

Canadian Pathology Quality Assurance

**CPQA**

**AQCP**

Assurance qualité canadienne en pathologie

# Cancer Diagnostics - Keeping Targeted Therapy on Target.

John Garratt, Director CPQA



**Canadian Pathology Quality Assurance - Assurance qualité canadienne en pathologie (CPQA-AQCP)**

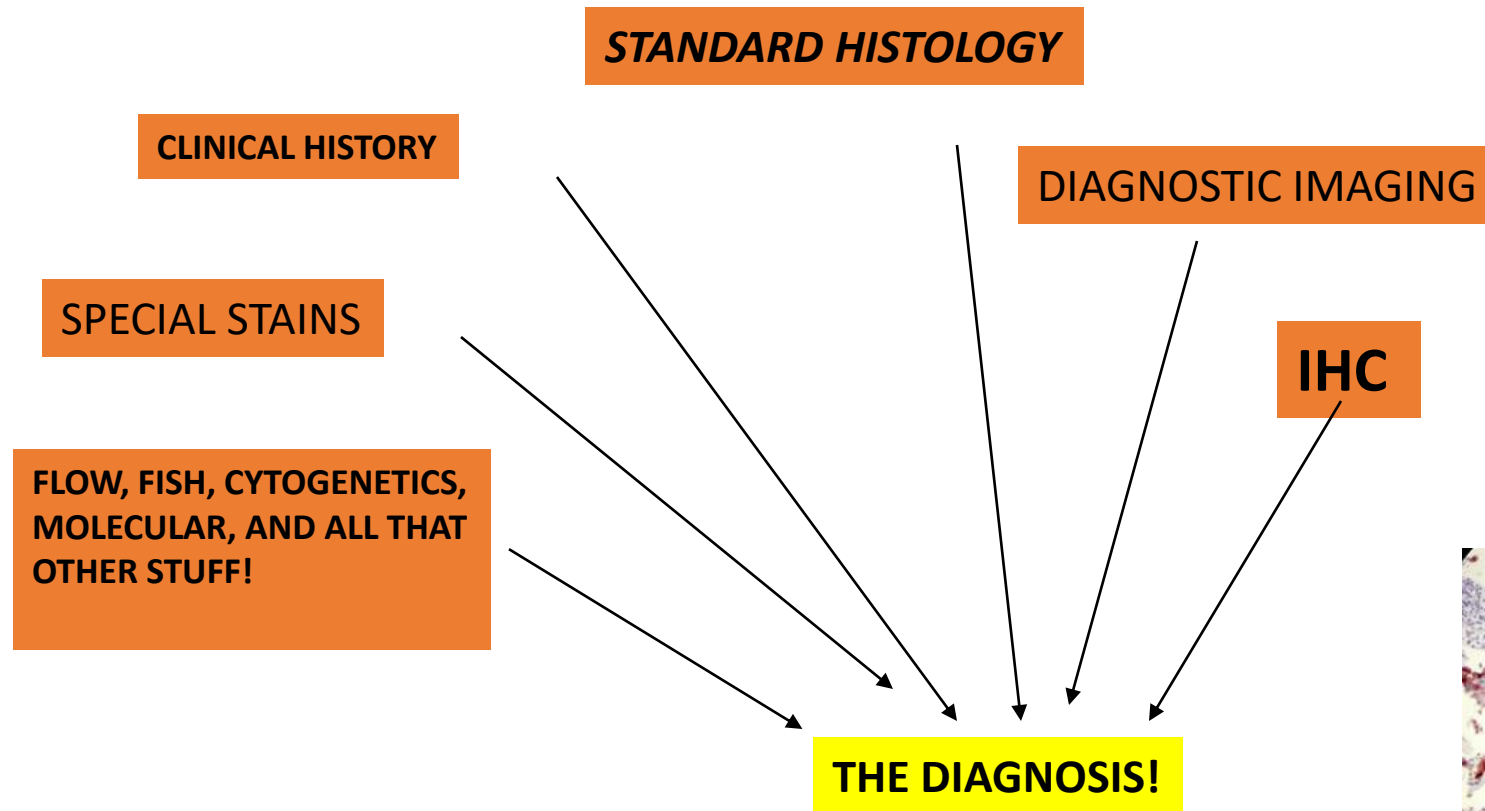
A not-for-profit corporation with its origin at the University of British Columbia, Vancouver, Canada

# CPQA – KEEPING TARGETED THERAPY ON TARGET

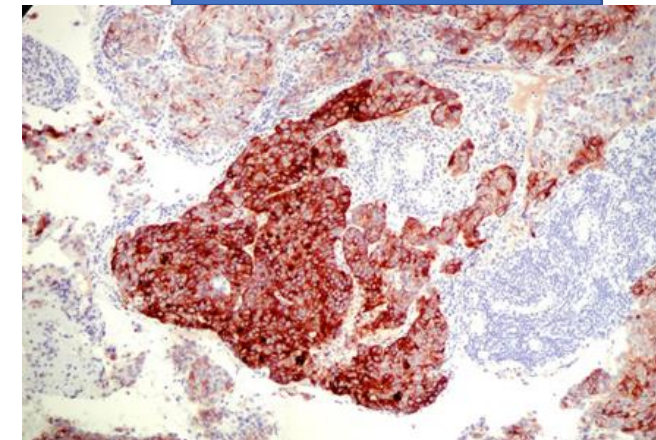
CPQA provides an external quality assurance (EQA) program within Canada and globally:

- Distributes clinically validated samples
- Participating labs monitor and improve the quality of their Immunohistochemistry (IHC) and molecular testing.

# DIAGNOSTIC ANATOMIC PATHOLOGY IS A COMPLEX, MULTIFACTORAL PROCESS



**IHC TELLS US WHAT PROTEINS A CELL IS EXPRESSING**





# CPQA Is A TMA Based EQA Program (mostly)

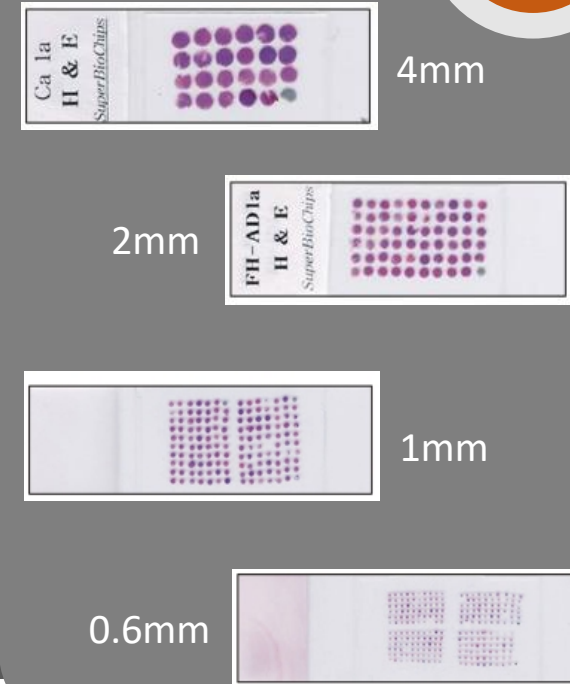
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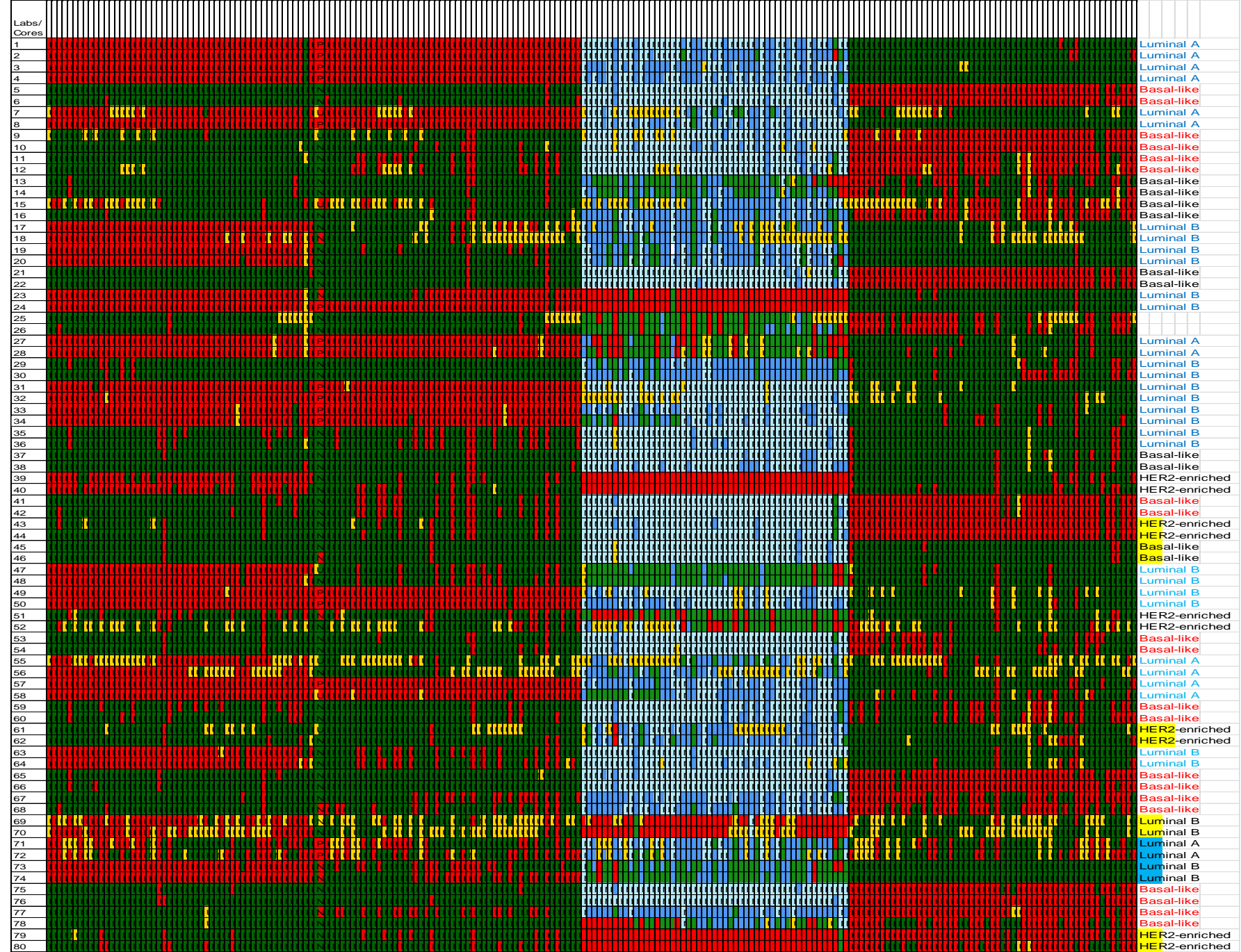


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TNBC  
Heat Map



# TMA Scorer – Web Based Data Entry Point

ER

HER2

PR

	1	2	3	4	5	6	7	8	9	10	11	12
1 row	P	U	N	P	P	N	N	U	P	N	P	N
2 row	24	23	22	21	20	19	18	17	16	15	14	13
3 row	25	26	27	28	29	30	31	32	33	34	35	36
4 row			46	45	44	43	42	41	40	39	38	37

1 row

1	Pos <input checked="" type="radio"/>	Neg <input type="radio"/>	Unsat <input type="radio"/>
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# Slide Expert Assessment and Final Report

## Assessment Team



# A sampling of CPQA 2021 EQA challenges

- H&E
- PD-L1
- Gastric HER2
- WT1
- CMV
- HSV
- p63/AMACR/keratin
- ER/PR/HER2 Breast
- MMR
- NTRK
- p53 endometrial
- p53 vulvar
- c-Myc lymphomas
- ROS1
- CD117
- BRAFV600E
- CD20
- p16
- ALK
- Ki67
- IDH1
- ATRX
- 1p19q FISH
- *RET* alterations

# Breast Cancer ER / PR / HER2

We have completed 34 Breast Ca EQA Challenges = 1530 slides = 61200 cores

## Breast Cancer biomarkers

2 out of 3 breast cancers are **ER** or **PR** positive. Their cells have hormone receptors which help cancer cells grow and spread.

Drugs: Tamoxifen, Toremifene, Fulvestrant

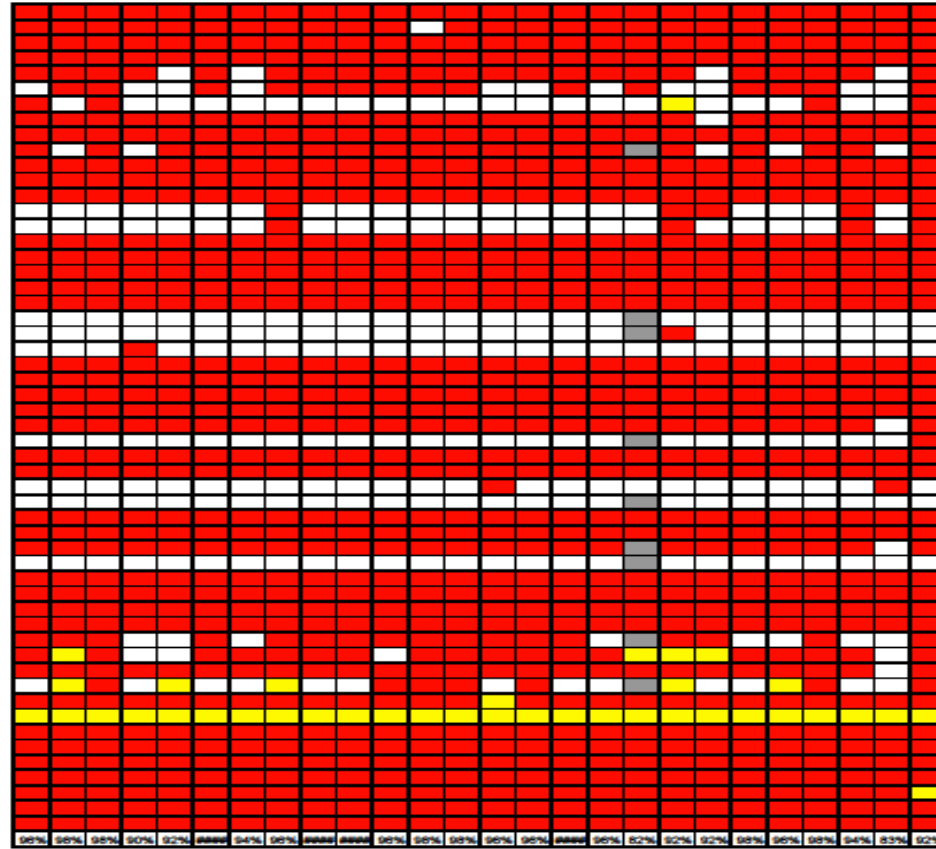
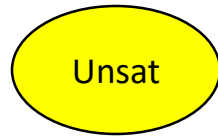
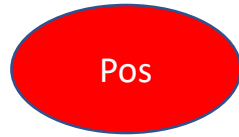
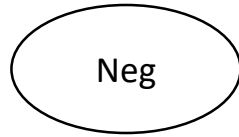
1 in 5 breast cancers have too much of a growth-promoting protein known as **HER2**. HER2 positive cancers tend to be aggressive.

Drugs: Herceptin and others drugs

# ESTROGEN RECEPTORS

Run 4 cIQc

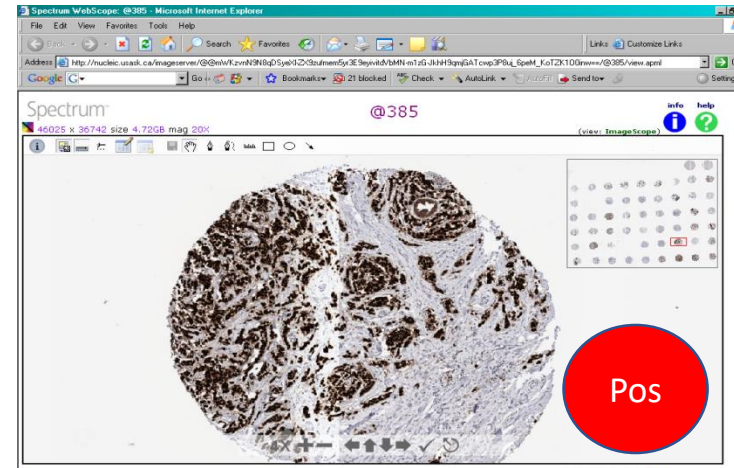
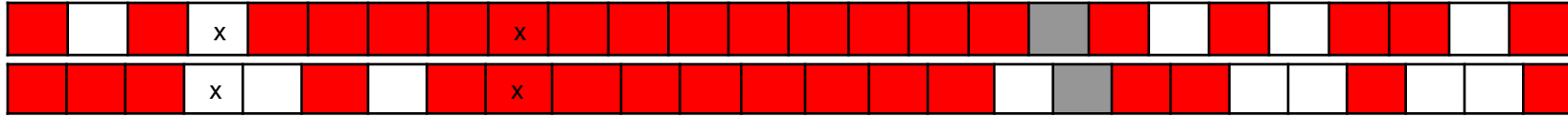
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# ESTROGEN RECEPTORS

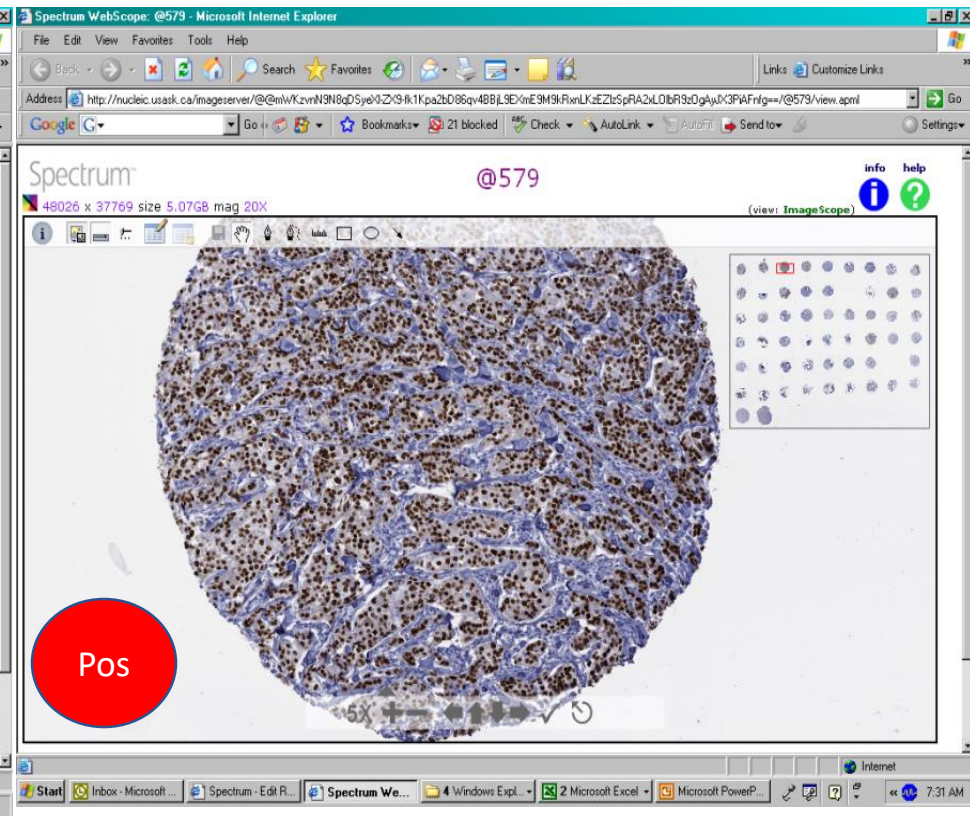
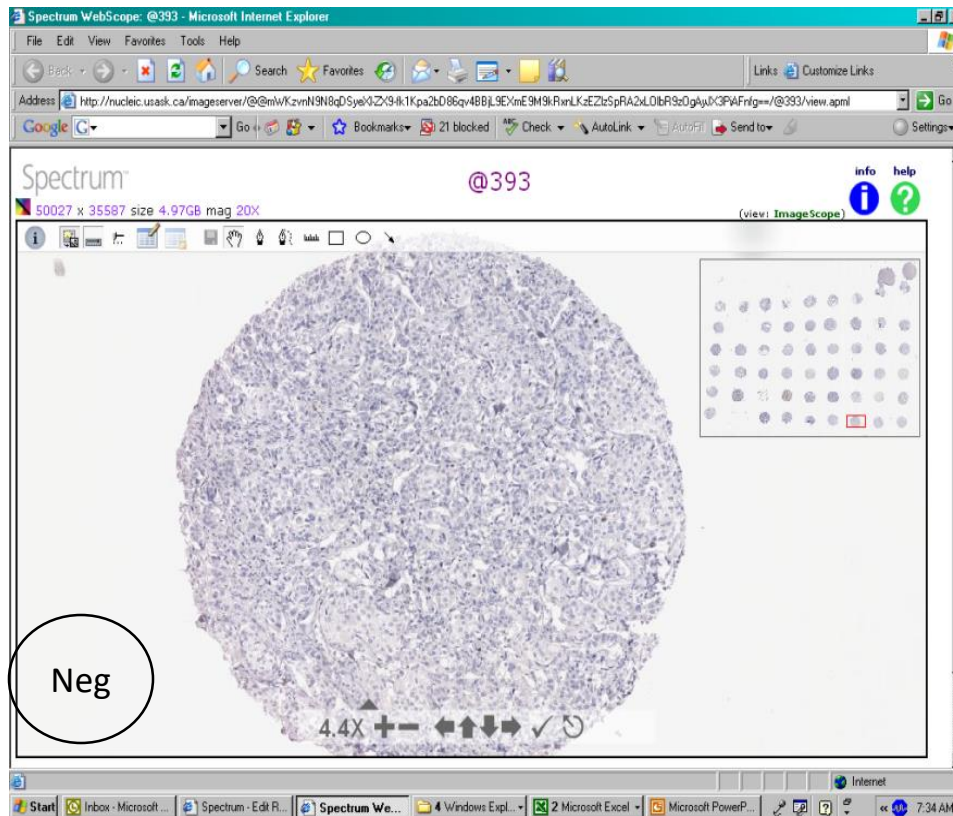
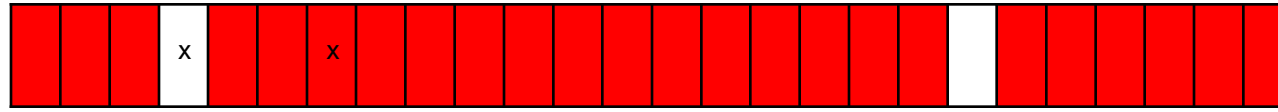
Run4/ Core 10 & 42





# Progesterone Receptor

clQc RUN 4/ core 3

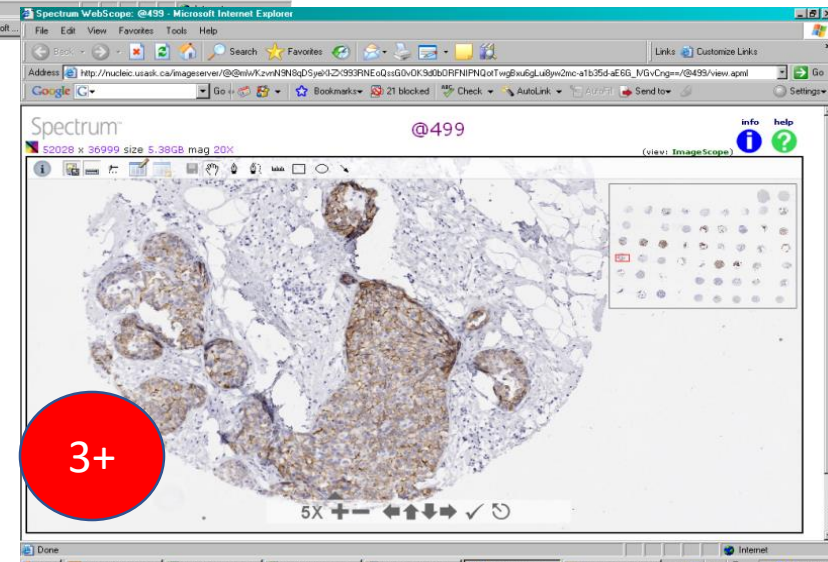
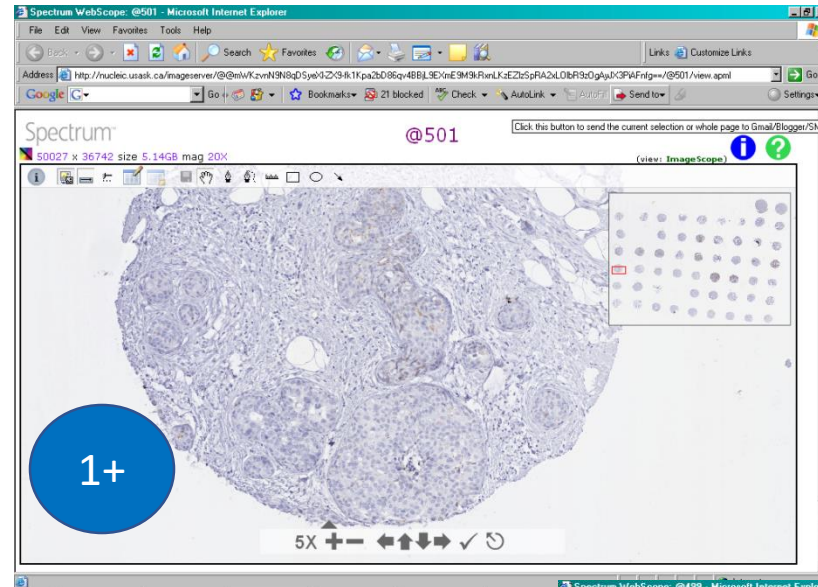






# HER2

clQc RUN 4/CORE 27

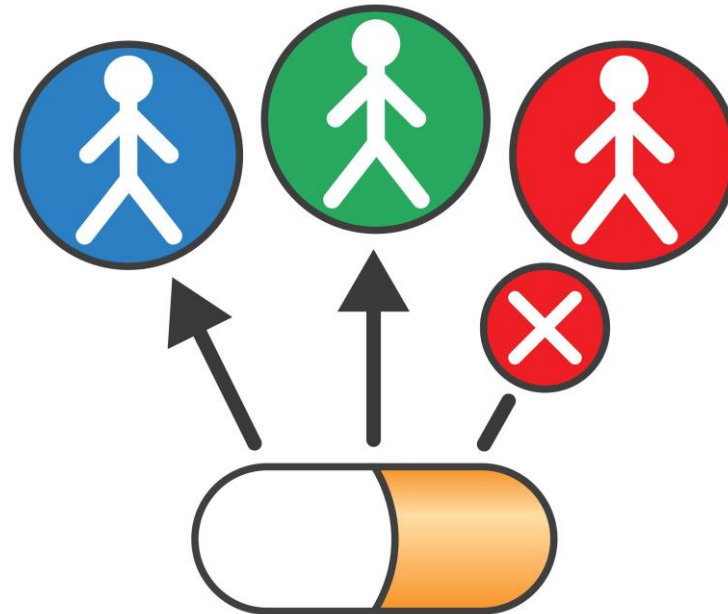


# KEEPING TARGETED THERAPY ON TARGET

COMPANION  
DIAGNOSTICS (CDx)

LAB DEVELOPED  
TESTS (LDT)

FDA  
APPROVED



# LABORATORY DEVELOPED TESTS (LDTs)

A LDT is a type diagnostic test that is designed, manufactured and used within a single laboratory.

- LDTs are diagnostic and prognostic
- Tests must be accurate so patients:
  - Do not receive unnecessary treatments
  - Treatment is not delayed
  - Are not exposed to inappropriate therapies.

CPQA is Protocol Agnostic – the majority of tests we review are LDTs

# COMPANION DIAGNOSTICS (CDx)

CDx - A term used by the FDA

- A companion diagnostic is defined in relation to a specific therapy
  - identifies patients who are most likely to benefit from the therapy
  - identifies patients at increased risk of serious side effects
  - monitors response to treatment
- FDA have 46 Companion Diagnostic Tests with 107 Drug Therapies dependent on the tests
- If the diagnostic test is inaccurate, then the treatment decision based on that test may not be optimal.



# HER2 - CDx Immunohistochemistry Tests

- INFORM HER-2/neu Ventana Medical Systems, Inc.  
Breast cancer - Herceptin (trastuzumab)
- PATHWAY antiHer2/neu (4B5) Rabbit Monoclonal Primary Antibody Ventana Medical Systems, Inc.  
Breast cancer - Herceptin (trastuzumab), Kadcyra (ado-trastuzumab emtansine)
- InSite Her-2/neu KIT Biogenex Laboratories, Inc.  
Breast cancer - Herceptin (trastuzumab)
- Bond Oracle HER2 IHC System, Leica Biosystems Breast cancer  
Breast cancer -Herceptin (trastuzumab)
- HercepTest Dako Denmark A/S,  
Breast cancer - Herceptin (trastuzumab) Perjeta (pertuzumab) Kadcyra (ado-trastuzumab emtansine)  
Gastric and gastroesophageal cancer- Herceptin (trastuzumab)

# HER2 - CDx Immunohistochemistry Protocols

Lab ID	Ag Retrieval Method	Time for Ag Retrieval (min)	Ab Clone	Ab Dilution	Ab Supplier/ Vendor	Ab Lot No.	Time for Ab Incubation (min)	Detection System	Amplification (y/n)	Enhancement (y/n)	Chromogen
101	EnV FlexTRS, High PH	30 min	4B5	1:8	ROCHE DIAGNOSTICS	F05675	15 min	DAKO Envision Flex	N	N	DAB
102	DAKO PT - HIGH PH	20	SP3	1:80	CELL MARQUE	50420	25"	DAKO ENVISION FLEX	NO	YES CUSO4	DAB+
103	CC1	36	4B5	PRE	VENTANA	F15240	16	ULTRA VIEW	NO	Y COPPER	DAB Ultraview
106	HIGH pH 97	30 MIN	4B5	1/5	ROCHE	F20661	20 MIN	FLEX	N	N	DAB
107	Dako FLEX TRS High pH	30	Polyclonal (Rabbit)	1:1000	Dako	20067288	12	Dako FLEX	N	N	DAB
111	HIER	36	4B5	PREDILUTE	VENTANA	F12738	32	ULTRAVIEW	N	Y	DAB
112	BOND ER2 pH 9.0	20 minutes	4B5	1:4 ratio of RTU	Ventana/Roche	F10545	15 MINUTES @ RT	bond Polymer Refine	no	no	DAB
113	CC1	36	SP3	1/50	Cell Marque	57447	20	Roche Ultraview	N	N	DAB
114	Envision Flex TRS, High pH	30	4B5	1:8	Roche	F15240	25	Envision FLEX DAKO Omnis	N	N	Envision Flex DAB
120	HIER	32 MINS	4B5	RTU	VENTANA	F20661	16 MINS	ULTRAVIEW	N	N	DAB
123	Roche CC1	36	4B5	predilute	Roche	F12738	24	Roche ultraView	N	Y	DAB
125	HIER	30	A0485	1/800	DAKO	20067288	10	DAB	N	N	DAB
127	HIER	36 MIN	4B5	PREDILUTE	VENTANA	F20661	24 MIN	ULTRAVIEW DAB	N	Y	DAB
129	ER 2- High pH retrieval	20	SP3	1:50	Thermo Scientific	UF2773162	15	Bond Refine Detection Kit	N	N	DAB
133	HIER	36	4B5	predilute	Roche	F12738	24	polymer-Ultraview	n	n	Dab
136	Dako Hercep Test buffer	40	A0485	RTU	Dako/ Agilent	200272143	30	Dako Hercep Test Kit	N	N	HT DAB
147	HIER PH 9	20	SP3	100	THERMO S	UI2843377	15	LOLYMER LEICA REFINE	N	N	DAB
151	BUFFER 9.0	20 MIN	SP3	1:50	THERMO	TL267341	15 MIN	BOND REFINE	N	N	DAB
160	CC1	36 MIN	4B5	RTU	VENTANA	F22519	16 MIN	ULTRAVIEW	N	Y	DAB
161	Herceptest epitope	40 Minutes	Rabbit anti-human HER protein	RTU	Dako	20072143	30 Minutes	Herceptest visualization reagent	Non	Non	Herceptest DAB chromogen
175	HIER	36	4B5	Pre dilute	Roche	F20902	16	Ultra DAB polymer	N	Y	DAB
186	HIER	20	c-erbB-2	1:400	DAKO	20067287	15	BOND POLYMER REFINE DETECTION	N	N	DAB
187	CC1	16	4B5	Predilute	Roche	F12738	24	Optiview	N	N	DAB
190	CC1	32	SP3	1:50	Thermo	9103S1711B	32	Optiview	N	N	DAB
194	CC1	36	4B5	RTU	ROCHE	F22519	12	ULTRAVIEW	N	Y	DAB
198	High pH HIER	30 min	4B5	1/5	Ventana/Roche	E25115M	20 min	Envision/Flex/HRP	N	N	DAB
199	ER2	30	SP3	1:300	Cell Marque	47174	15	Refine	N	N	Dab
202	HIER PH6.0	40	ERBB2	RTU	DAKO	20072143	30	HERCEPTEST FOR AUTOMATED LINK PLATFORMS VISUALIZATION	N	N	DAB
207	on line CC1	36	4B5	prediluted	Ventana	F20661	16	Ultraview	N	Y	DAB
220	HIER	36	4B5	PRE DILUTE	VENTANA	F18078	12	VENTANA ULTRAVIEW	N	Y	DAB
230	HIER	32	4B5	predilute	Roche	F20661	16	Ultraview	N	N	DAB
233	HIER CC1	36	4B5	NA	Roche	F108078	16	Ultraview Universal DAB	N	Y	Ultraview DAB





# ALK GENE REARRANGEMENT

ALK gene rearrangements are found in approximately 2% to 7% of patients with NSCLC\*

ALK gene rearrangements represent a fusion between ALK and partner genes.

Once this fusion occurs, the gene acts as a driver of lung tumorigenesis and oncogenic activity

VENTANA ALK (D5F3) CDx Assay

Non-small cell lung cancer

Zykadia (ceritinib), Xalkori (crizotinib), Alecensa (alectinib), Lorbrina (lorlatinib)

\*Kwak EL, Bang YJ, Camidge DR, et al. Anaplastic lymphoma kinase inhibition in non-small-cell lung cancer. *N Engl J Med*. 2010;363:1693-1703.

# ALK Protocols

## LDTs tests for biomarkers ALK Run 107

**Table S1.** Self-reported ALK IHC staining protocols.

Lab ID	Ag Retrieval Method	Time for Ag Retrieval (min)	Ab Clone	Ab Dilution	Ab Supplier/ Vendor	Ab Lot No.	Time for Ab Incubation (min)	Detection System	Amplification (Y/N)	Enhancement (Y/N)	Chromogen
101	EnV FlexTRS, High PH	1 hour	5A4	1:25	Leica	6056459	40 min	DAKO Envision Flex	Y	N	DAB
102	DAKO PT - HIGH PH	20	5A4	1:40	LEICA	6064412	60" RT	DAKO ENVISION FLEX+	YES	YES CUSO4	DAB+
107	Dako FLEX TRS High pH	60	5A4	1:25	Novocastra	6071624	40	Dako FLEX	N	N	DAB
110	DAKO PT High ph 9.0@97 C	20 min	5A4	1:50	Biocare	82718	30 min	Dako Envision Flex	Y	N	DAB
112	BOND Epitope Retrieval 2 pH 9.0	30 minutes	5A4	1:25	Leica (Novocastra)	6069219	30 minutes	BOND polymer refine detection	none	none	DAB
113	High pH	30	5A4	1/25	Leica	6071624	27.5	DAKO Envision Flex HRP	N	N	DAB
114	Envision Flex TRS, High pH	60	5A4	1:25	Leica (novocastra)	6065605	40	Envision FLEX DAKO Omnis	Y	N	Envision Flex DAB
115	Envision Flex High PH	30 min	D5F3	1/100	Cell Signaling	3633S	30 min	Envision Flex	Y	N	DAB
120	HIER Waterbath	20	5A4	1:40	Biocare	21219	30	Dako Envision Flex	y	N	DAB
123	Roche CC1	92	5A4	1/100	Novocastra	6071624	60	Roche OptiView	Y	Y	DAB
136	Dako High pH	20	5A4	1:50	Leica	6071624	30	Dako Envision FLEX +	Y	N	DAB
146	FLEX TRS High	20	5A4	1:100	Biocare	112019	25	FLEX	n	n	DAB
149	high pH OMNIS	20 min at 97 C	OT11A4	1:1000	Origene	0F004	26	EnVision Flex OMNIS	Yes	No	DAB
160	CC1	64 MIN	5A4	1/10	LEICA	6069219	32 MIN	OPTIVIEW	Y	Y	DAB
194	CC1	92	D5F3	RTU	ROCHE	E11917	16	OPTIVIEW	Y	Y	DAB
202	HIER PH9.0	20	5A4	10	NCL	6071624	15	BOND POLYMER REFINE DETECTION KIT	N	N	DAB
207	on line-high PH	30	OT11A4	1/1000	Cederlane	W003	30	DAB Envision Flex	Y	N	DAB
220	HIER	92	5A4	1/30	NOVOCAST RA/LEICA	6071624	80	VENTANA OPTIVIEW	Y	Y	DAB
230	HIER	80	5A4	predilute	LEICA	66021	64	Optiview	Y	N	DAB





# PD-L1 Programmed Death-Ligand 1

- PD-L1 is associated with the activation of T-Cells and with immune response.
- PD-L1 is expressed in numerous tumour types and binds with the PD-1 receptor on T-Cells, deactivating the T-Cell and preventing an immune response against the tumour.
- A number of drugs have been developed to inhibit PD-L1 and have been used in Melanoma and NSCLC therapy.
- The overexpression of PD-L1 can be considered a biomarker of tumour response to immunotherapy.

# PD-L1 Programmed Death-Ligand 1

PD-L1 IHC 28-8 pharmDx, Dako North America, Inc.

Non-small cell lung cancer (NSCLC)

OPDIVO (nivolumab) in combination with YERVOY (ipilimumab)

PD-L1 IHC 22C3 pharmDx, Dako North America, Inc.

Non-small cell lung cancer (NSCLC), gastric or gastroesophageal junction adenocarcinoma, cervical cancer, urothelial carcinoma, head and neck, squamous cell carcinoma (HNSCC), esophageal squamous cell carcinoma (ESCC), triple-negative breast cancer (TNBC)

KEYTRUDA (pembrolizumab), Libtayo (cemiplimab-rwlc)

VENTANA PD-L1 (SP142) Assay, Ventana Medical Systems, Inc.

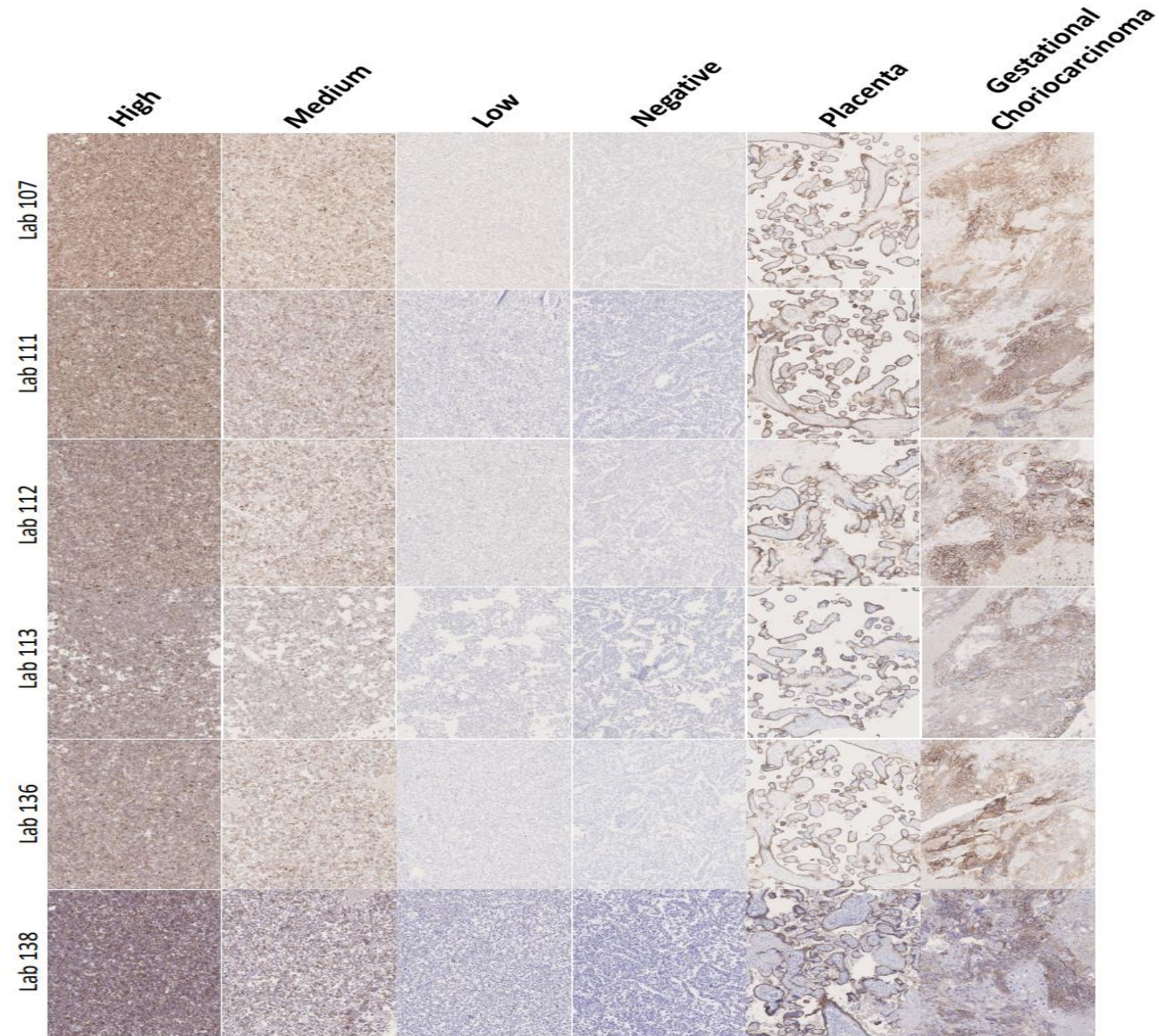
Urothelial carcinoma, Triple-Negative Breast Carcinoma (TNBC) and Nonsmall cell lung cancer (NSCLC)

TECENTRIQ (atezolizumab)

# Protocols - Run 132 PD-L1

Lab ID	Platform/instrument	LDT or IHC Kit	Ag Retrieval Method	Time for Ag Retrieval (min)	Ab Clone	Ab Dilution	Ab Supplier/ Vendor	Ab Lot No.	Time for Ab Incubation (min)	Detection System	Amplification (Y/N)	Enhancement (Y/N)	Chromogen
107	Dako Autostainer Link 48	IHC Kit	EnVision FLEX TRS, low pH: 97°C	20	22C3	RTU	DAKO	11202433	30	Envision FLEX HRP	N	Y	DAB
111	Dako Autostainer Link 48	IHC Kit	EnVision FLEX TRS, low pH: 97°C	20	22C3	RTU	DAKO	11166452	30	Envision FLEX HRP	N	N	DAB
112	Dako Autostainer Link 48	IHC Kit	EnVision FLEX TRS, low pH: 97°C	60	22C3	RTU	DAKO	11202433	30	Envision FLEX HRP	N	N	DAB
113	Dako Autostainer Link 48	IHC Kit	EnVision FLEX TRS, low pH: 97°C	20	22C3	RTU	DAKO	11198363A	30	Envision FLEX HRP	Y	Y	DAB
114 SP142	Dako Omnis	LDT	EnVision FLEX TRS, low pH: 97°C	60	SP142	1:25	Spring Bioscience	GR3208476 21	40	Envision FLEX HRP	Y	N	DAB
114 SP263	Dako Omnis	LDT	EnVision FLEX TRS, low pH: 97°C	30	SP263	1:5	Ventana Roche		20	Envision FLEX HRP	Y	N	DAB
136	Dako Autostainer Link 48	IHC Kit	EnVision FLEX TRS, low pH: 97°C	20	22C3	RTU	DAKO	11202433	30	Envision FLEX HRP	Y	Y	DAB
138	Dako Autostainer Link 48	IHC Kit	EnVision FLEX TRS, low pH: 97°C	20	22C3	RTU	DAKO	11202433	30	Envision FLEX HRP	Y	y	DAB
149	Dako Omnis	IHC Kit	EnVision FLEX TRS, low pH: 97°C	20	22C3	RTU	DAKO	11202433	30	Envision FLEX HRP	Y	N	DAB
184 GE006	Dako Omnis	GE006	EnVision FLEX TRS, low pH: 97°C	40	22C3	RTU	DAKO	11211282	40	Envision FLEX HRP	N	Y	DAB
184 SK005	Dako Autostainer Link 48	SK005	EnVision FLEX TRS, low pH: 97°C	20	28-8	RTU	Agilent	11256998	30	Envision FLEX HRP	N	Y	DAB
184 SK006	Dako Autostainer Link 48	IHC Kit	EnVision FLEX TRS, low pH: 97°C	20	22C3	RTU	DAKO	11265194	30	Envision FLEX HRP	N	Y	DAB
194	Leica Bond III	LDT	ER2 (pH9)	40	22C3	1/20	DAKO	11175306	30	Refine	N	Y	DAB
202	Dako Autostainer Link 48	IHC Kit	EnVision FLEX TRS, low pH: 97°C	20	22C3	RTU	DAKO	11139863	30	Envision FLEX HRP	N	Y	DAB
207	Dako Omnis	LDT	EnVision FLEX TRS, low pH: 97°C	60	22C3	1/30	DAKO	11199937	60	Envision FLEX HRP	Y	N	DAB
220	Ventana BenchMark Ultra	LDT	CC1	48	22C3	1/40	DAKO	11175306	64	OPTIVIEW	N	Y	DAB
230	Ventana BenchMark Ultra	LDT	CC1	32	SP263	RTU	Roche Diagnostics	G03096	16	OPTIVIEW	N	N	DAB
249	Ventana BenchMark Ultra	IHC Kit	CC1	48	SP142	None	Ventana	G27114	16	OPTIVIEW	Y	N	DAB

# Educational Run - PD-L1 22C3



**Figure X.** Composite images of participant staining using PD-L1 clone 22C3.



## MMR Immunohistochemistry

MMR enzymes play a role in recognizing and repairing erroneous base pairings that arise during DNA replication.

Four MMR enzymes (MLH1, MSH2, MSH6 and PMS2) are of clinical relevance.

Loss of MMR expression in the tumors of patients with colorectal or endometrial carcinoma identifies patients at increased risk for Lynch Syndrome (LS), an autosomal dominant cancer susceptibility syndrome that accounts for approximately 4% of cases of colorectal and endometrial carcinoma.

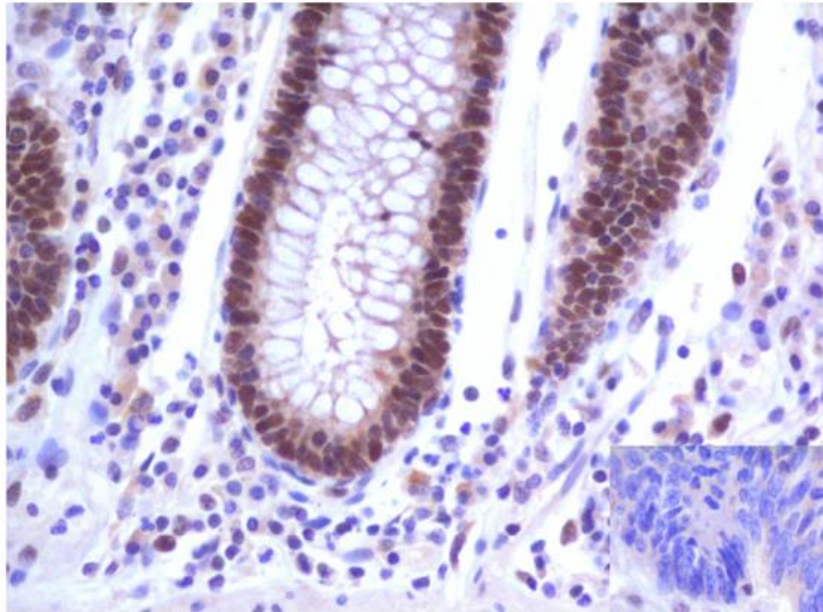
Lynch syndrome patients in a 50 to 80 percent lifetime risk of developing colorectal cancer.

CDx: VENTANA MMR Endometrial Carcinoma (EC) RxDx Panel Jemperli (dostarlimab-gxly)

Mismatch repair deficient (dMMR) Solid tumors Jemperli (dostarlimab-gxly)

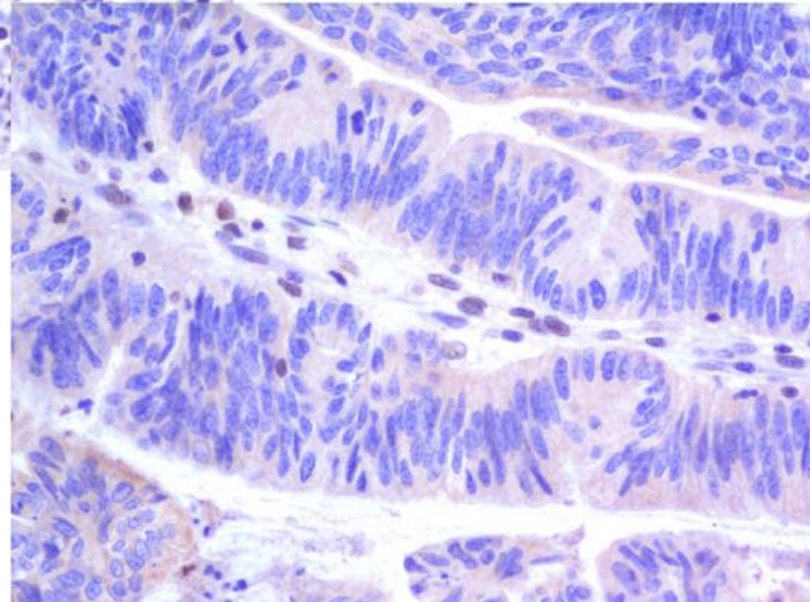
Plus: Loss of expression of any MMR proteins - predictive of response to chemotherapy in colorectal carcinoma.

# MMR Staining – When Positive is Negative



**MLH 1**

Expression



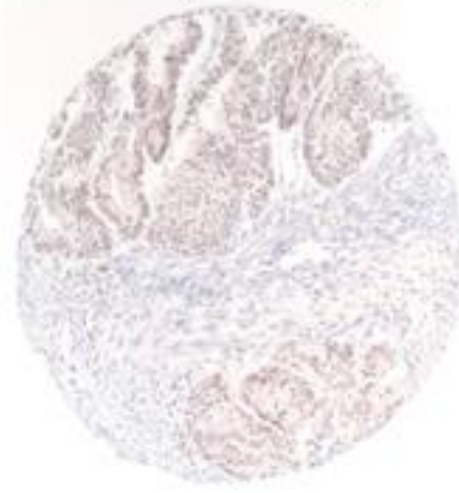
Absent

E	Expression			
A	Absence of Expression			
F	Failed			
U	Unsatisfactory			



# Run 70 Core 15 MLH1

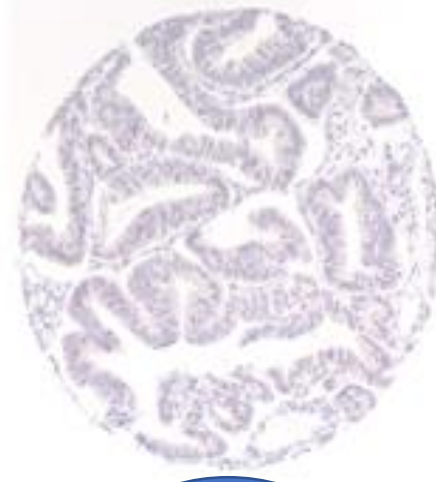
Lab 101 (weak staining)



Lab 110 (nice staining)

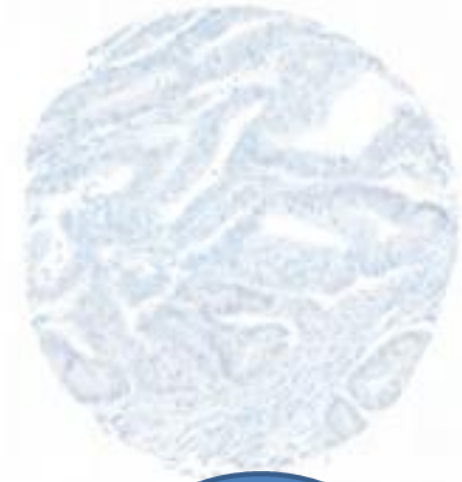


Lab 114 (very weak staining)



failed

Lab 124 (extremely weak staining)



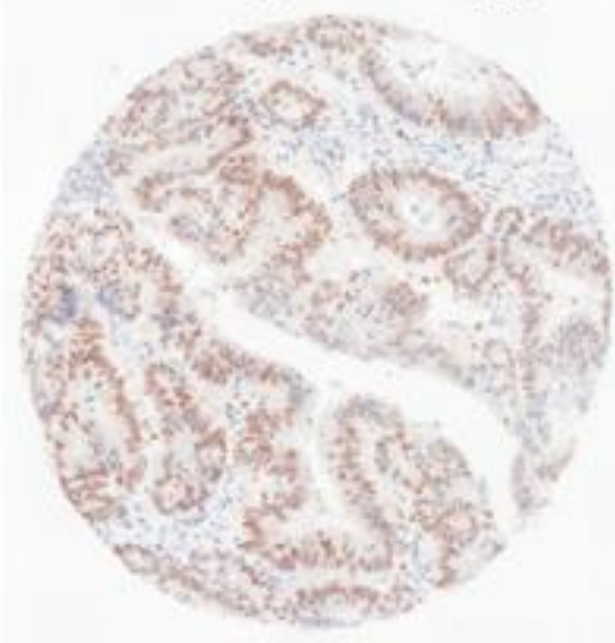
failed



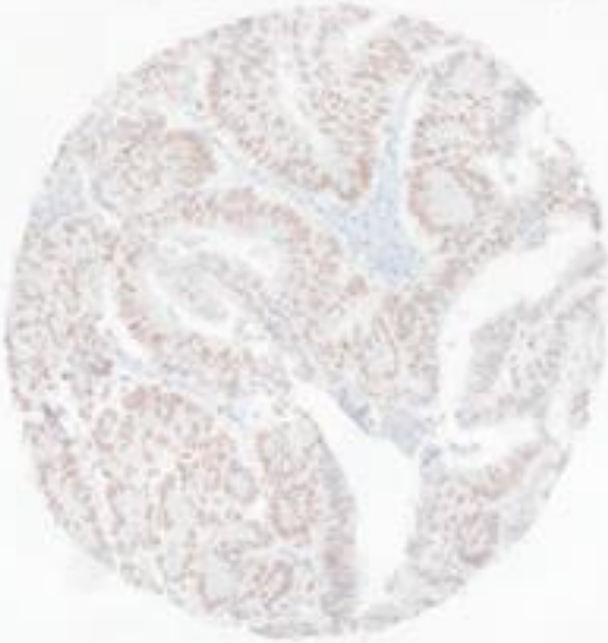


# Run 70 PMS2 Core 8

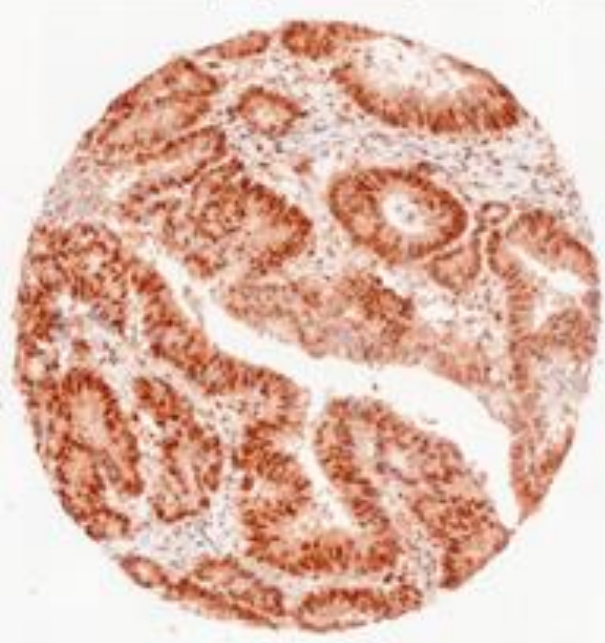
**Lab 125 (nice staining)**



**Lab 207 (very weak staining)**



**Lab 217 (high background)**



E	Expression		
A	Absence of Expression		
F	Failed		
U	Unsatisfactory		

# Run 70 MSH2

Lab/ Core	101	102	103	104	106	107	109	110	111	112	114	115	116	123	124	125	126	138	141	144	145	149	175	181	186	189	202	207	217	220	222	231	MMR status		
1	E	E	E	E	E	E	E	E	E	E	E	E	E	U	U	E	E	E	U	E	E	E	E	E	E	E	E	E	E	E	E	U	MLH1		
2	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	MSH6	
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7	U	U	E	E	E	E	E	E	E	E	E	E	E	E	E	U	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	MLH1	
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15	F	E	E	E	E	F	E	E	F	E	F	E	F	F	F	E	E	E	E	E	F	E	E	E	F	E	A	A	F	F	F	F	F	MSH6	
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21	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	MLH1
22	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	MLH1
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27	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	F	E	F	E	E	E	E	E	E	E	MLH1/MSH6
32	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	MLH1
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# Run 70 MSH6

Lab/ Core	101	102	103	104	106	107	109	110	111	112	114	115	116	123	124	125	126	138	141	144	145	149	175	181	186	189	202	207	217	220	222	231	MMR status	
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33	E	E	E	E	E	E	E	E	E	E	E	E	U	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	PMS2
34	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	MLH1
38	A	A	A	A	A	A	A	A	A	A	E	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	F	A	A	A	A	A	MSH2



**"I HAVE TO TELL YOU  
ABOUT THE FUTURE"**

# THE CHALLENGES AHEAD FOR LABS & EQA

- New biomarkers and technologies are continually arriving. Labs are under pressure to quickly adapt diagnostic processes whilst maintaining quality
- EQA schemes are increasingly in demand and have limited resources
- The interaction of labs and industry is fragmented would benefit from coordination
- Well-designed EQA/PT schemes are an important mechanism for high quality clinical implementation of biomarker testing and improves patient care - Keeping precision medicine precise
- Adaption of new tools like AI

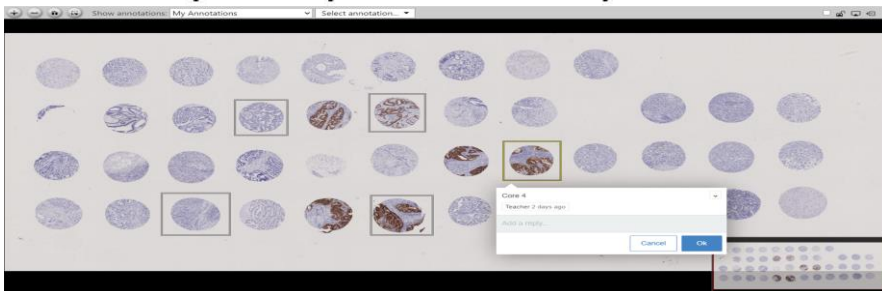


# THE CHALLENGES AHEAD- KEEPING PRECISION MEDICINE PRECISE

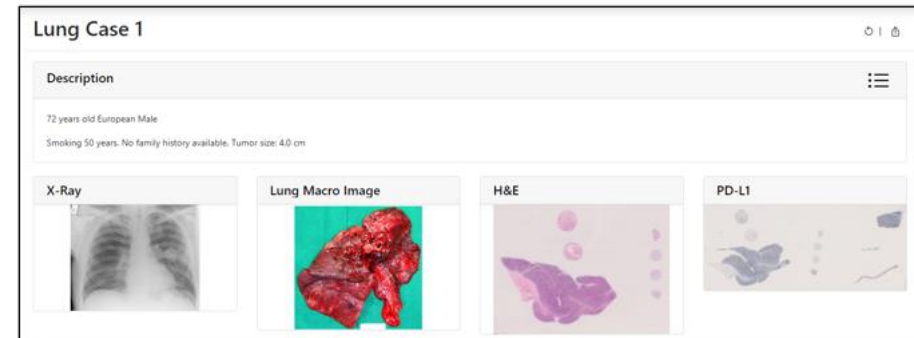


Online platform for teaching, training and quality assurance in pathology

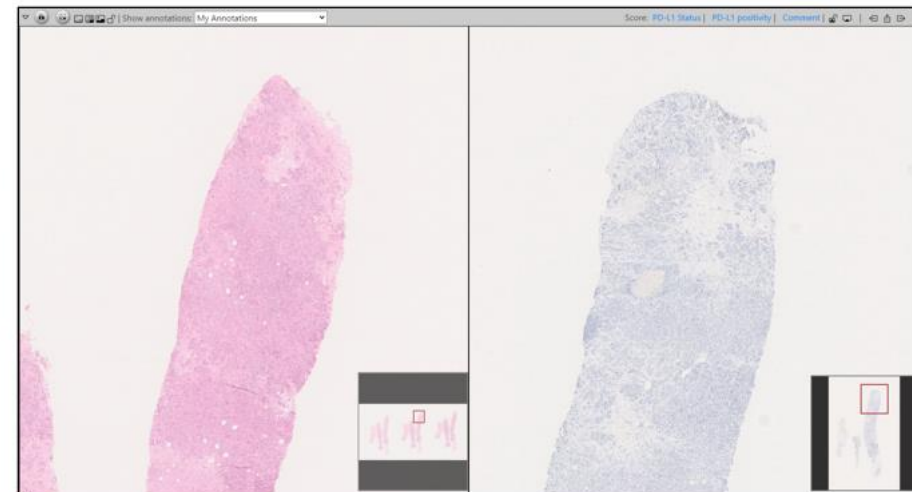
- Build modules by linking images with questions, annotations and guidance documents
- Combine clinical information with macroimages, X-rays/scans and whole slide images to build complete patient cases
- Split TMA slides to work with individual cores
- Invite admins and participants, or make the module publicly available as you wish



Build patient cases



Split-view for linking with H&E

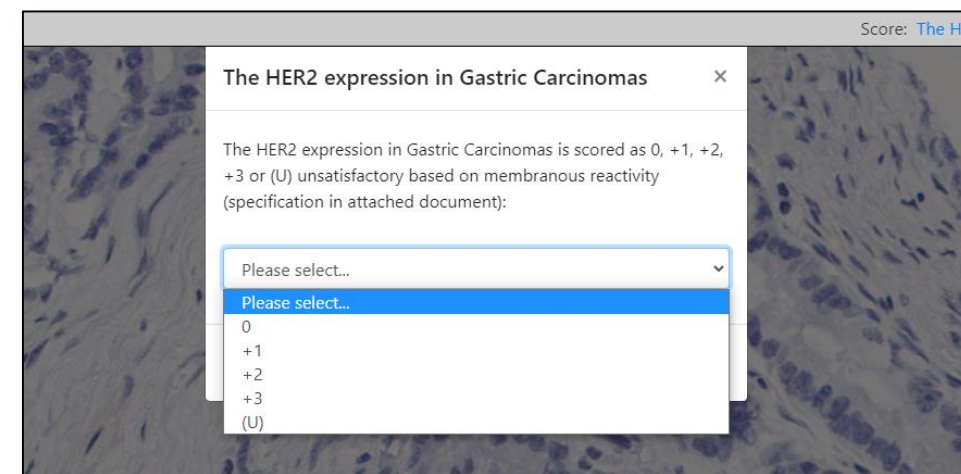
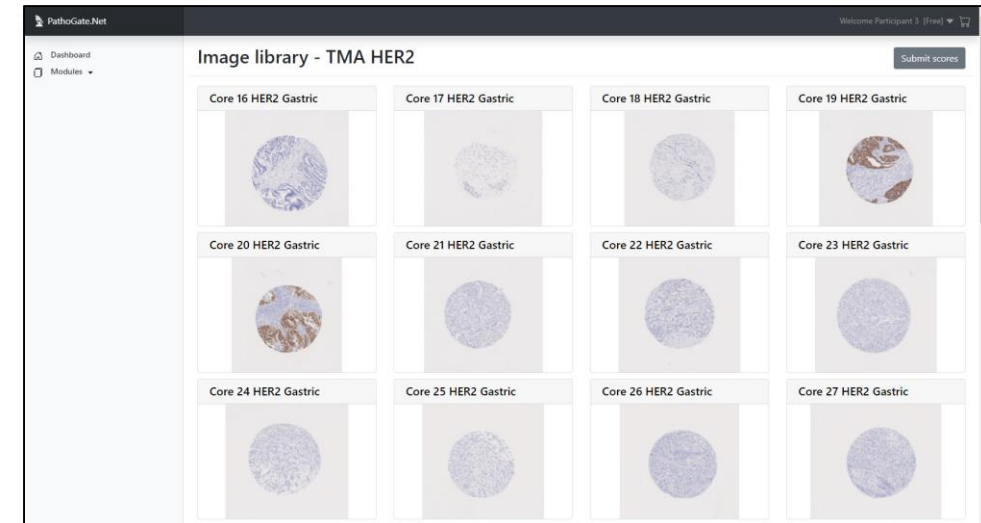
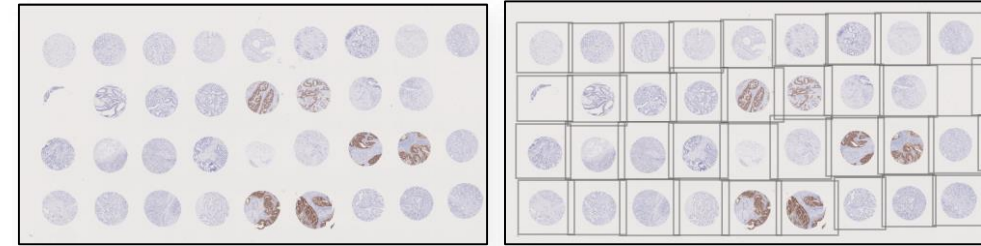
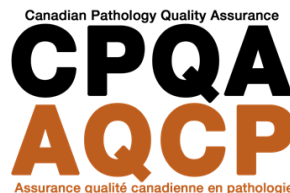
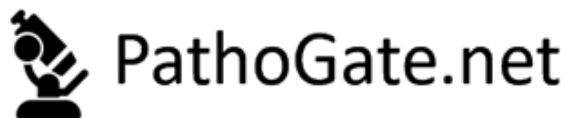


# KEEPING PRECISION MEDICINE PRECISE

## CPQA collaboration with PathoGate.net

To provide online educational and self-assessment modules for a series of IHC biomarkers

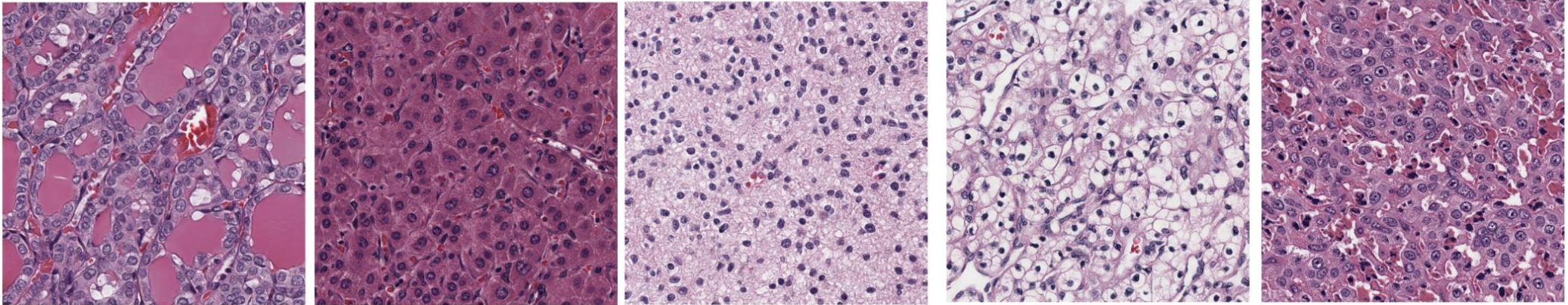
- Material is based on CPQA collection of TMA slides from previous quality runs
- TMAs are split to individual cores using simple annotations generated on the platform
- Relevant questions are assigned to the images
- Participants will get access to a training set and an assessment set for each marker



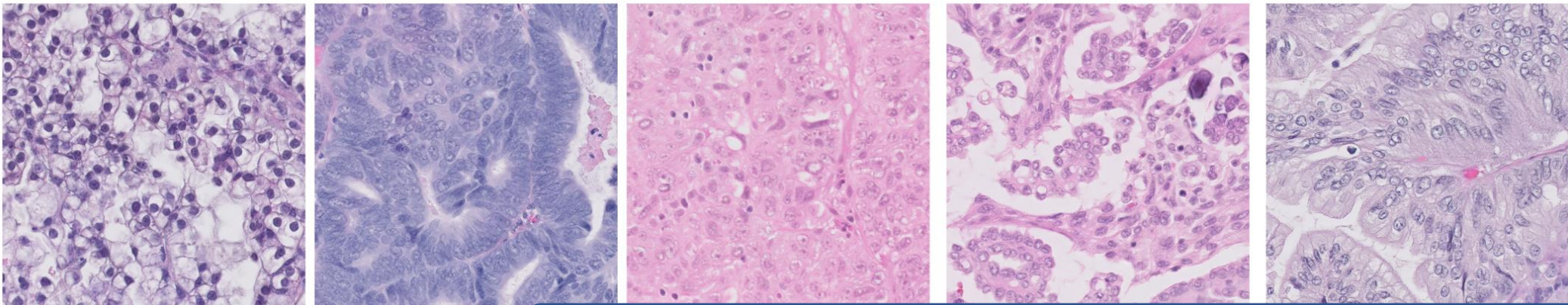


# Synthetic Clinical Grade Cancer Images

**a**



**b**



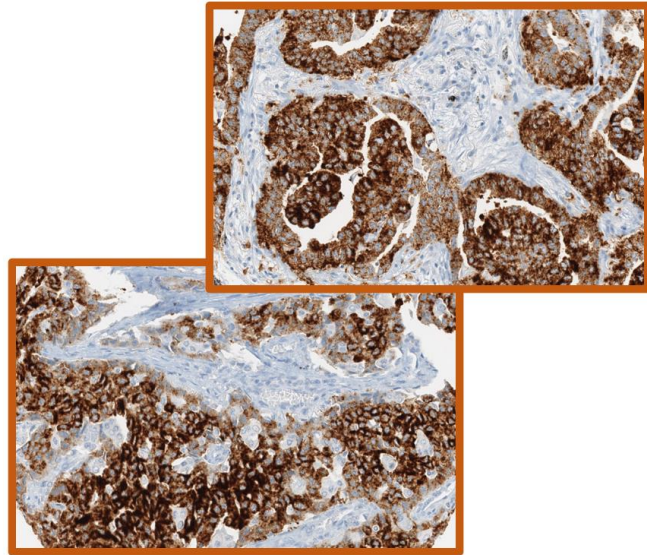
Levine AB, Peng J, Farnell D, et al. Synthesis of diagnostic quality cancer pathology images by generative adversarial networks. *J Pathol* [Internet] 2020; Available from: <http://dx.doi.org/10.1002/path.5509>



# THE CHALLENGES AHEAD – NEW BIOMARKERS

## *ROS1* Rearrangement

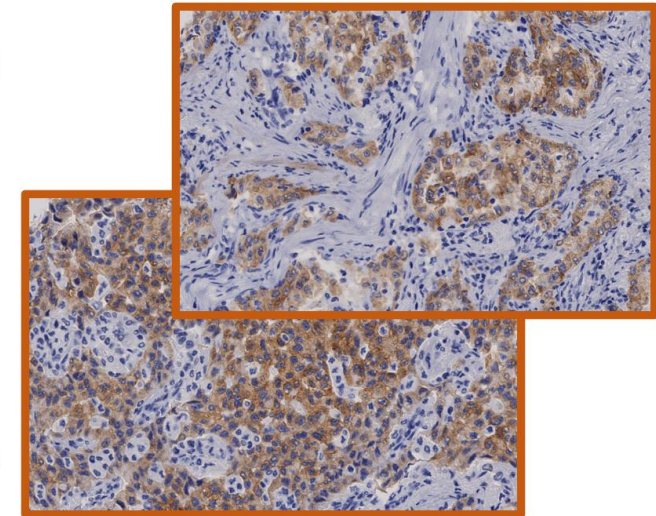
The frequency of *ROS1* rearrangement in non-small cell lung cancers has been reported to range from 1.6% to 2.3%.



Suryavanshi, Moushumi, et al. "ROS1 rearrangement and response to crizotinib in Stage IV non-small cell lung cancer." *Lung India: official organ of Indian Chest Society* 34.5 (2017): 411.

## *ALK* Rearrangement

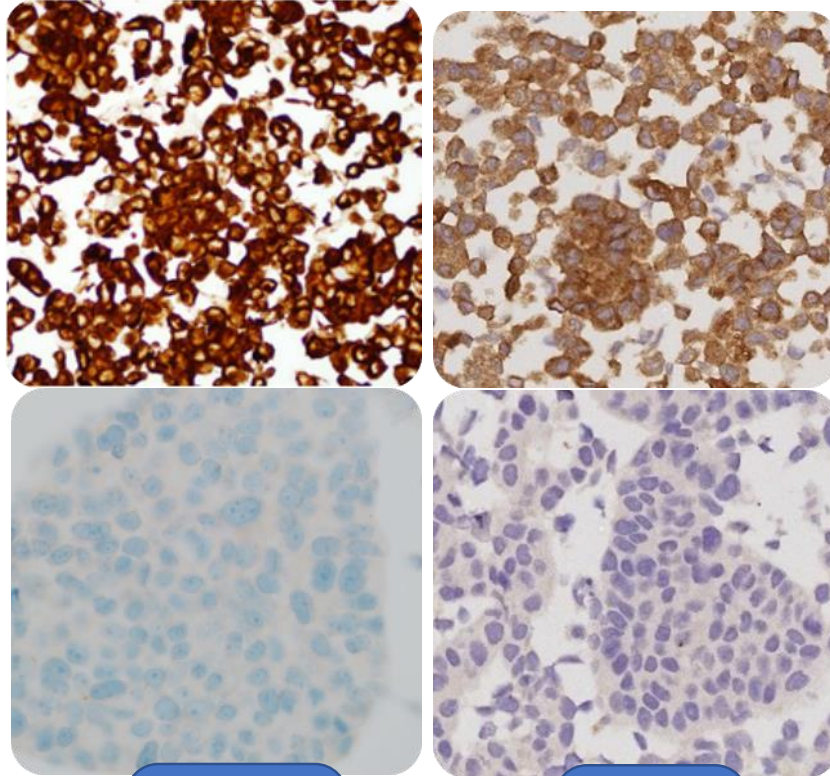
*ALK* rearrangements are found in approximately 2% to 7% of patients with NSCLC.



Kwak EL, Bang YJ, Camidge DR, et al. Anaplastic lymphoma kinase inhibition in non-small-cell lung cancer. *N Engl J Med*. 2010;363:1693-1703.

# ALK Cell Lines

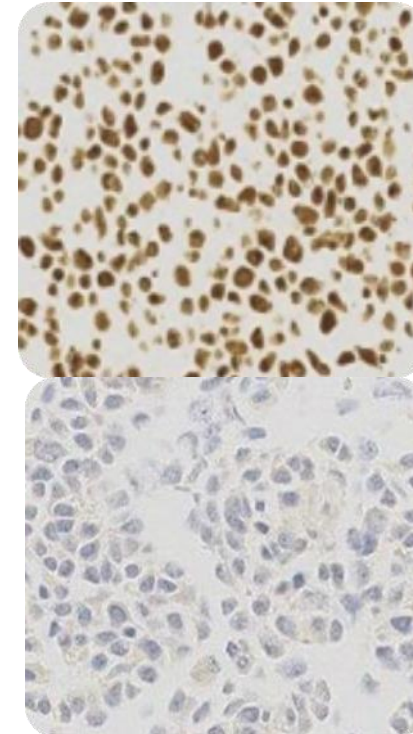
Lung: EML4-ALK translocation



Ventana  
D5F3

Leica  
4A5

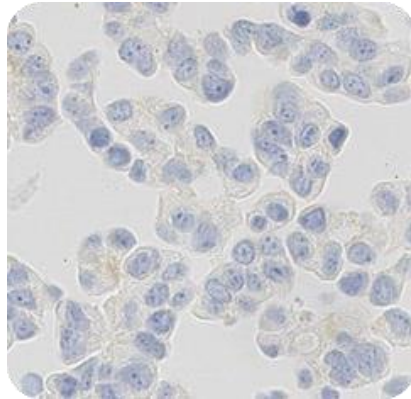
Lymphoma NPM-ALK translocation



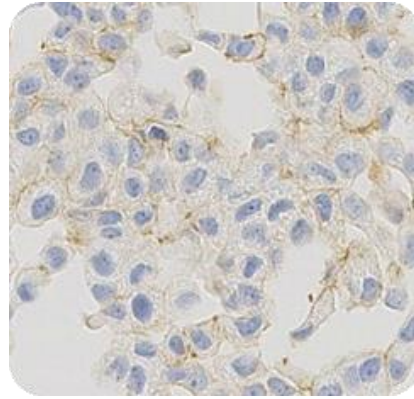
Ventana  
P80ALK



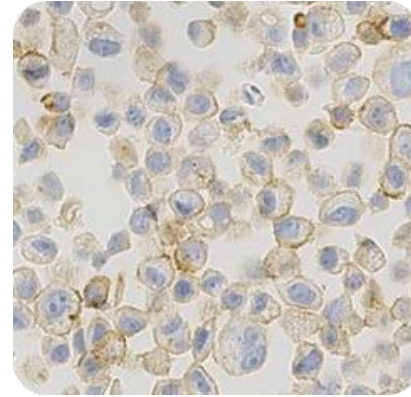
# Quantitative HER2 Analyte Control Cell Lines



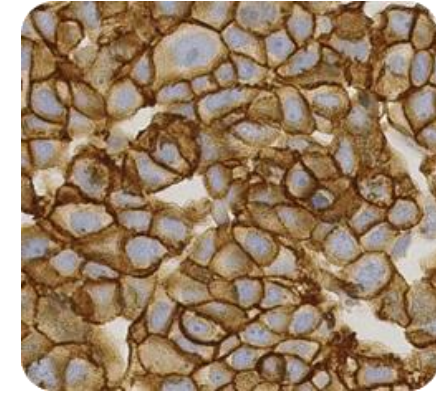
Neg



1+



2+



3+



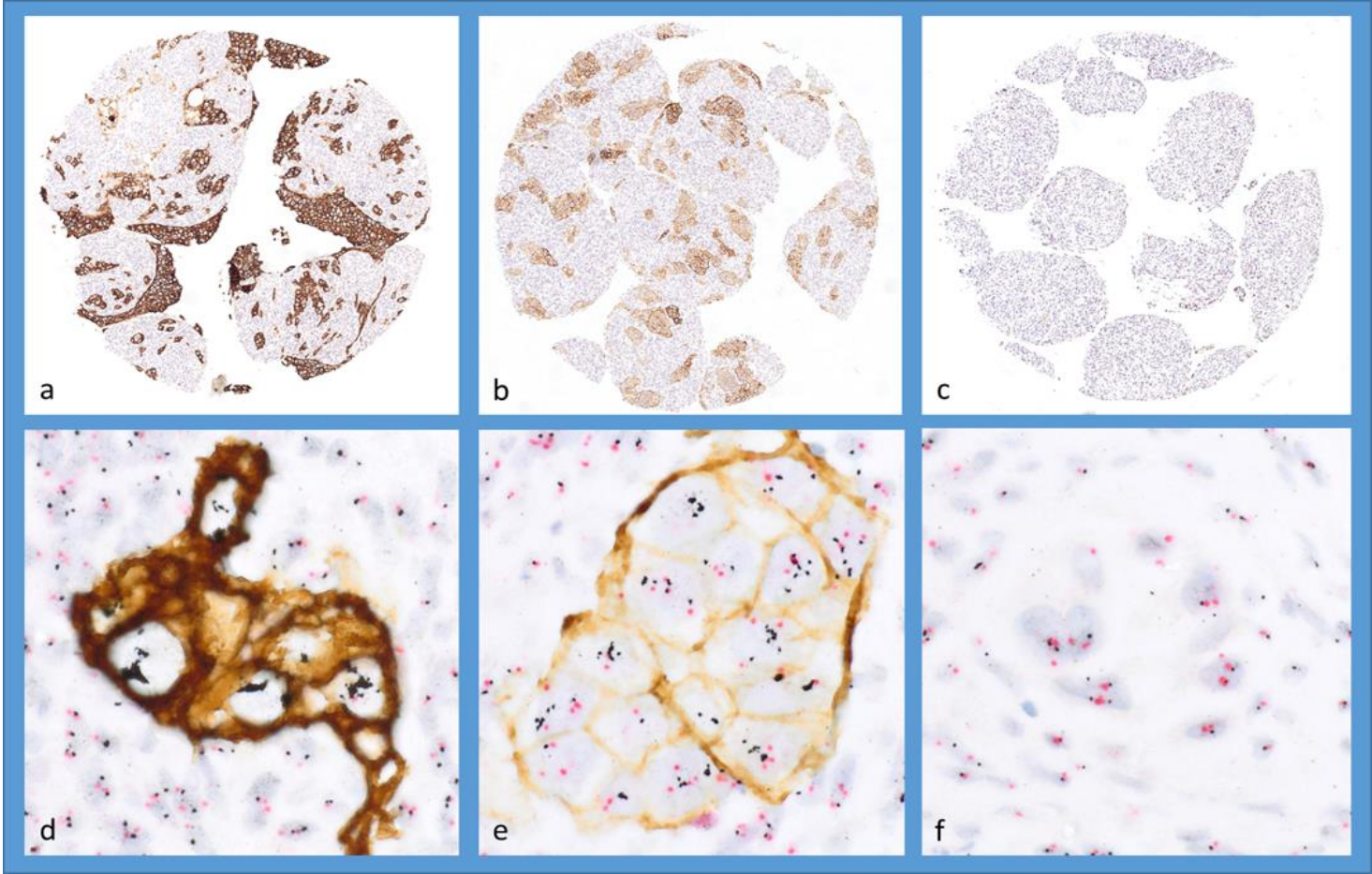
Quality in Control

<http://www.histocyte.com/>

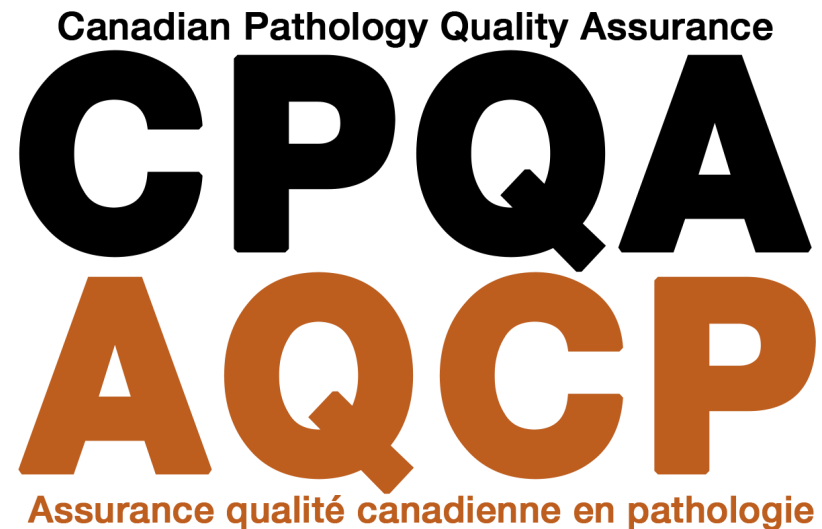


# Histoids for Quantitative Positive Control

Histoids are tumour cell lines grown in a matrix of normal stromal cells to give the appearance of tissue. [www.statlab.com](http://www.statlab.com)



# The Challenges Ahead -TRK (pan-TRK) Collaboration

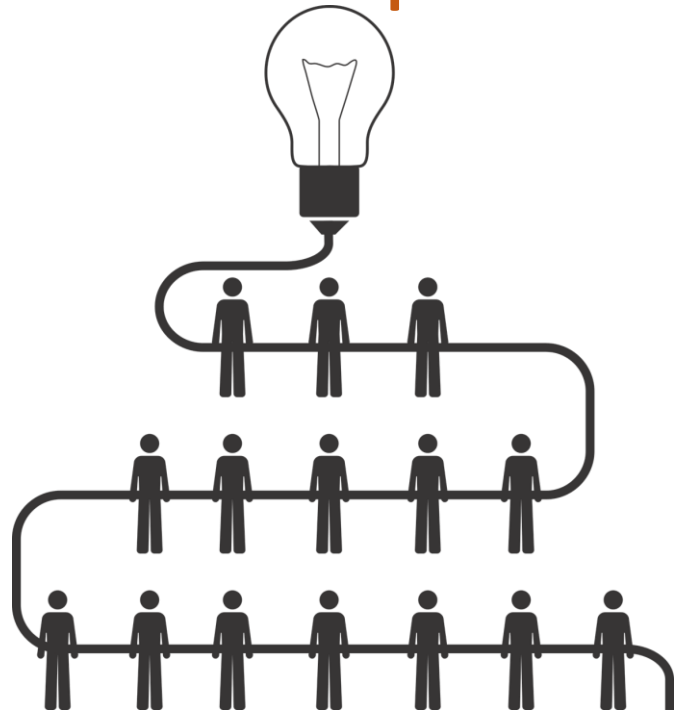


- ▶ TRK fusion cancers occurs when NTRK gene fuses with another gene and creates overexpression of the TRK protein which results in tumour growth.
- ▶ TRK fusion cancer occurs across a broad range of different tumours.
- ▶ Low incidence in certain cancers ( ie CRC 1.5%)
- ▶ Larotrectinib (Bayer) is considered to be tissue agnostic developed and approved to treat any cancer containing N-TRK fusions.

**“First treatment for TRK fusion cancer approved.”**

Bayer

# Global crowd-sourcing hard to locate biosamples



Helping labs by coordinating and assisting with biomarker test validation and provide them a vigilant EQA program



T H A N K  
Y O U

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Canadian Pathology Quality Assurance

**CPQA**  
**AQCP**

Assurance qualité canadienne en pathologie

**The CPQA-AQCP Team**

Dr. Blake Gilks

Dr. Bob Wolber

Ms. Vidya Beharry

Mr John Garratt

Dr. Jennifer Won