRL-7676™</a>
Primary Ductal Carcinoma	Mammary gland; breast	HCC38	<a href="#">CRL-2314™</a>	Peripheral Blood	HCC38.BL	<a href="#">CRL-2346™</a>
Primary Ductal Carcinoma	Mammary gland; breast	HCC1143	<a href="#">CRL-2321™</a>	Peripheral Blood	HCC1143.BL	<a href="#">CRL-2362™</a>


ATCC | Credible leads to Incredible®

Page 1

# HCC1395 and HCC1395BL reference cell lines

www.nature.com/scientificdata

## scientific data

OPEN

DATA DESCRIPTOR

### Whole genome and exome sequencing reference datasets from a multi-center and cross-platform benchmark study

Yongmei Zhao *et al.*<sup>#</sup>

With the rapid advancement of sequencing technologies, next generation sequencing (NGS) analysis has been widely applied in cancer genomics research. More recently, NGS has been adopted in clinical oncology to advance personalized medicine. Clinical applications of precision oncology require accurate tests that can distinguish tumor-specific mutations from artifacts introduced during NGS processes or data analysis. Therefore, there is an

Check for updates

Whole-genome (WGS) and whole-exome sequencing (WES) data sets generated through the SEQC2 consortium project, which is an FDA-led consortium for advancing the quality control of targeted next-generation sequencing assays for precision oncology.

Reference sample	Sample type	Platform	Data set
 Normal cell line HCC1395BL	Fresh DNA	WGS <ul style="list-style-type: none"> <li>• Hi Seq</li> <li>• NovaSeq</li> <li>• PacBio</li> <li>• 10X Genomics</li> </ul> WES <ul style="list-style-type: none"> <li>• HiSeq</li> <li>• Ion Torrent</li> </ul> AmpliSeq <ul style="list-style-type: none"> <li>• MiSeq</li> </ul> Microarray <ul style="list-style-type: none"> <li>• Affymetrix CytoScan</li> </ul>	Reproducibility: <ul style="list-style-type: none"> <li>• Intra-center WGS</li> <li>• Inter-center WGS</li> <li>• Cross-platform</li> </ul> Library preparation: <ul style="list-style-type: none"> <li>• Library kit</li> <li>• DNA input amount</li> </ul> Validation <ul style="list-style-type: none"> <li>• Confirmation</li> <li>• Specificity</li> <li>• Sensitivity</li> </ul>
	FFPE DNA Mixture DNA	WGS <ul style="list-style-type: none"> <li>• HiSeq</li> </ul> WES <ul style="list-style-type: none"> <li>• HiSeq</li> </ul>	FFPE process: <ul style="list-style-type: none"> <li>• Fixing time: 1h, 2h, 6h, 24h</li> <li>• DNA damage</li> </ul> Tumor purity: <ul style="list-style-type: none"> <li>• 75%, 50%, 20%, 10%, 5%</li> </ul>
	Fresh cells	scCNV <ul style="list-style-type: none"> <li>• 10X Genomics</li> </ul>	Number of cells: <ul style="list-style-type: none"> <li>• HCC1395BL: 983</li> <li>• HCC1395: 1465</li> </ul>

Zhao Y, et al. Sci Data 8(1): 293, 2021. PubMed: 34753956

# Predictive immunotherapy biomarkers

*Cancer immunotherapy has revolutionized the field of oncology*

Predictive immunotherapy biomarkers are already established as routine testing

- Programmed death ligand-1 (PD-L1)
- Mismatch repair (MMR) and microsatellite instability (MSI)
- Tumor mutational burden (TMB) is emerging

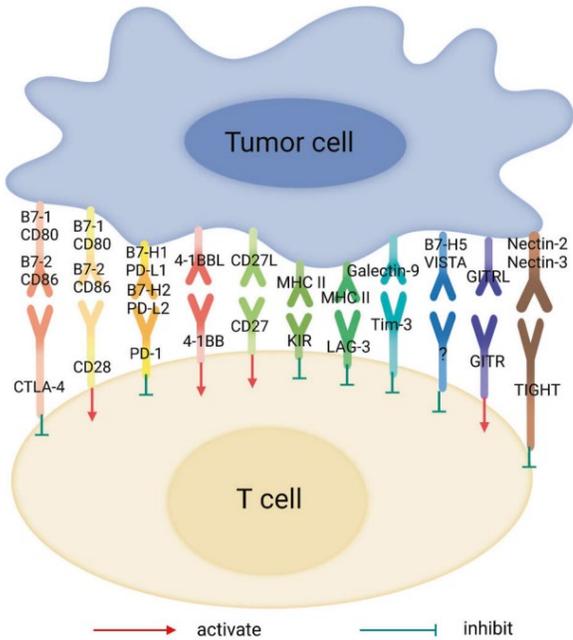
Several challenges still to be overcome in the diagnostic setting

- PD-L1 heterogeneity (intra- and intertumoral)
- MSI - requires normal tissue comparison from the same individual, accurate data interpretation
- TMB - technical/analytic burden, lack of standardized methods and controls for TMB calculation

A need for established, fully characterized, globally accepted reference materials

# IO checkpoint profiling of ATCC® cancer cell lines

Immune checkpoint inhibitors and their receptors



Wang DR, et al. Signal Transduct Target Ther 7(1): 331, 2022. PubMed: 36123348

Comprehensive checkpoint molecular profiling (Ex. PD-L1) in many ATCC® cancer cell lines

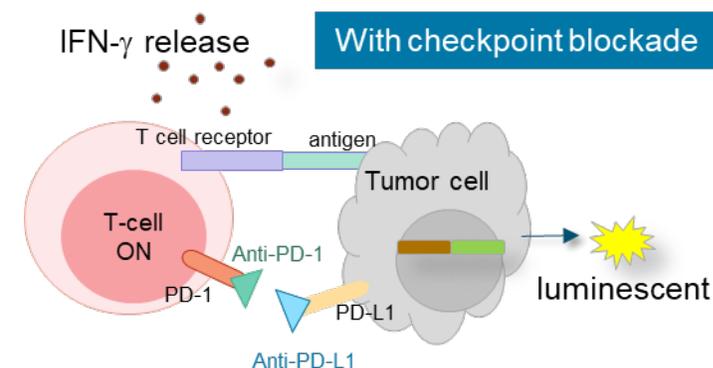
PD-L1

Cancer type	Cell lines	ATCC® catalog #	HLA typing		Inhibitory checkpoint molecule ligands										Co-stimulatory checkpoint molecule ligands										
			HLA class I	HLA class II	PD-L1 -	PD-L1 +	PD-L2 -	PD-L2 +	B7-H3 -	B7-H3 +	B7-H4 -	B7-H4 +	HVEM -	HVEM +	4-1BBL -	4-1BBL +	ICOS-L -	ICOS-L +	CD155 -	CD155 +	CD80 -	CD80 +	CD86 -	CD86 +	
Bladder cancer	5637	HTB-9™	+	-	52096	143325	49	2594	60004	52945	0	0	1593	1783	3085	2831	1322	1464	68780	85293	2092	3069	1909	1993	
	HT-1197	CRL-1473™	+	-	40740	45361	1368	6891.5	21853	16451	0	0	1785	2838	0	1852	1682	1837	105114	127213	4220	6126	2120	2878	
	HT-1376	CRL-1472™	+	-	27135	51493	1692	8578	74668	66185	0	0	365	1790	0	0	3440	6322	36478	44828	4293	4179	1233	1707	
	RT4	HTB-2™	+	-	0	5054	52	518	143148	139442	0	42	717	1602	2395	2961.5	5676	7754	40953	48452	883	1097	1482	1954	
	TCCSUP	HTB-5™	+	+	30543	48394	4325	9664	131058	123270	930	822	526	1422	3016	3758	315	366	271088	282653	3912	3573	3917	3933	
Brain cancer	SK-N-BE(2)	CRL-2271™	+	-	245	6837	0	258	15903	17884	156	123	262	237	626	528	228	240	5236	6395	452	350	923	778	
	U-87 MG	HTB-14™	+	-	321	2990	249	246	73474	72722	338	263	4718	3312	2804	3010	339	454	30877	33809	2926	2597	2080	1968	
	U-87 MG-Luc2	HTB-14-LUC2™	+	-	15061	40367	0	0	29967	29009	1508	1374	487	706	1717	1370	141	219	36063	43417	1851	1491	984	753	
Breast cancer	AU565	CRL-2351™	+	-	2428	11013	0	0	9476	8169	3514	2925	307	831	1289	841	633	856	37017	35953	983	1027	433	454	
	BT-20	HTB-19™	+	-	6082	17072	886	4614	44830	44507	711	761	0	0	7297	8831	300	136	203815	235198	8916	9398	1172	1244	
	DU4475	HTB-123™	+	-	1912	3232	1082	3774	59238	54996	1941	1317	4014	4293	8298	6525	0	0	36382	32343	8865	6426	2523	1278	
	HCC38	CRL-2314™	+	-	13009	126059	3097	16705	220234	208819	2300	1565	6396	7267	1912	3050	1525	1855	132767	134741	5751	4437	2143	1906	
	MCF7	HTB-22™	+	-	53	1802	0	0	46613	42793	4324	2944	2197	1972	4821	4165	1583	2402	23280	22977	5720	4584	2867	2424	
	MCF7-Luc2	HTB-22-LUC2™	+	-	0	3116	0	0	2793	56518	53829	575	936	1331	1723	3902	5935	465	1037	20258	22678	1724	5297	1215	2149
	MDA-MB-231	HTB-26™	+	-	11359	20492	986	1880	12979	11668	149	125	456	1031	531	777	14	37	38583	53188	563	428	346	234	
MDA-MB-468	HTB-132™	+	-	221	5046	115	380	16180	16342	806	575	140	438	740	769	401	747	36560	43422	475	464	308	290		
Bone cancer	T-47D	HTB-133™	+	-	72	6355	0	0	32581	24851	828	594	597	703	3140	1990	859	683	39364	37651	3038	2166	1620	1325	
	HOS	CRL-1543™	-	+	13031	41473	2927	9075	60530	61277	289	305	211	552	1127	1210	0	0	99713	124829	841	815	443	400	
	MG-63	CRL-1427™	-	+	0	7362	0	0	84745	79181	443	819	368	730	4326	4901	0	0	303805	268365	2894	6552	1339	2968	
	Saos-2	HTB-85™	+	-	6082	32705	0	0	7455	7136	332	239	897	1244	2525	1975	0	0	58992	70813	1726	1733	1644	1525	
Colon cancer	U-2 OS	HTB-96™	+	-	5929	36019	290	5915	63080	64082	548	333	830	1152	2321	2660	784	778	112962	124648	2554	1174	3008	3045	
	Caco-2 [Caco2]	HTB-37™	+	-	0	471	0	0	32201	30175	1315	1209	1900	1817	4255	5817	1060	661	44423	39942	6756	4849	4146	3170	
	HCT-15	CCL-225™	-	+	474	3790	35	0	12896	12520	137	94	513	947	369	251	0	21	33045	34475	411	140	441	335	
Head & Neck cancer	LoVo	CCL-229™	-	+	468	17697	0	0	20338	19572	347	346	975	2481	1581	1647	775	1080	24870	36144	903	1271	1044	1010	
	A-253	HTB-41™	+	-	2070	16019	123	3176	43926	41341	18	0	45	477	1431	2558	3380	3887	67935	83057	3303	3051	731	985	
	FaDu	HTB-43™	+	-	2733	37007	205	13372	39475	31090	0	0	138	855	1640	0	3643	4161	60462	62858	2728	2720	1904	1951	
Liver cancer	FaDu-Luc2	HTB-43-LUC2™	+	-	6965	29601	0	0	24921	20048	269	333	421	448	1159	1591	484	557	35527	40460	1019	1334	2147	2183	
	C3A [HepG2/C3A]	CRL-10741™	+	-	0	2114	0	2698	18098	16938	441	453	1362	2682	1243	2171	394	511	54751	59271	1079	1914	1136	1100	
	SK-HEP-1	HTB-52™	+	-	2428	11013	0	0	9476	8169	3514	2925	307	831	1289	841	633	856	37017	35953	983	1027	433	454	
Lung cancer	A549	CCL-185™	+	-	1512	9611	0	2476	34719	33139	0	0	764	752	943	1345	2547	3209	87047	88786	719	1227	810	1078	
	Calu-1	HTB-54™	+	-	53834	114947	3528	10080	18438	19072	588	604	921	2119	2993	3444	0	0	94510	114947	3240	3268	1210	1254	
	NCI-H1650 [H-1650, H1650]	CRL-5883™	+	-	3491	15369	1050	5615	127539	134041	1738	1422	263	476	8605	9501	0	0	353964	391949	9642	7584	1455	916	
	NCI-H226 [H226]	CRL-5826™	-	+	49391	145367	10744	24379	73920	101793	640	767	0	672	2378	2758	3006	2629	136158	229665	2143	2477	1202	897	
	NCI-H441 [H441]	HTB-174™	+	-	13424	34487	359	1782	34363	32832	887	1044	383	829	2762	2540	246	260	59151	73580	2841	3133	3440	3250	
	NCI-H460 [H460]	HTB-177™	+	-	7193	19574	921	2778	55359	49738	885	1089	0	742	2375	3040	189	615	78046	86814	2342	3040	3792	3223	
	HCC827	CRL-2868™	+	-	9795	60468	3725	8478	41249	47178	1817	1721	879	0	3726	3399	162	0	58497	105562	5176	7123	2222	1917	
	NCI-H1299	CRL-5803™	+	-	278	3436.5	0	92	37817	36030	0	0	0	0	2768	3391	2961	4373	196936	184904	3765	3790	909	662	
	NCI-H1975 [H-1975, H1975]	CRL-5908™	+	-	2483	23447	490	4677	70851	62007	0	0	368	1729	227	208	535	1455	168919	175547	3665	4409	1160	1412	
	NCI-H596 [H596]	HTB-178™	+	-	18669	40780	1275	3245	84320	77592	0	0	0	275	0	0	3410.6	3890	255616	311989	5243	2880	1349	1078	
Melanoma	A-375 [A375]	CRL-1619™	+	-	1255	27782	0	433	52580	40341	0	0	566	1127	0	0	755	544	30126	37903	3133	2863	1237	1077	
	A375-KRAS	CRL-1619G-1™	+	-	40740	45361	1368	6891.5	21853	16451	0	0	1785	2838	0	1852	1682	1837	105114	127213	4220	6126	2120	2878	
	A375-KRAS-Luc2	RL-1619G-1-LUC2™	+	-	109294	117180	0	966	12826	13191	735	816	0	60	3526	3450	0	0	128469	160467	4777	5130	1723	1784	
	RPMI-7951	HTB-66™	+	-	10229	26724	2662	8763	65180	80081	0	0	523	1646	0	0	1930	1297	66083	91229	883	1097	1482	1954	
	SH-4	CRL-7724™	+	-	1291	12124	0	0	54016	44759	0	68	2556	3350	108	2006	1142	760	66235	65168	3429	4481	932	1507	
Ovarian cancer	SK-MEL-24	HTB-71™	-	+	400	17538	1000.5	750	26932	17137	27	60	236	1187	2903	3177	6613	5316	45197	75332	888	826	2945	2605	
	ES-2	CRL-1978™	+	-	57764	89033	718	5906	11970	11255	405	390	1161	1368	2730	1971	188	0	92087	122142	1453	1620	3210	3510	
	AsPC-1	CRL-1682™	-	+	0	6325	155	2800	28044	26743	297	397	1147	2666	1415	1444	310	546	32180	49052	825	1290	3033	3095	
Pancreas cancer	PANC-1	CRL-1469™	+	-	1049	0	0	0	20419	21694	421	473	1276	976	2031	2093	331	196	33618	34518	2265	2625			

# Immuno-oncology luciferase reporter cells

## Checkpoint Luciferase Reporter Cells

Designation	ATCC® No.	Disease	Biomarker	Tissue of origin
HCC827-GAS-Luc2	<a href="#">CRL-2868-GAS-LUC2™</a>	Adenocarcinoma	PD-L1	Lung
MG-63-GAS-Luc2	<a href="#">CRL-1427-GAS-LUC2™</a>	Osteosarcoma	CD-155	Bone
NCI-H1650-GAS-Luc2	<a href="#">CRL-5883-GAS-LUC2™</a>	Adenocarcinoma	B7-H3	Lung
SUP-T1 [VB]-NFAT-Luc2	<a href="#">CRL-1942-NFAT-LUC2™</a>	Lymphoblastic Lymphoma	PD-1	Pleural effusion

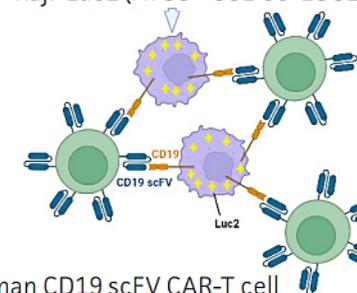


## CAR-T Target Luciferase Reporter Cell Lines

Designation	ATCC® No.	Disease	Target
WIL2-S-Luc2	<a href="#">CRL-8885-LUC2™</a>	B Cell Lymphoma	CD19
Raji-Luc2	<a href="#">CCL-86-LUC2™</a>	Burkitt's Lymphoma	CD19
Daudi-Luc2	<a href="#">CCL-213-LUC2™</a>	Burkitt's Lymphoma	CD20
Farage-Luc2	<a href="#">CRL-2630-LUC2™</a>	Non-Hodgkin's B Cell Lymphoma	CD20
BT-474-Luc2	<a href="#">HTB-20-LUC2™</a>	Breast Ductal Carcinoma	HER2

### CHIMERIC ANTIGEN RECEPTOR

WIL2-S-Luc2 (ATCC® CRL-8885-LUC2™) or  
Raji-Luc2 (ATCC® CCL-86-LUC2™)



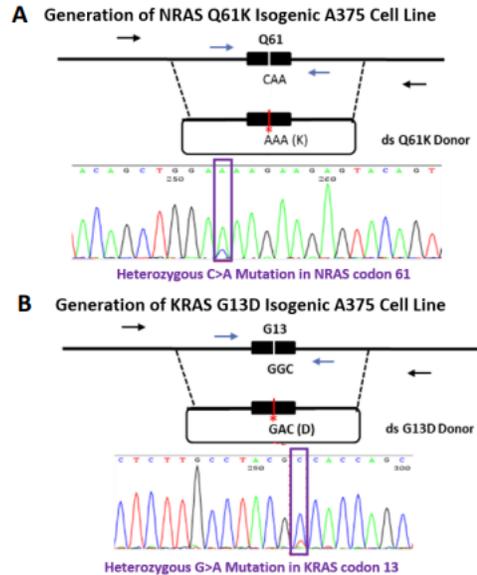
Find out  
More



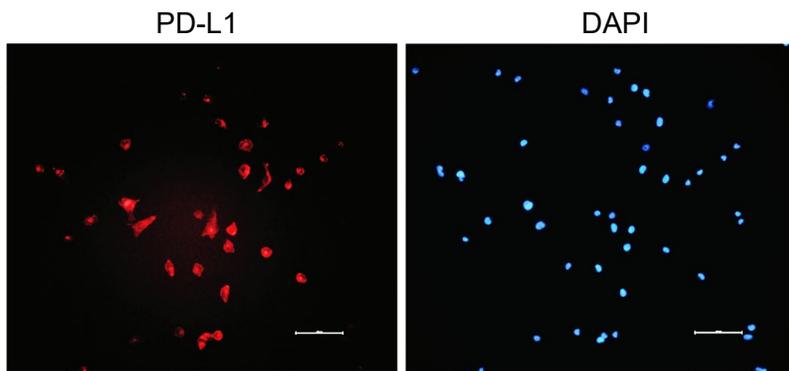
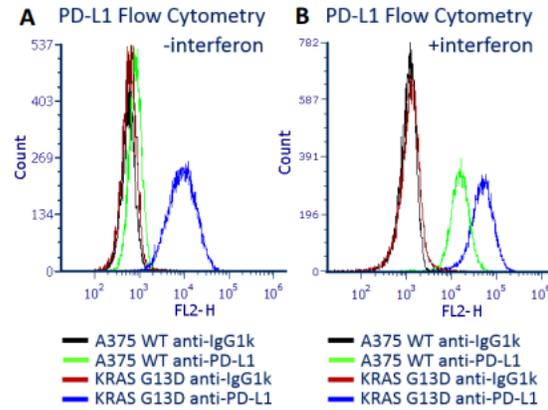
# PD-L1 high expression cell line: ATCC® CRL-1619IG-1™

**KRAS G13D A375 cell line**  
**ATCC® CRL-1619IG-1™**

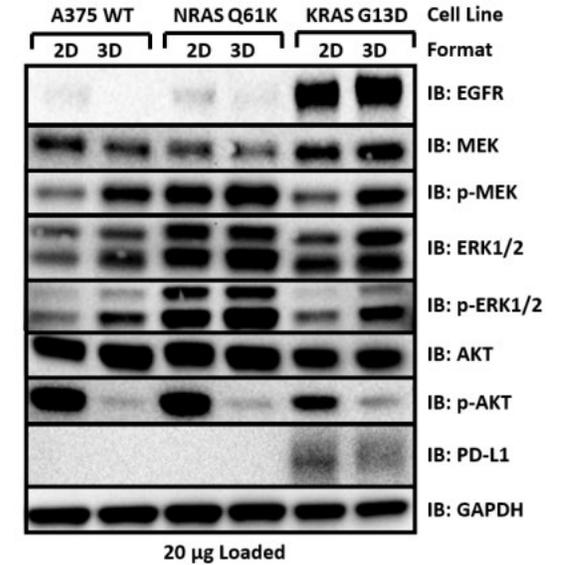
## CRISPR Editing Strategy and Sequencing of NRAS Q61K and KRAS G13D Isogenic Lines



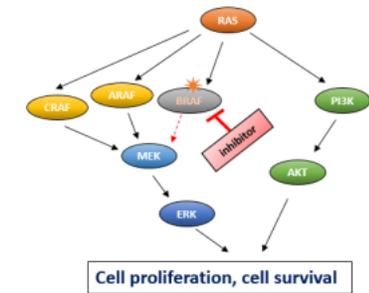
## Effect of KRAS G13D Mutation on Basal PD-L1 Expression in A375 Cells



## Impact of 3D Culture Format on RAS-RAF-MAPK Signaling in A375 Isogenic RAS Mutant Lines



## RAS-mediated Resistance to BRAF Inhibitor in Melanoma



Tuner E, et al. *Cancers* 14(21), 5449, 2022. PubMed: 36358868

# Summary

## We offer a range of products to accelerate your Oncology diagnostic assay development & validation projects

- ATCC<sup>®</sup> patient-derived cell lines and genomic DNA products offer a robust set of reference standards ideal for the development and validation of NGS-based pan-cancer and IO diagnostic assays:
  - Quantitated human gDNA from authenticated tumor cell lines with clinically-validated oncology biomarkers
  - Also available as cancer cell line-derived ATCC<sup>®</sup> certified reference materials
  - Well-characterized tumor-normal matched cell line pairs facilitate NGS IO diagnostic assay development & validation