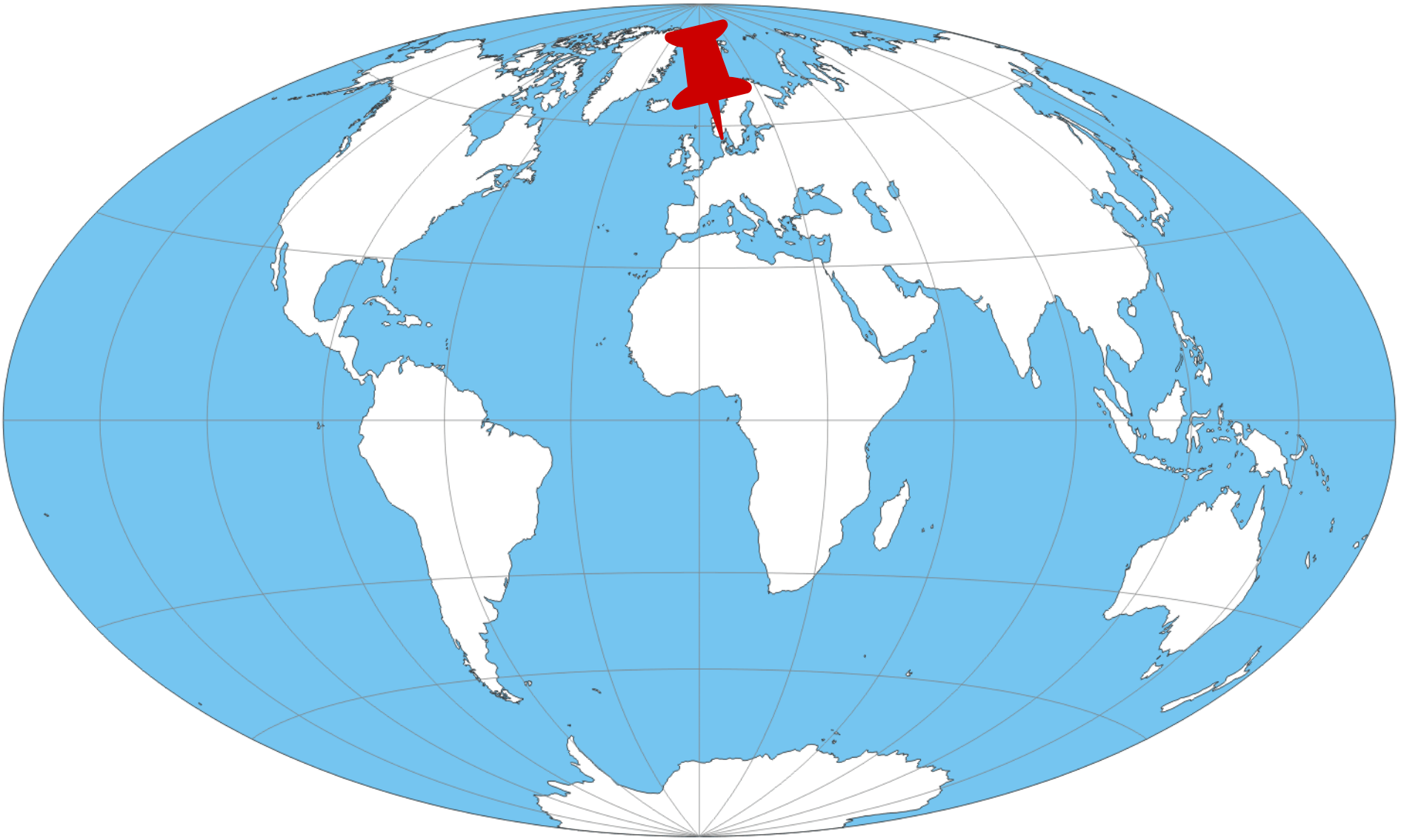
NordiQC

Workshop in Diagnostic Immunohistochemistry
Aalborg University Hospital, October 5-7th 2022

Welcome To Aalborg

Søren Nielsen
Director, NordiQC
Aalborg University Hospital, Denmark

IHC – NordiQC workshop 2022



IHC – NordiQC workshop 2022

IHC – NordiQC workshop 2022

IHC – NordiQC workshop 2022

Workshop in Diagnostic Immunohistochemistry
Aalborg University Hospital, October 5-7th 2022

63 participants - 10 countries

Workshop frames:

- Approximately 16 lecture hours
- Focus on technical parameters influencing IHC results
- Review on diagnostic / clinical use of IHC

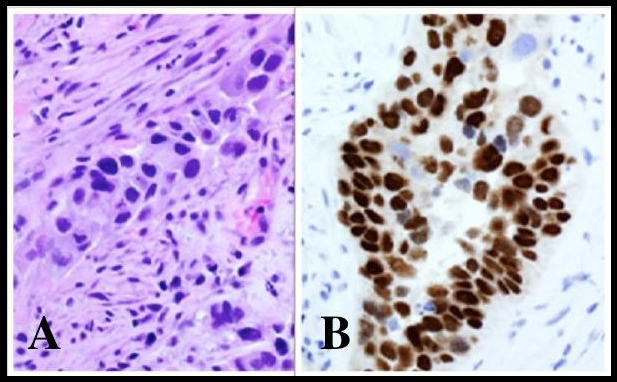
IHC – Potential in lung cancer pathology

Primary or secondary

TTF1, Calretinin, CDX2, GATA3, ….

NSCLC or SCLC

CGA, SYP, CD56, INSIM1….

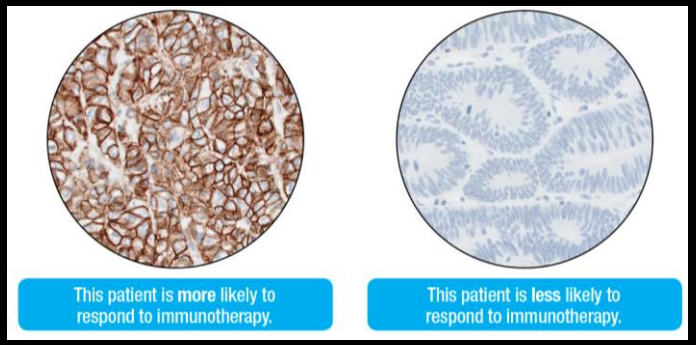


Adenocarcinoma or squamous

TTF1, Napsin A, CK5, p40….

Predictive

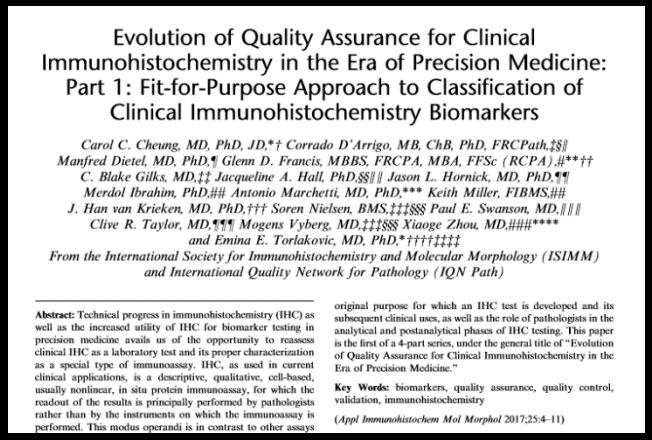
ALK, PD-L1, ROS1….



IHC – NordiQC workshop 2022

Original nomenclature and grouping of IHC tests:

- Type I / Class I IHC tests: Interpreted in the context of histo- or cytomorphologic and clinical data. Results interpreted and used by pathologists. E.g. CD45, TTF1, PAX8, SOX10, CDX2, p40 etc
- Type II / Class III, US) IHC tests: Stand-alone tests being interpreted (largely) to provide predictive and prognostic information. Results interpreted by pathologists and used by clinicians to give tailored treatment. E.g. ER, ALK, HER2, MMR, BRAF, PD-L1 etc .



Evolution of Quality Assurance for Clinical Immunohistochemistry in the Era of Precision Medicine: Part 1: Fit-for-Purpose Approach to Classification of Clinical Immunohistochemistry Biomarkers

Carol C. Cheung, MD, PhD, JD,† Corrado D'Arrigo, MB, ChB, PhD, FRCPath,‡§‖ Manfred Dietel, MD, PhD,¶ Glenn D. Francis, MBBS, FRCPA, MBA, FFSc (RCPA),#**†† C. Blake Gilks, MD,‡‡ Jacqueline A. Hall, PhD,§§‖‖ Jason L. Hornick, MD, PhD,¶¶ Merdol Ibrahim, PhD,## Antonio Marchetti, MD, PhD,*** Keith Miller, FIBMS,## J. Han van Krieken, MD, PhD,††† Soren Nielsen, BMS,‡‡‡§§§ Paul E. Swanson, MD,‖‖‖ Clive R. Taylor, MD,¶¶¶ Mogens Vyberg, MD,‡‡‡§§§ Xiaoge Zhou, MD,###**** and Emina E. Torlakovic, MD, PhD,*†††‡‡‡‡*

From the International Society for Immunohistochemistry and Molecular Morphology (ISIMM) and International Quality Network for Pathology (IQN Path)

Abstract: Technical progress in immunohistochemistry (IHC) as well as the increased utility of IHC for biomarker testing in precision medicine avails us of the opportunity to reassess clinical IHC as a laboratory test and its proper characterization as a special type of immunoassay. IHC, as used in current clinical applications, is a descriptive, qualitative, cell-based, usually nonlinear, in situ protein immunoassay, for which the readout of the results is principally performed by pathologists rather than by the instruments on which the immunoassay is performed. This modus operandi is in contrast to other assays original purpose for which an IHC test is developed and its subsequent clinical uses, as well as the role of pathologists in the analytical and postanalytical phases of IHC testing. This paper is the first of a 4-part series, under the general title of "Evolution of Quality Assurance for Clinical Immunohistochemistry in the Era of Precision Medicine."

Key Words: biomarkers, quality assurance, quality control, validation, immunohistochemistry

(*Appl Immunohistochem Mol Morphol* 2017;25:4–11)

AJCP / Special Article

Am J Clin Pathol 2010;133:354-365

CME/SAM

Canadian Association of Pathologists–Association canadienne des pathologistes National Standards Committee/Immunohistochemistry

Best Practice Recommendations for Standardization of Immunohistochemistry Tests*

Emina Emilia Torlakovic, MD, PhD,[1] Robert Riddell, MD, FRCPath, FRCPC,[2] Diponkar Banerjee, MBChB, FRCPC, PhD,[3] Hala El-Zimaity, MD, MS, FRCPC,[4] Dragana Pilavdzic, MD, FRCPC,[5] Peter Dawe, MS,[6] Anthony Magliocco, MD, FRCPC,[7] Penny Barnes, MD, FRCPC,[8] Richard Berendt, MD, FRCPC,[9] Donald Cook, MD, FRCPC,[10] Blake Gilks, MD, FRCPC,[11] Gaynor Williams, MD, PhD,[12] Bayardo Perez-Ordonez, MD, FRCPC,[13] Bret Wehrli, MD, FRCPC,[14] Paul E. Swanson, MD,[15] Christopher N. Otis, MD,[16] Søren Nielsen, HT, CT,[17] Mogens Vyberg, MD,[17] and Jagdish Butany, MBBS, MS, FRCPC[13]

IHC – NordiQC workshop 2022

Type II / Class III, IHC companion diagnostics (CDx):

IHC	Area	Demonstration	Drug
ER	Breast	Estrogen receptor	Tamoxifen, …
HER2	Breast and gastric	HER2 protein overexpression	Herceptin,…
CD117	GIST	Protein second to gene mut.	Glivec,…
ALK, ROS1	NSCLC	Fusion protein from gene mut.	Crizotinib,…
PD-L1	NSCLC	PD-1 receptor	Pembrolizumab,..
PD-L1	TNBC	PD-L1 receptor	Azetolizumab
MMR	Solid carcinoma	PD-L1 receptor	Pembrolizumab
……			

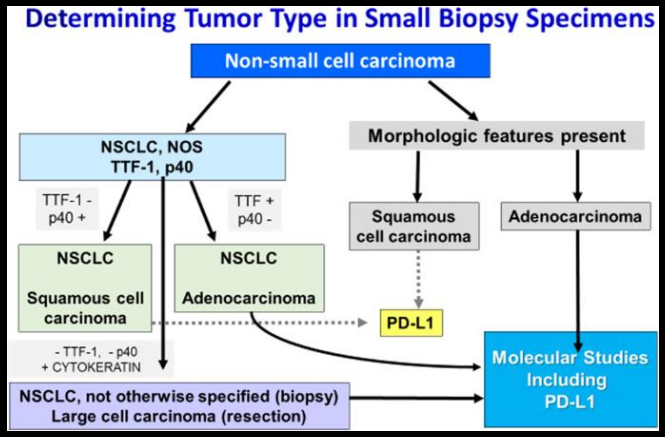
IHC – NordiQC workshop 2022

In practice more and more IHC tests become Type II tests: Directly indicated

IHC	Area	Type I	Type II	Comment
ALK	Lymphoma	ALCL	Crizotinib	Type II: Lung NSCLC
CD30	Lymphoma	HL, ALCL	Brentuximab	Type II: HL, ALCL
CD56	Carcinoma	Neuroendo.	Lorvotuzumab	Type II: Lung SCLC
MMR	CRC	Lynch	Pembrolizumab	Type II: Solid carc.

Indirectly indicated typically due to personalized treatment e.g.

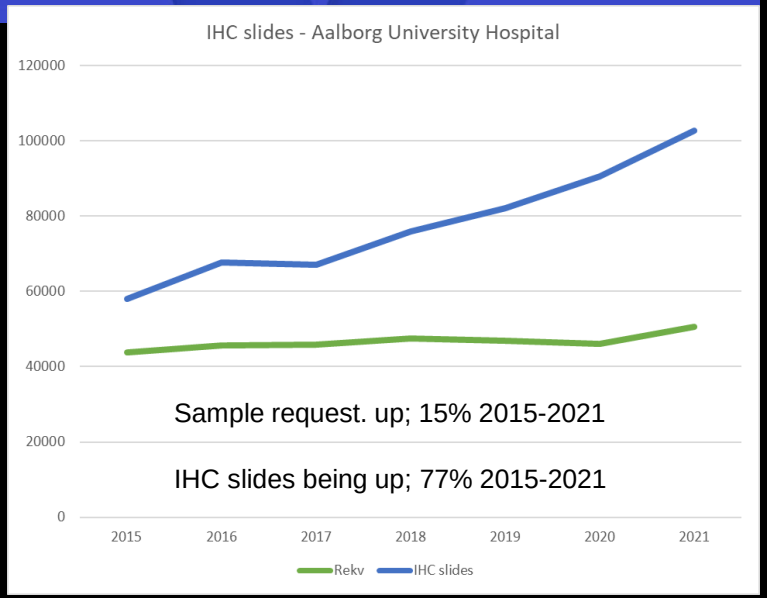
IHC	Area	Type I	Type II	Comment
p40 - lung	Carcinoma	Squamous		
TTF1- lung	Carcinoma	Adeno	Crizotinib,….	ALK, EGFR, ROS1…

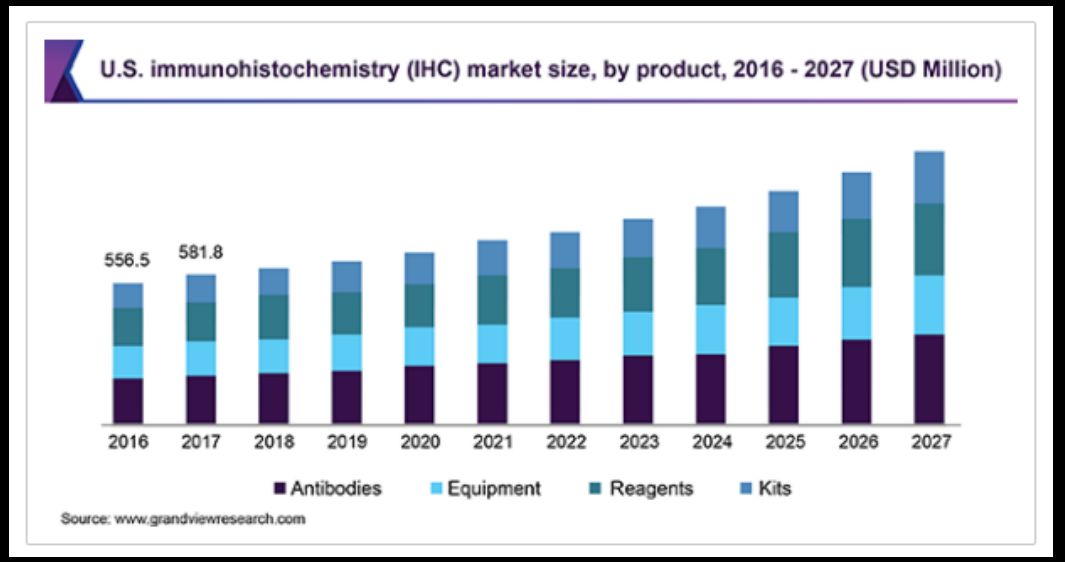


IHC – NordiQC workshop 2022

Does IHC have a future???

Molecular testing is here and can replace IHC!!!





IHC – NordiQC workshop 2022

… The biomarker protocol trap – Caution: not for faint-hearted lab personel !!!!!

Fixation
Time, Type, Volume

Decalcification
Preparation

Pre-analytic

Pre-treatment

Primary antibody
Clone, Dilution
Buffer, Time, Temp

Tissue
Type,
Laser
De-dif

Analytic

With 3 cho
variables in ea
4 million pr

icity

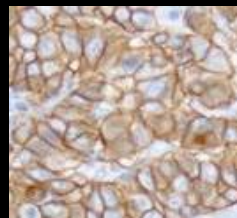
Development
Sensitivity,
Localization

Controlment

Post-analytic

Quantification
Reporting

Interpretation
Localization
Positive/Negative - cut-off level



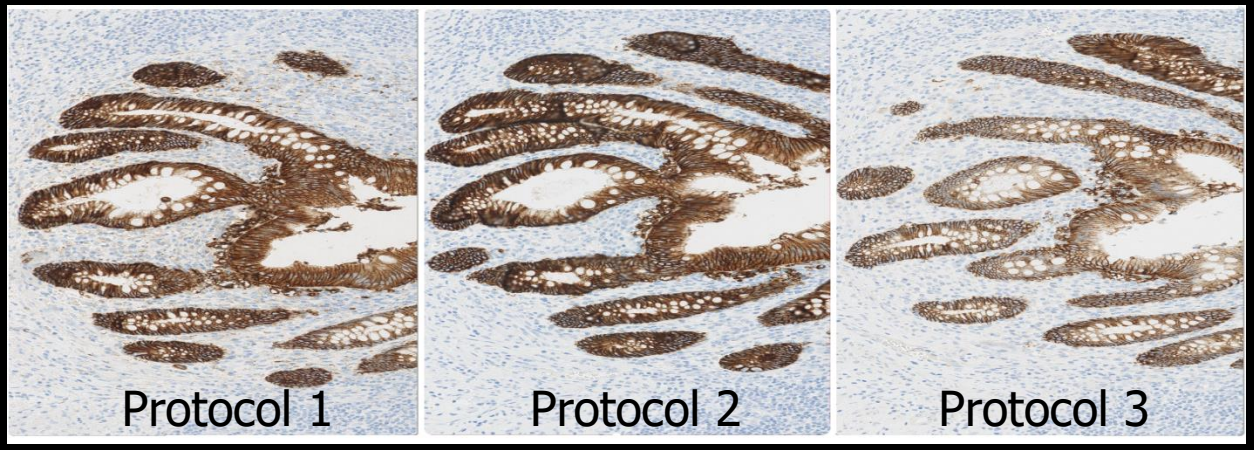
IHC – NordiQC workshop 2022

- IHC staining quality may vary between different laboratories depending on the individual calibration of methods and level of technical expertise present

- The quality of commercial available products for IHC as antibodies, ancillary reagents and guidelines for their use may be varying

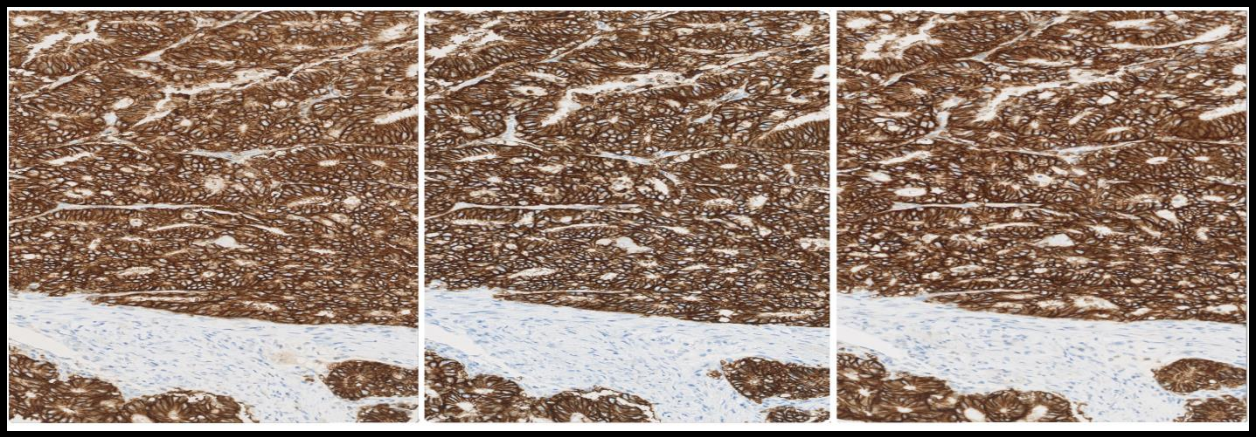
- Internal quality control will often not identify a poorly calibrated IHC system or varying quality of products giving insufficient or aberrant staining results

IHC – NordiQC workshop 2022

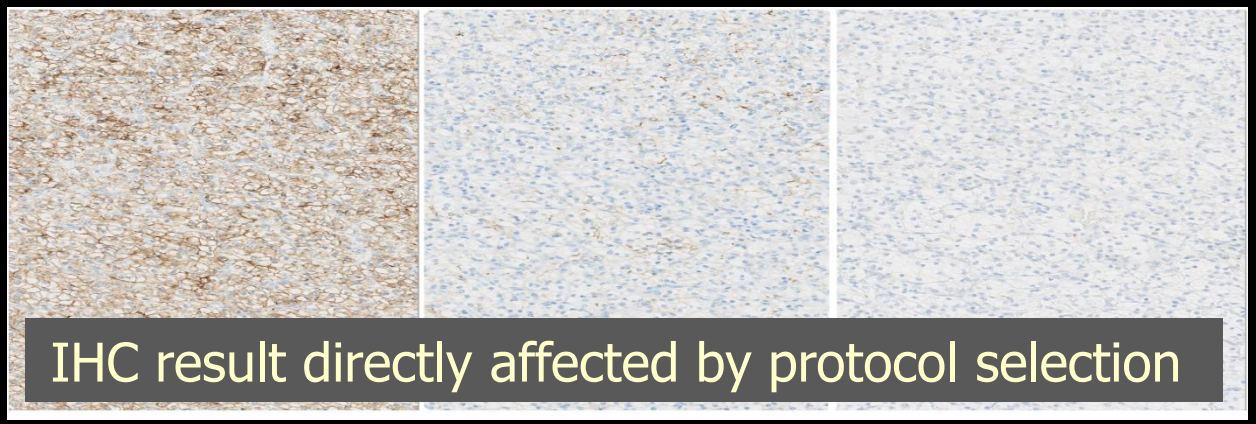


EPCAM calibration & validation challenge

Normal colon mucosa (6/6), (6/6), (6/6)



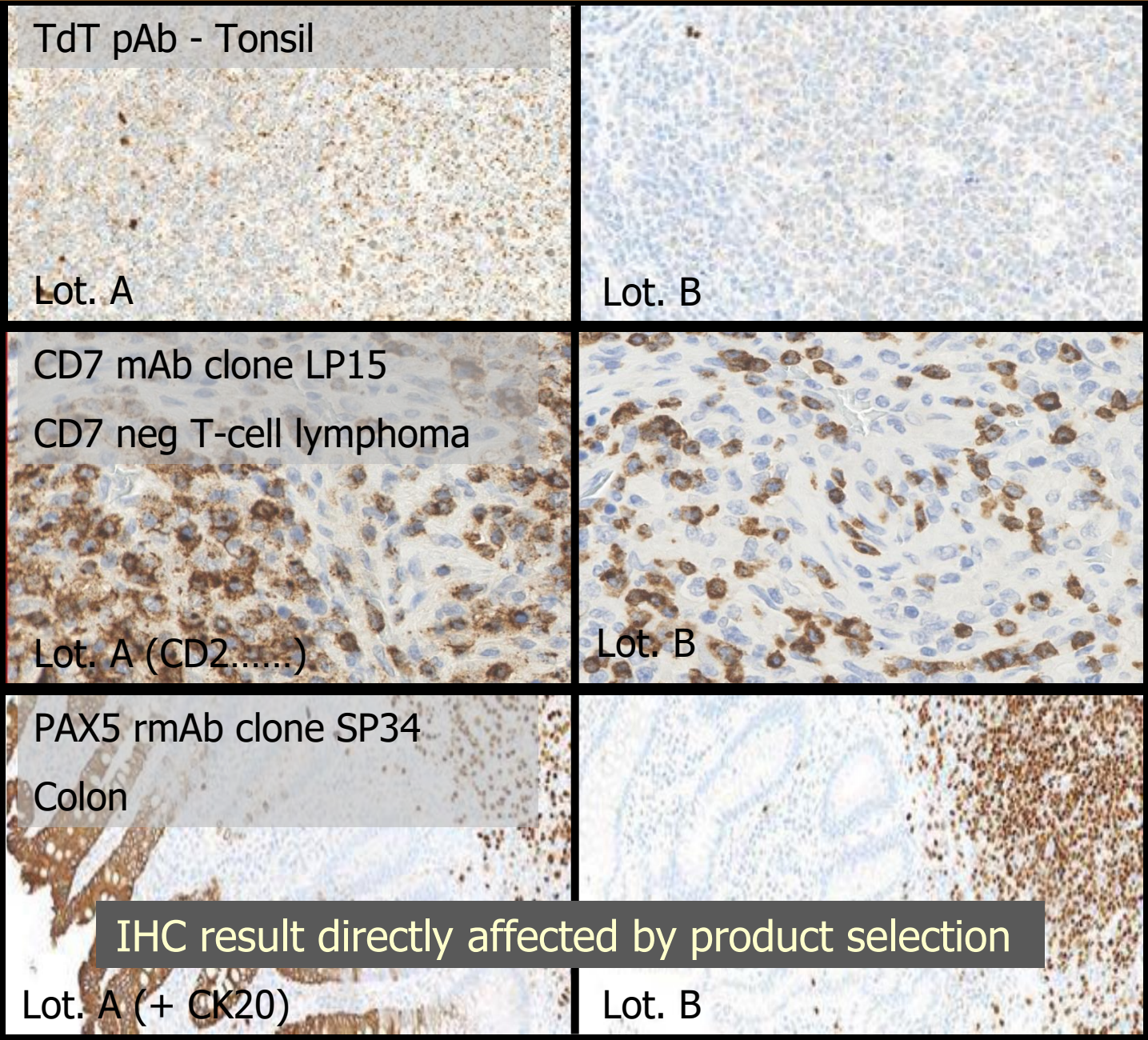
Colon adenocarcinoma (63/64), (63/64), (62/64)



Renal clear cell carc. (4/5), 2(5), (0/5)

IHC result directly affected by protocol selection

IHC – NordiQC workshop 2022

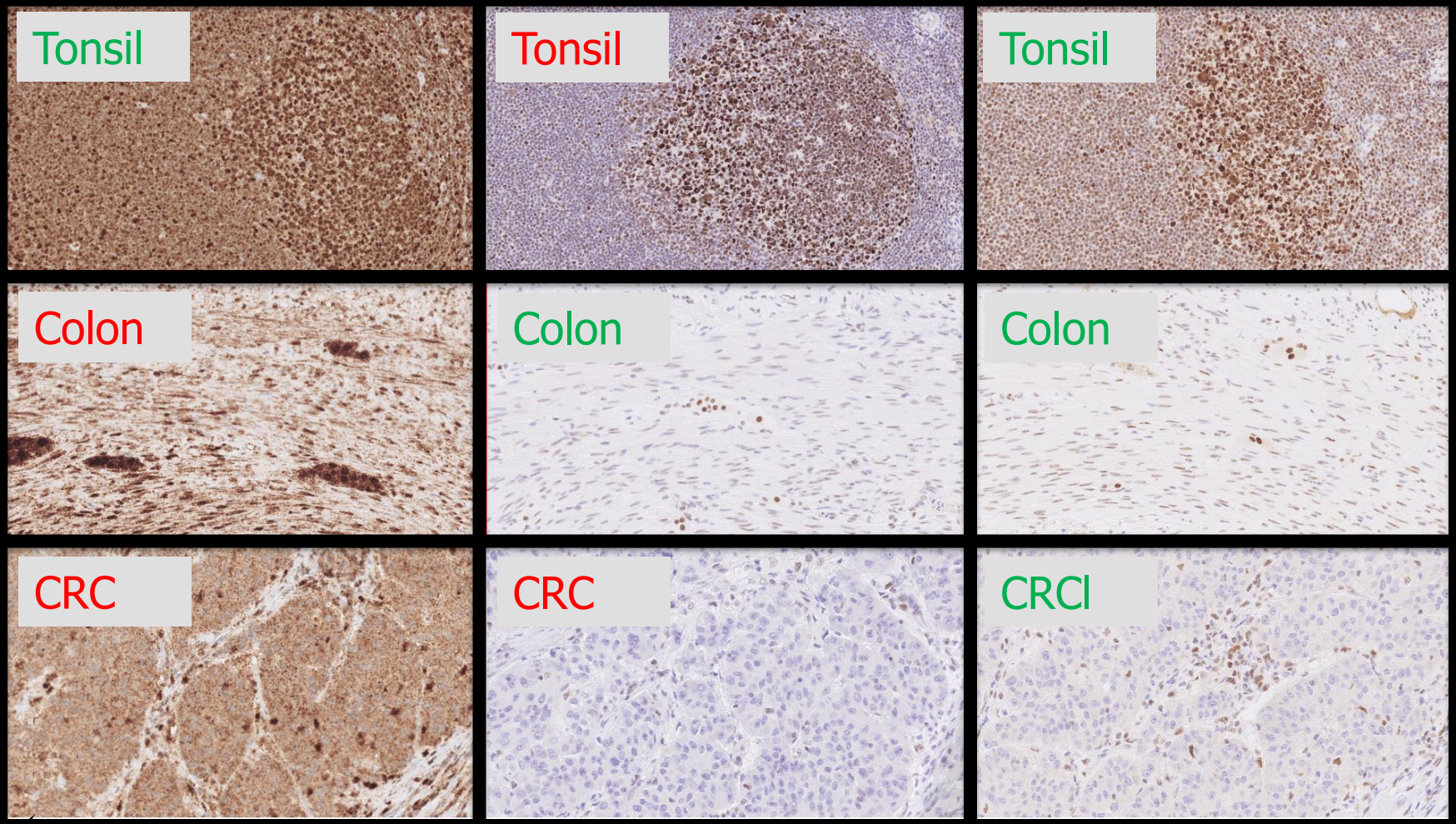


FP staining reactions

Not identified by negative reagent controls or use of recommneded positive tissue controls.

The FP reaction would only be identified by use of different neg. tissue controls. Neg. reagent control would give a neg. reaction thus provide a ”false security”

IHC – NordiQC workshop 2022



IHC MMR – PMS2

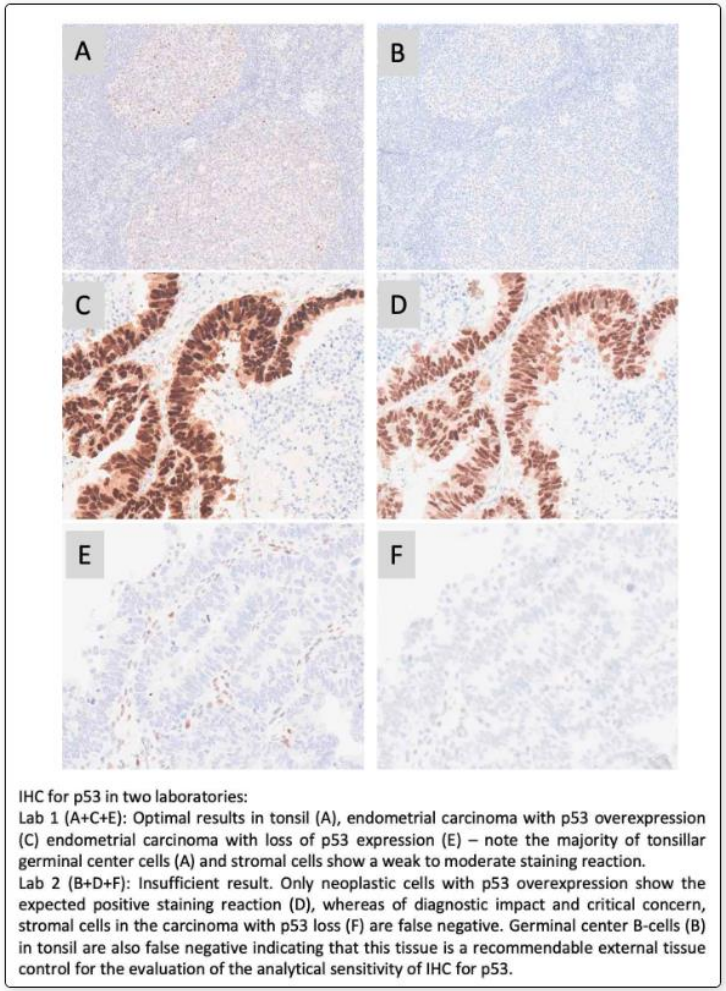
Control tissues to monitor level of technical sensitivity & specificity

IHC result verified by right control selecetion

www.nordiqc.org

NordiQC

Info ▾ Modules ▾ Assessments Protocols Controls Events ▾ Login



IHC for p53 in two laboratories:
Lab 1 (A+C+E): Optimal results in tonsil (A), endometrial carcinoma with p53 overexpression (C) endometrial carcinoma with loss of p53 expression (E) – note the majority of tonsillar germinal center cells (A) and stromal cells show a weak to moderate staining reaction.
Lab 2 (B+D+F): Insufficient result. Only neoplastic cells with p53 overexpression show the expected positive staining reaction (D), whereas of diagnostic impact and critical concern, stromal cells in the carcinoma with p53 loss (F) are false negative. Germinal center B-cells (B) in tonsil are also false negative indicating that this tissue is a recommendable external tissue control for the evaluation of the analytical sensitivity of IHC for p53.

Results - Run 65, C11

11-Jul-2022
The results for the runs 65, C1 are now available on the website. Individual results can be seen after logging in. Protocol submission for the next runs 66, B34, H22, C12 is already open.

All news

Events

NordiQC Workshop in Diagnostic Immunohistochemistry 2022
5–7 Oct 2022: Aalborg, Denmark

NordiQC Workshop in Diagnostic Immunohistochemistry 2023
4–6 Oct 2023: Aalborg, Denmark

Important dates

Run 66, B34, H22, C12
Slide return deadline
10 Oct 2022
Publication of results
17 Dec 2022

Questions

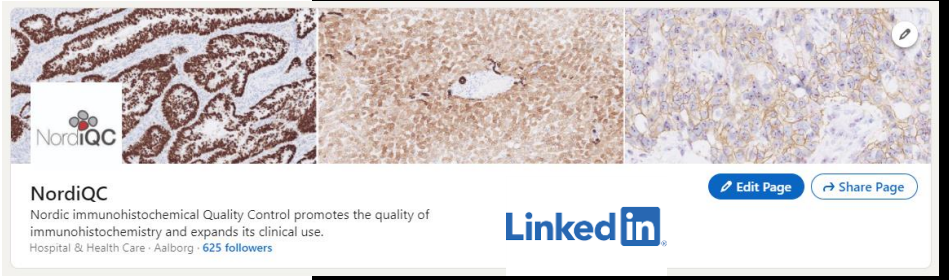
Check out our FAQ (Frequently asked questions) or contact us

Overview

Number of active labs: 623
from 58 different countries.

Participants by module

Module	n	Countries
General Module	458	48
Breast Cancer Module	497	52
HER2-ISH Module	282	43
Companion Diagnostic Module	295	42



IHC – NordiQC focus areas & working principles

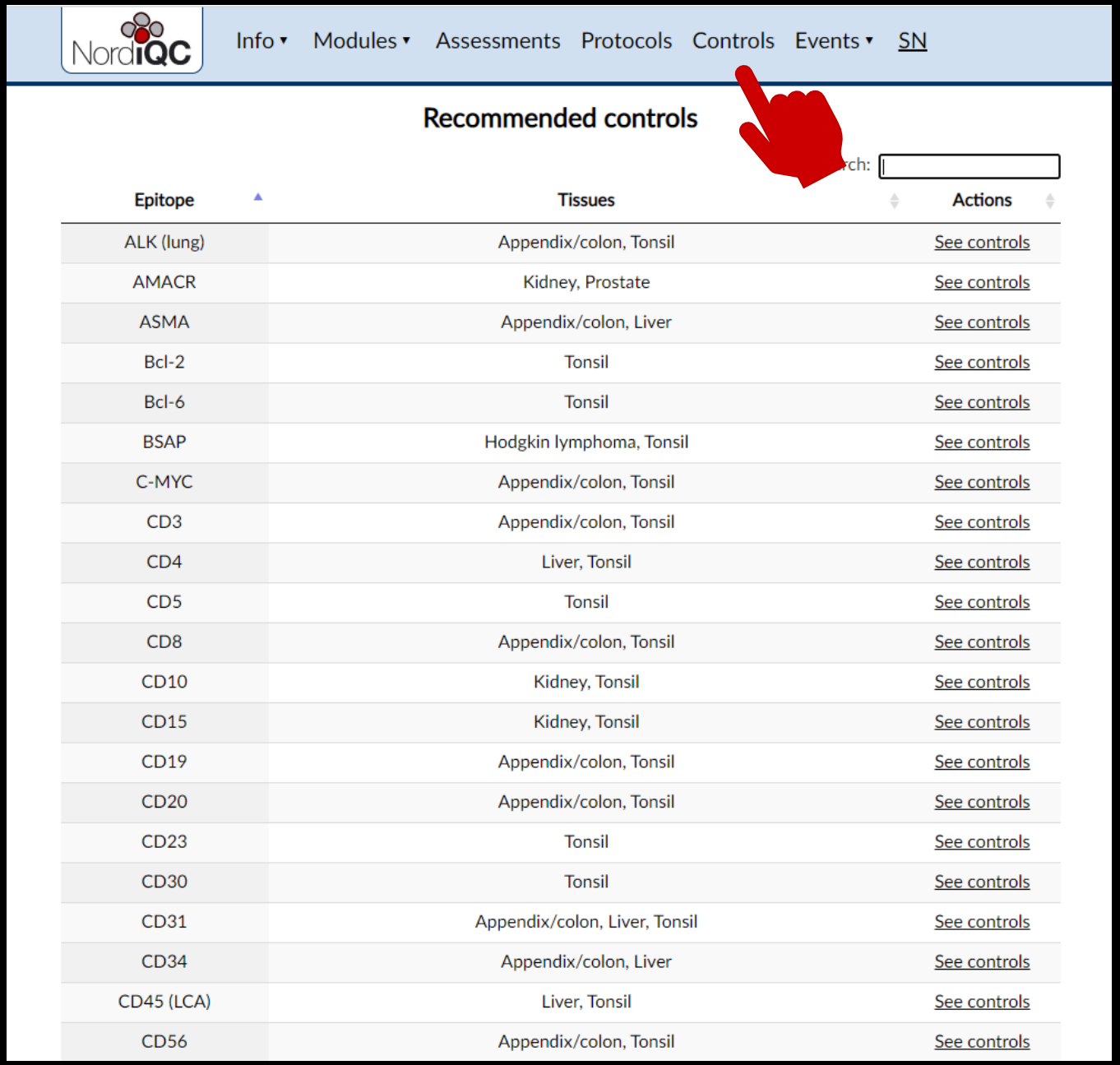
Central assessment with consensus between experienced pathologists and biomedical scientists

- Correlate staining results with central protocol parameters in order to identify
  - Successful and less successful Abs
  - Appropriate and inappropriate protocol settings
  - Staining platform issues
  - Reliable control tissues

- Publish general results on an open website

- E-mail individual results to the participants
  - Specific explanations for insufficient results
  - Tailored recommendations for improvement

IHC – NordiQC workshop 2022



NordiQC Info ▾ Modules ▾ Assessments Protocols Controls Events ▾ SN

Recommended controls

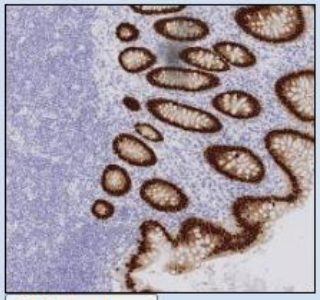
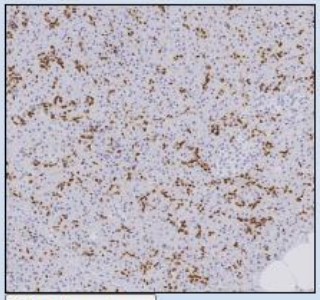
rch:

Epitope	Tissues	Actions
ALK (lung)	Appendix/colon, Tonsil	See controls
AMACR	Kidney, Prostate	See controls
ASMA	Appendix/colon, Liver	See controls
Bcl-2	Tonsil	See controls
Bcl-6	Tonsil	See controls
BSAP	Hodgkin lymphoma, Tonsil	See controls
C-MYC	Appendix/colon, Tonsil	See controls
CD3	Appendix/colon, Tonsil	See controls
CD4	Liver, Tonsil	See controls
CD5	Tonsil	See controls
CD8	Appendix/colon, Tonsil	See controls
CD10	Kidney, Tonsil	See controls
CD15	Kidney, Tonsil	See controls
CD19	Appendix/colon, Tonsil	See controls
CD20	Appendix/colon, Tonsil	See controls
CD23	Tonsil	See controls
CD30	Tonsil	See controls
CD31	Appendix/colon, Liver, Tonsil	See controls
CD34	Appendix/colon, Liver	See controls
CD45 (LCA)	Liver, Tonsil	See controls
CD56	Appendix/colon, Tonsil	See controls

IHC – NordiQC workshop 2022

NordiQC Info ▾ Modules ▾ Assessments Protocols Controls Events ▾ SN

CDX2 - CDX2

Control type	Positive tissue control High expression level	Positive tissue control Low expression levels	Negative tissue control
Tissue	Appendix/colon	Pancreas	Tonsil
Description	All epithelial cells must show a strong nuclear staining reaction. *Note, a weak cytoplasmic staining reaction in CDX2 positive cells can be seen and should be accepted if signal-to-noise ratio otherwise is acceptable.*	The vast majority of epithelial cells of intercalated ducts must show a weak to moderate nuclear staining reaction.	No staining reaction should be seen. *Note, dispersed lymphocytes can show a faint nuclear staining reaction.*
Example	 Click to enlarge	 Click to enlarge	 Click to enlarge

Back

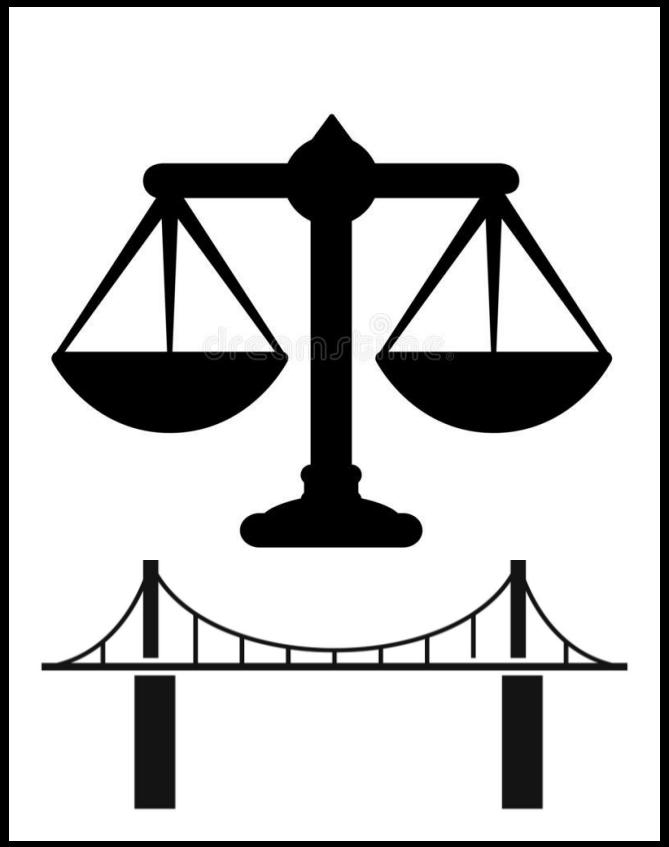
- Available for NordiQC participants
- Tissues
- Purpose
- Reaction patterns
- Online scans accessible

IHC – NordiQC workshop 2022

Aim for Workshop 2022 is to focus on knowledge sharing

Scientists

Heidi
Tanya
Irena
Michael
Donald
Søren



Pathologists

Rasmus
Steve
Anne Vibeke
Henrik

IHC – NordiQC workshop 2022

Workshop in Diagnostic Immunohistochemistry
Aalborg University Hospital, October 5-7th 2022

PROGRAM

Wednesday, October 5th

09:15 – 10:00		*Arrival and registration, coffee*	
10:00 – 10:15	**15**	Welcome – Introduction	SN
10:15 – 11:00	**45**	IHC principles: The technical test approach – pre-analytical phase	SN
11:15 – 12:00	**45**	IHC principles: The technical test approach - analytical phase I	MB
12.00 – 12:15	**15**	Discussion and summary of lectures	
12:15 – 13:15	**60**	*Lunch*	
13:15 – 14:00	**45**	IHC principles: The technical test approach - analytical phase II	MB
14:15 – 14:30	**15**	Discussion and summary of lectures	
14:30 – 15:15	**45**	IHC principles: The technical test approach – Tissue tool box for controls	SN
15:15 – 15.35	**20**	*Coffee*	
15.35 – 16:20	**45**	Validation and verification process for IHC – what, why and how?	DVH
16:20 – 16:30	**10**	Discussion and summary of lecture	
16.30 – 18.00		*Social arrangement (optional)*	

IHC – NordiQC workshop 2022

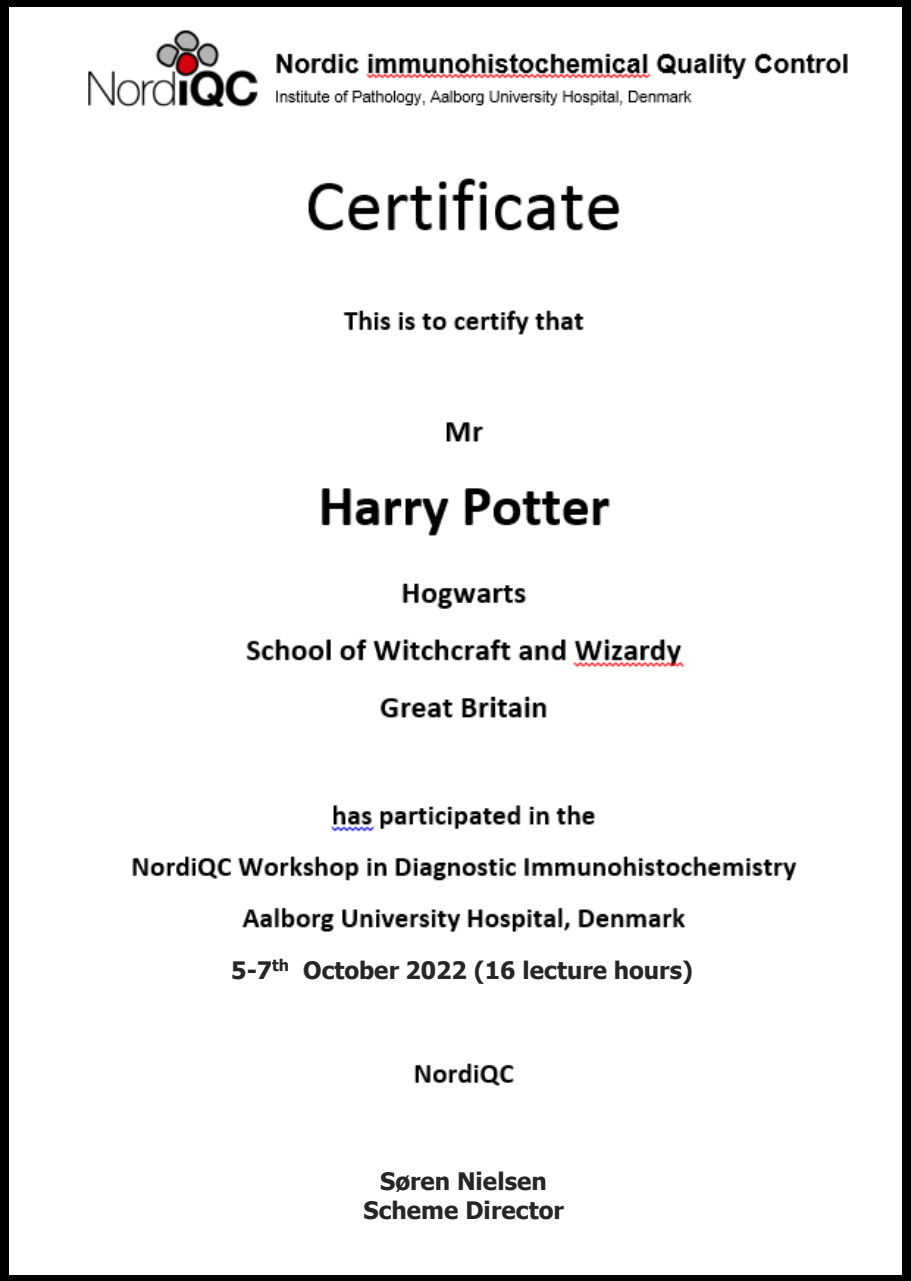
Thursday, October 6th			
08:30 – 09:15	**45**	The ur…iagnostic use	RR
09:25 – 09:50	**25**	Nordi…ocols and controls	TJ
09:50 – 10:10	**20**	*Coffee*	
10:10 – 10:55	**45**	Hemat…gnostic use	SH
11:05 – 11:30	**25**	Nordi…ocols and controls	TJ
11.30 – 11:45	**15**	Discussion and summary of lectures	
11:45 – 12:30	**45**	Breast cancer: IHC for diagnostic use	AVL
12:30 – 13:30	**60**	*Lunch*	
13:30 – 13:55	**25**	NordiQC data: Antibody selection, pr…	
14.10 – 14:55	**45**	Lung cancer: IHC for diagnostic use	
14.55 – 15:10	**20**	Coffee	
15:10 – 15:35	**25**	NordiQC data: Antibody selection, pr…	
15:40 – 16:10	**30**	"The antibody graveyard"; Goodbye …	
16:10 – 16:30	**20**	Discussion and summary of lectures	
18:00 –		*Workshop dinner* – *Mortens Kro*	

The challenging day…….

IHC – NordiQC workshop 2022

Friday, October 7th			
08:15 – 09:05	**45**	Immunocytochemistry – overview, considerations and applications	ISK
09:05 – 09:50	**40**	Double/Multiplex staining – overview, considerations and applications	MB
09:50 – 10:10	**20**	*Coffee*	
10.10 – 10:50	**35**	IHC stainers – overview, pros and cons	SN
10:50 – 11:35	**40**	IHC in the time of molecular era – Predictive, diagnostic and prognostic markers	HH
11.35 – 11.50	**15**	Discussion and summary of lectures	
11:50 – 12:35	**40**	In Situ Hybridization – novel techniques	MB
12:35 – 13.00	**25**	Discussion and evaluation	
13:00 –		*Lunch (on-site or to-go), departure*	

IHC – NordiQC workshop 2022



Nordic immunohistochemical Quality Control
Institute of Pathology, Aalborg University Hospital, Denmark

Certificate

This is to certify that

Mr

Harry Potter

Hogwarts

School of Witchcraft and Wizardy

Great Britain

has participated in the

NordiQC Workshop in Diagnostic Immunohistochemistry

Aalborg University Hospital, Denmark

5-7th October 2022 (16 lecture hours)

NordiQC

Søren Nielsen
Scheme Director

Will be e-mailed

IHC – NordiQC workshop 2022

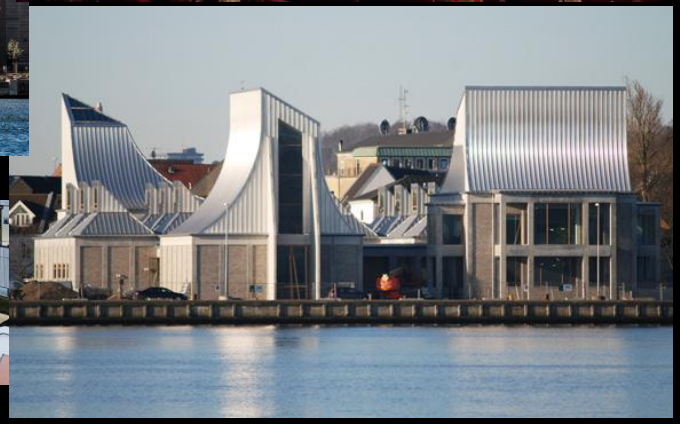
These are the 19 happiest cities in Europe, according to the people who live there

BUSINESS INSIDER

Will Martin

Feb. 6, 2016, 8:05 AM 312,207

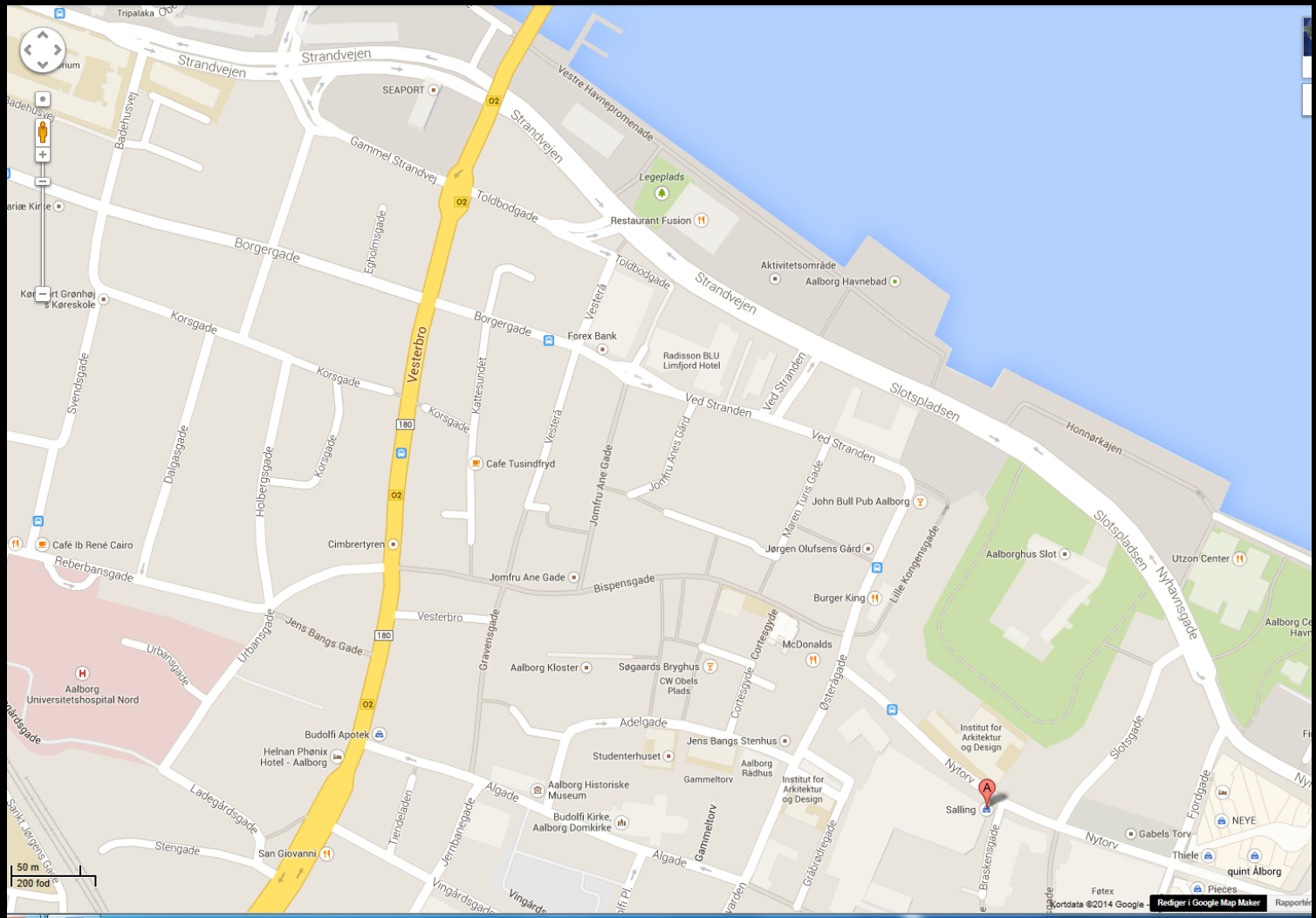
1. Aalborg – 72% very satisfied, 24% satisfied. The industrial city in the north of Denmark isn't exactly world famous, but utilities like a symphony orchestra, a world class university, and a beautiful waterfront, make it not surprising that Aalborg's citizens are the most satisfied in Europe.



IHC – NordiQC workshop 2022

IHC – NordiQC workshop 2022

Shops open till 17.30
Salling (warehouse) till 19.00



IHC – NordiQC workshop 2022

Wifi: network; AKKC Guest password; kongres2022

All final presentations will be available on www.nordiqc.org

Coffee / Tea / Water will be available all day long – "base" outside the lecture room.

Lunch served in the restaurant downstairs.

Toilets – just outside.