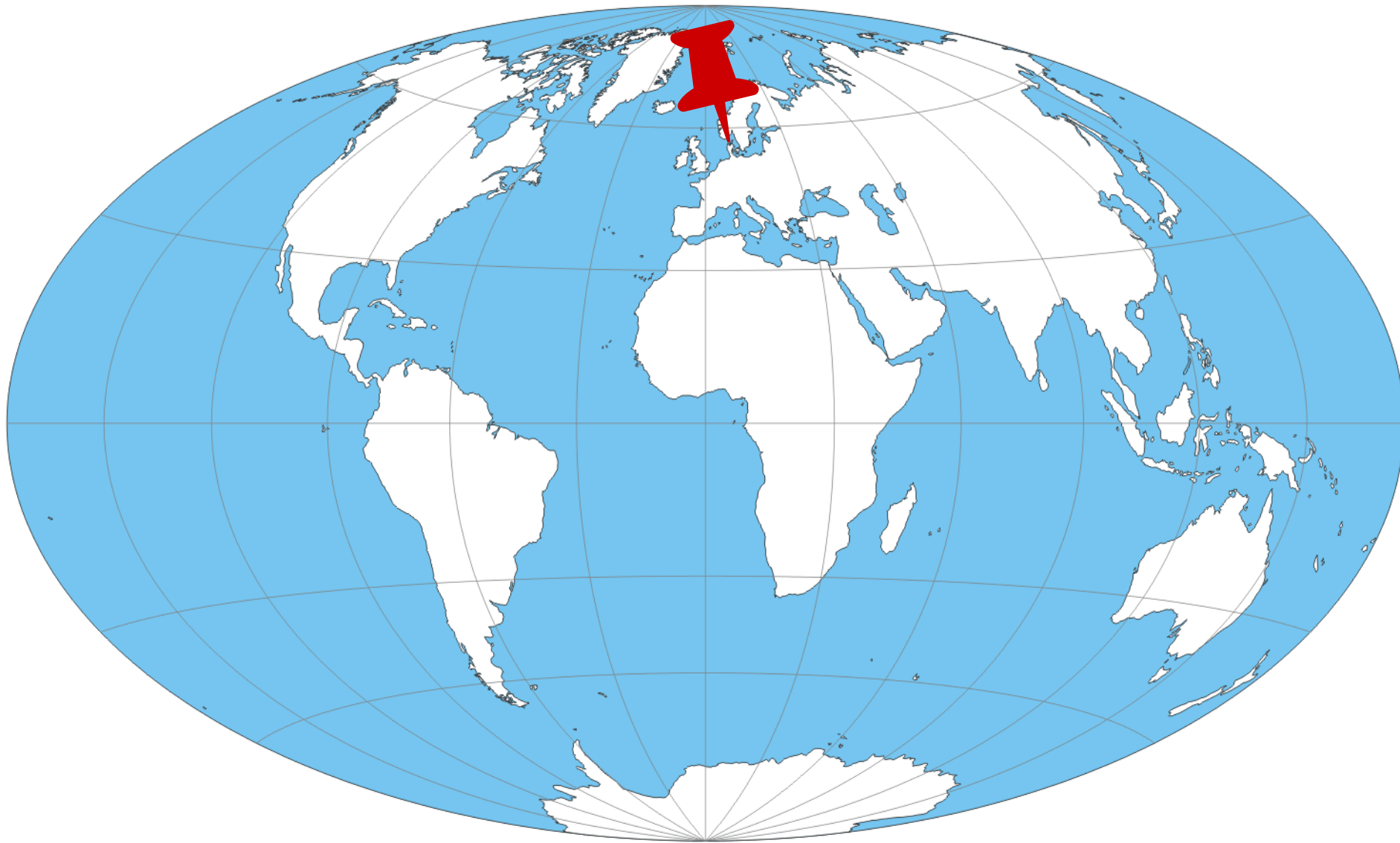




Workshop in Diagnostic Immunohistochemistry
Aalborg University Hospital, 29 Sept. - October 1 2021

Welcome To Aalborg

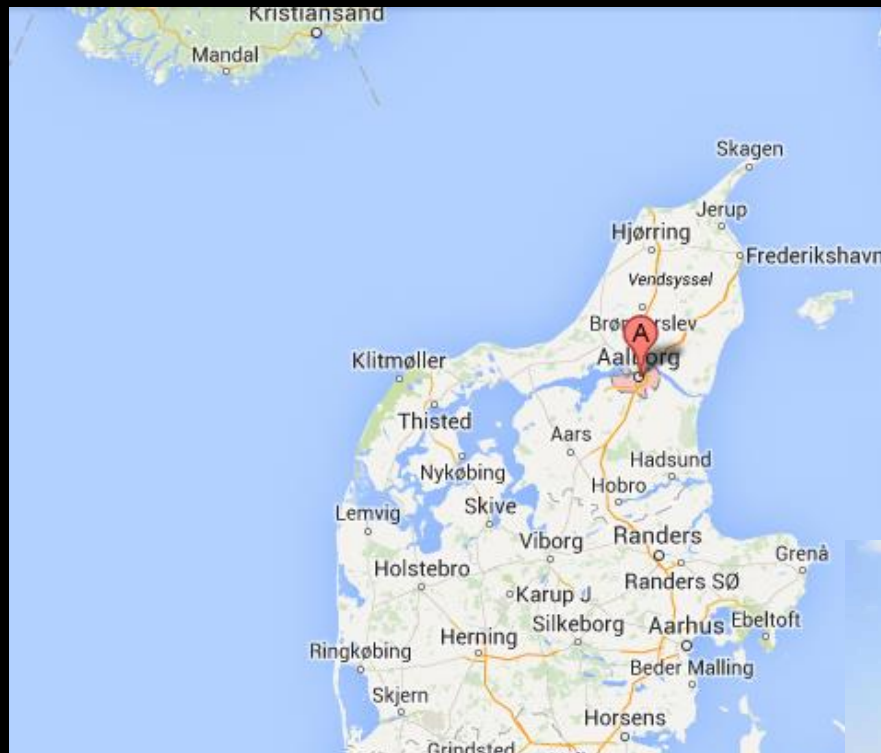
Søren Nielsen
Director, NordiQC
Aalborg University Hospital, Denmark



IHC – NordiQC workshop 2021



IHC – NordiQC workshop 2021





**Workshop in Diagnostic Immunohistochemistry
Aalborg University Hospital, 29 Sept. - October 1 2021**

59 participants - 14 countries

Workshop frames:

Approximately 16 lecture hours

Focus on technical parameters influencing IHC results

Review on diagnostic / clinical use of IHC

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,††† Søren 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

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 Berendr, MD, FRCPC,⁹ Donald Cook, MD, FRCPC,¹⁰
Blake Gilks, MD, FRCPC,¹¹ Gaynor Williams, MD, PhD,¹² Bayardo Perez-Ordóñez, 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, FRCPC¹³

CME/SAM

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
.....			

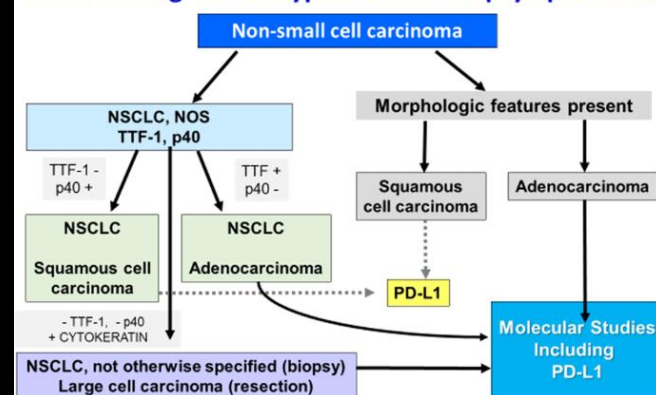
In practice more and more IHC tests become Type II tests:
Directly indicated

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.

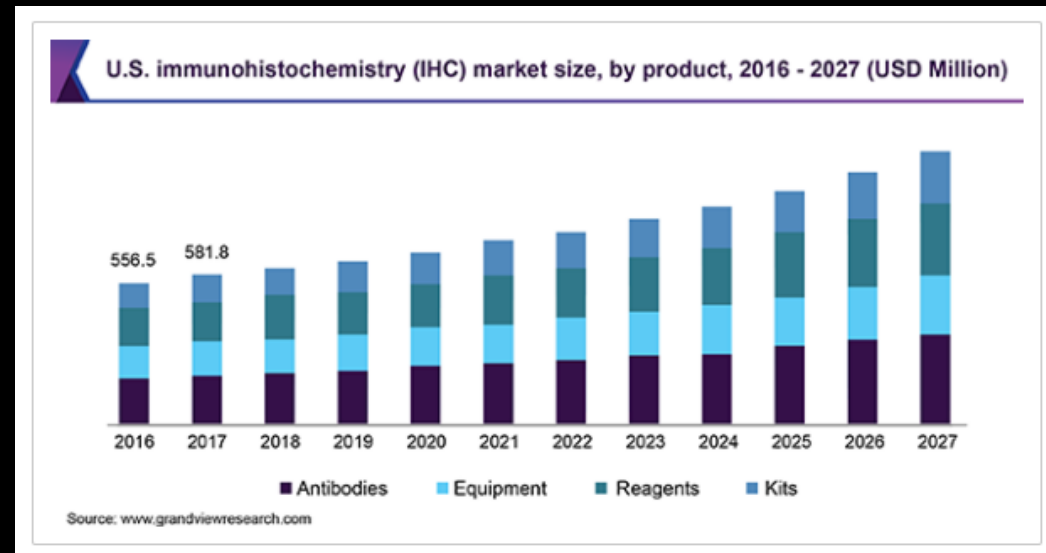
IHC	Area	Type I	Type II	Comment
p40 - lung	Carcinoma	Squamous		
TTF1- lung	Carcinoma	Adeno	Crizotinib,....	ALK, EGFR, ROS1...

Determining Tumor Type in Small Biopsy Specimens



Does IHC have a future???

Molecular testing is here and can replace IHC!!!



... 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

THE SUM OF ALL FEARS

Analytic

With 3 choices
variables in each
4 million possibilities

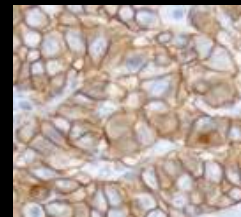
Specificity
Development
Sensitivity,
Localization

Controiment

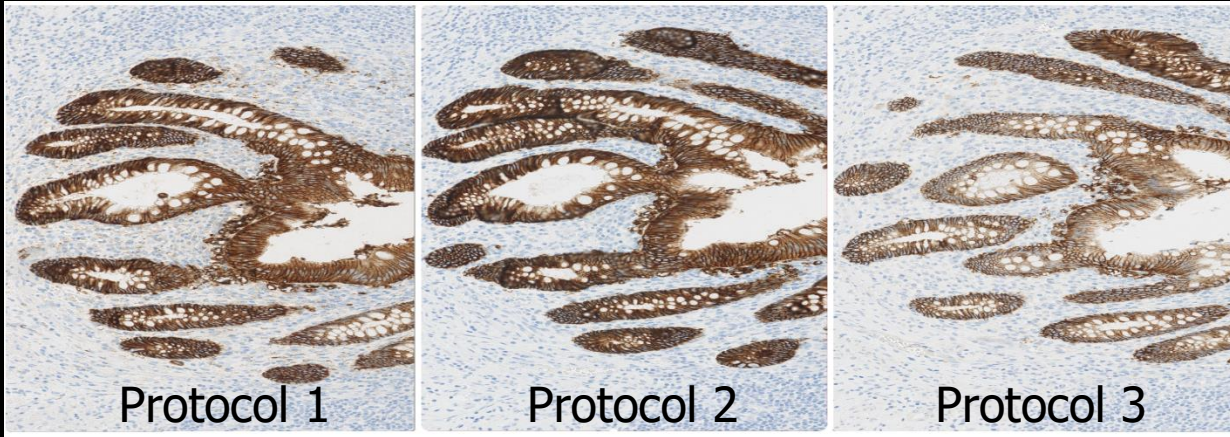
Post-analytic

Interpretation
Localization
Positive/Negative - cut-off level

Quantification
Reporting

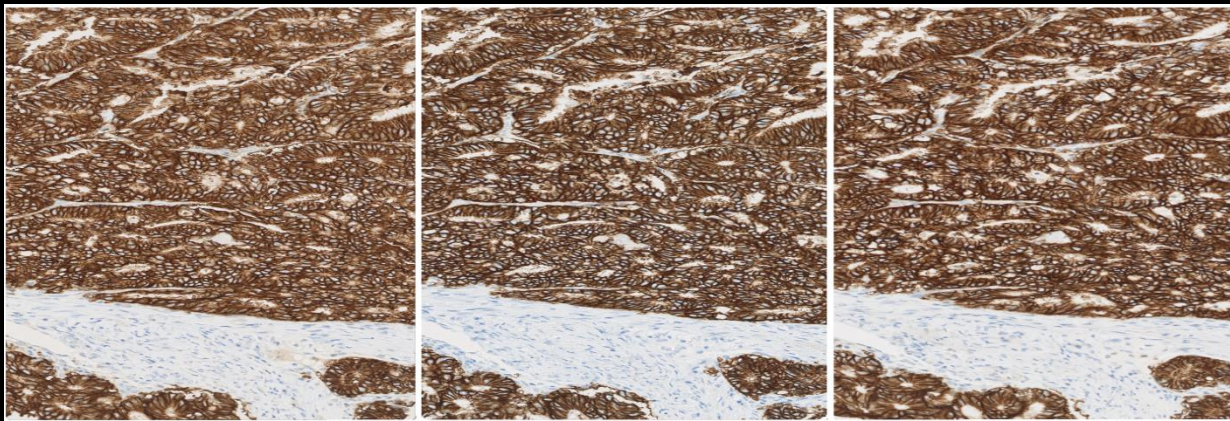


- IHC staining quality may vary between different laboratories depending on the individual calibration of methods and level of technical expertise present
- The quality of commercial available products for IHC as antibodies, ancillary reagents and guidelines for their use may be varying
- Internal quality control will often not identify a poorly calibrated IHC system or varying quality of products giving insufficient or aberrant staining results



EPCAM calibration & validation challenge

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

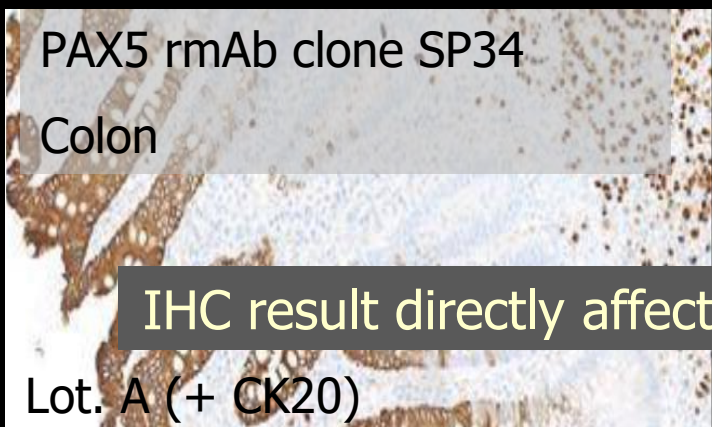
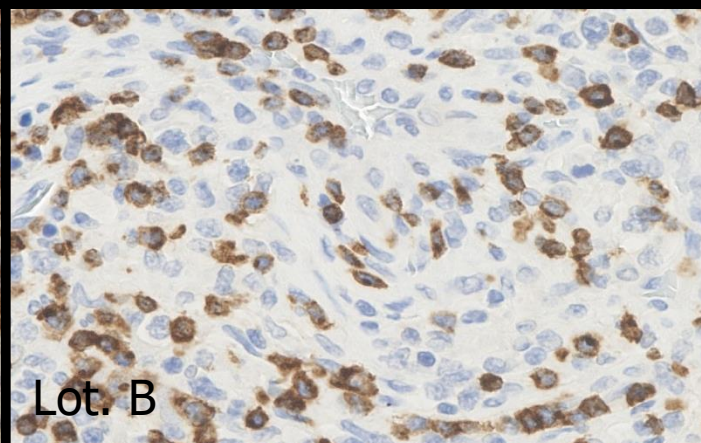
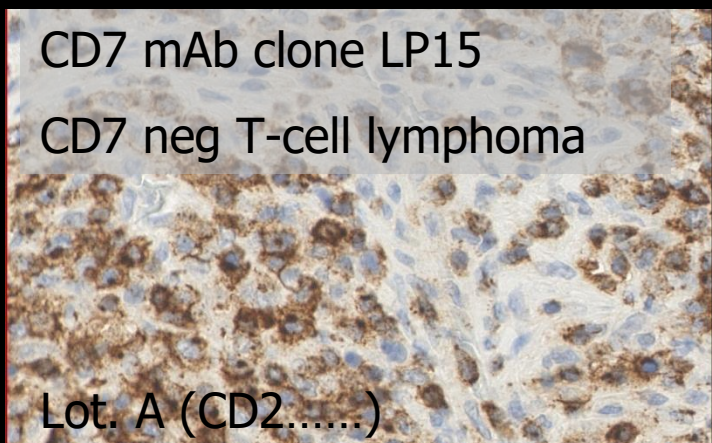
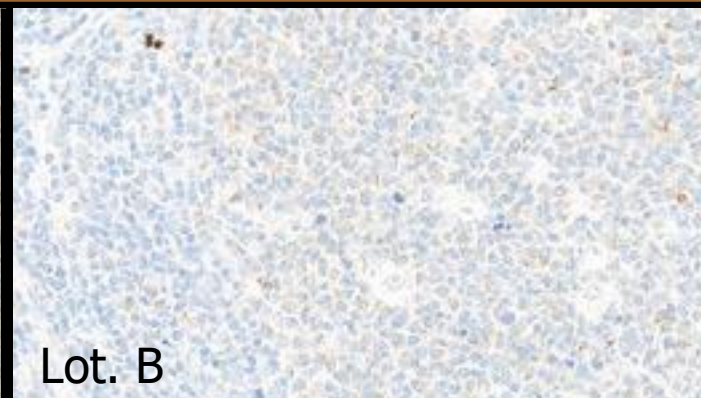
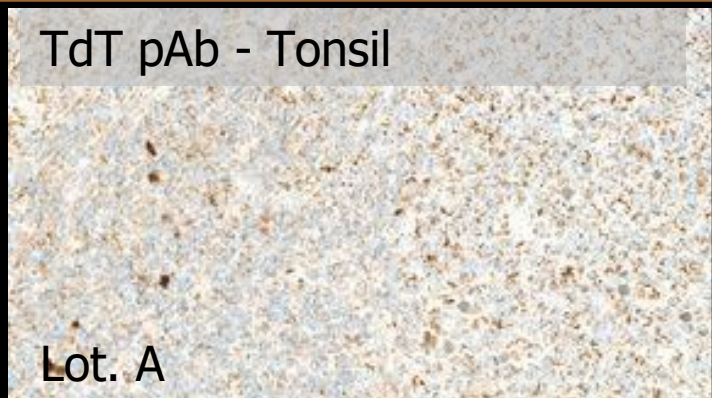


**Colon adenocarcinoma
(63/64), (63/64), (62/64)**



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

IHC result directly affected by protocol selection

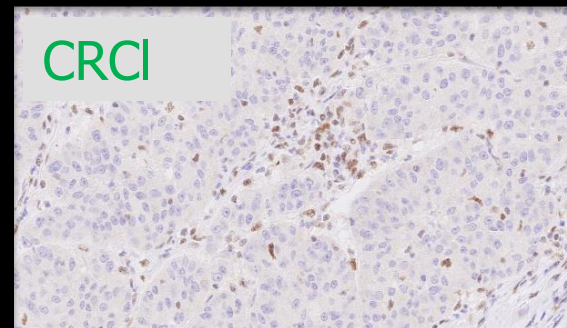
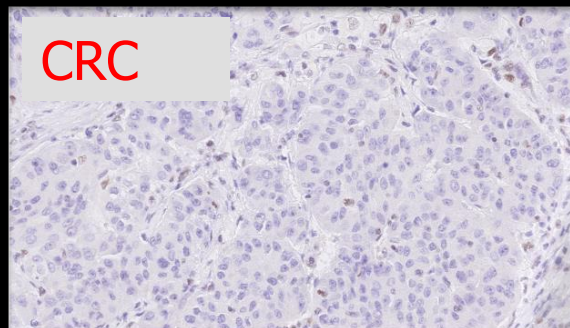
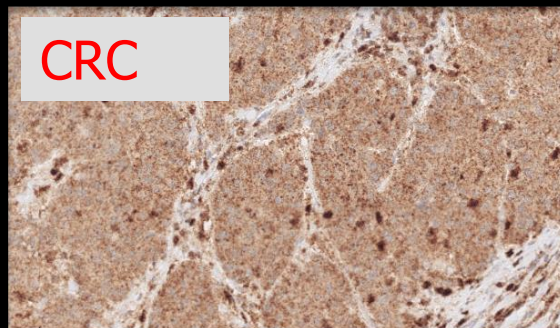
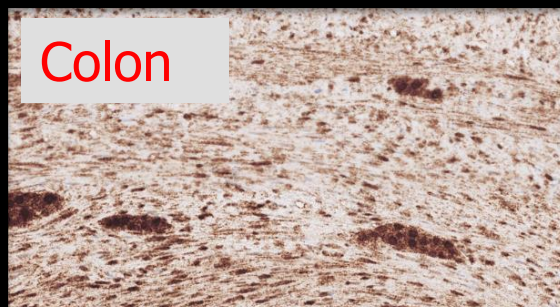
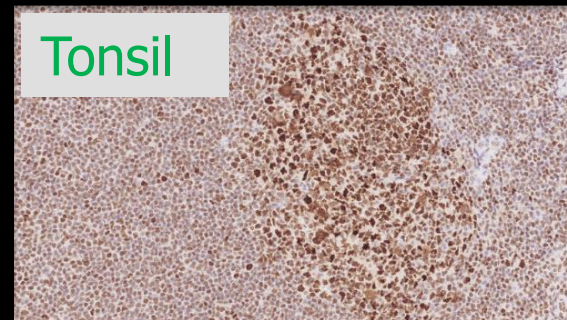
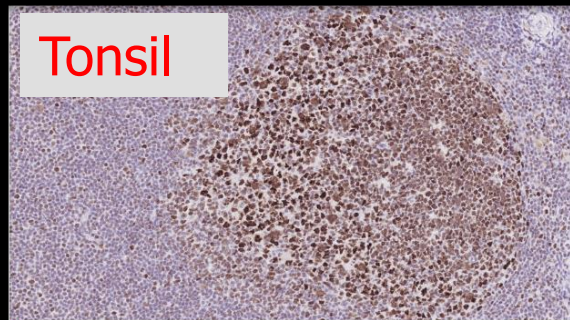
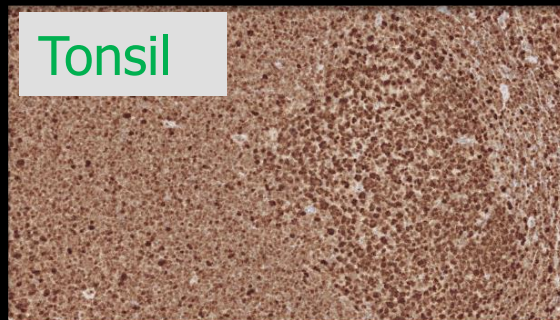


IHC result directly affected by product selection

FP staining reactions

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

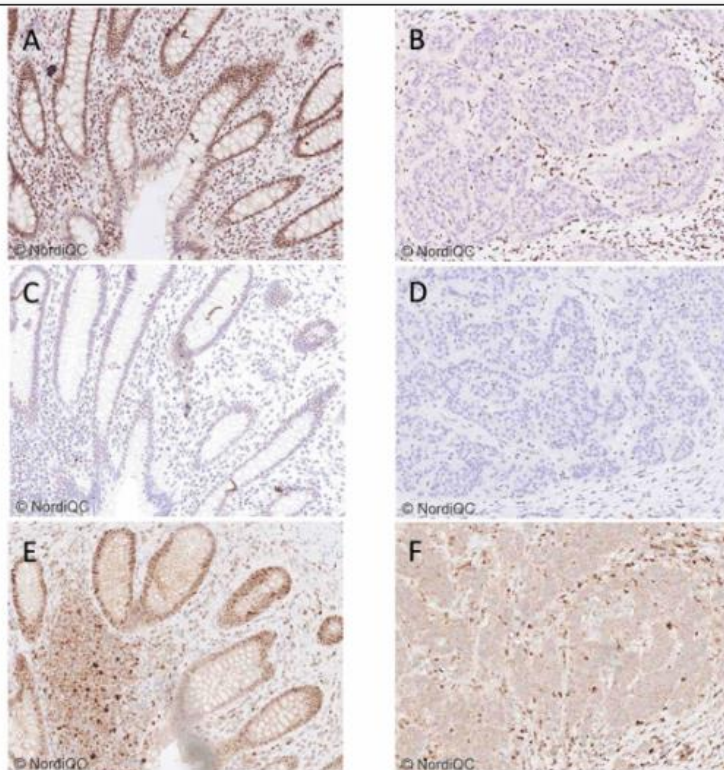
The FP reaction would only be identified by use of different neg. tissue controls. Neg. reagent control would give a neg. reaction thus provide a "false security"



IHC MMR – PMS2

Control tissues to monitor level of technical sensitivity & specificity

IHC result verified by right control selection



IHC for PMS2 in three laboratories:

Lab 1 (A+B): Optimal results in appendix (A) and colon adenocarcinoma with loss of PMS2 (B) using the rmAb clone EP51 within an accurately calibrated IHC assay.

Lab 2 (C+D): Insufficient result using the rmAb clone EP51 by protocol settings with too low level of analytical sensitivity. Stromal cells being internal control in the colon adenocarcinoma are false negative.

Lab 3 (E+F): Insufficient result using the mAb clone A16-4 giving an excessive cytoplasmic staining reaction compromising the evaluation of nuclear PMS2 expression in the colon adenocarcinoma.

Events

[NordiQC Workshop in Diagnostic Immunohistochemistry 2021](#)

29 Sep 2021 – 1 Oct 2021: Aalborg, Denmark

[NordiQC Workshop in Diagnostic Immunohistochemistry 2022](#)

5–7 Oct 2022: Aalborg, Denmark

Important dates

Run 63, B32, H20, C10

Slide return deadline

10 Oct 2021

Publication of results

10 Dec 2021

Questions

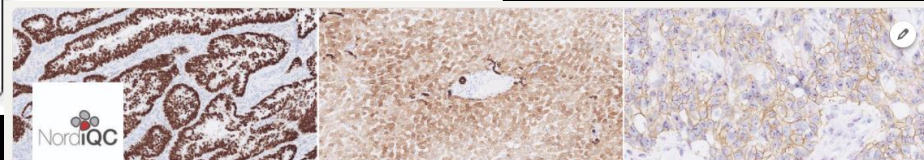
Check out our [FAQ](#) (Frequently asked questions) or [contact us](#)

Overview

Number of active labs: 648
from 64 different countries.

Participants by module

Module	n	Countries
General Module	429	48
Breast Cancer Module	475	54
HER2-ISH Module	272	48
Companion Diagnostic Module	327	44



NordiQC

Nordic immunohistochemical Quality Control promotes the quality of immunohistochemistry and expands its clinical use.
Hospital & Health Care · Aalborg · 625 followers

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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



Info ▾ Modules ▾ Assessments Protocols Controls Events ▾ [SN](#)

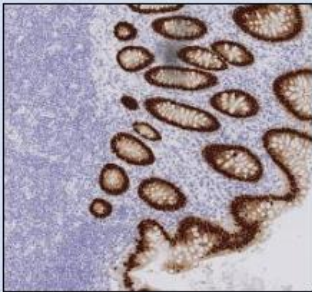
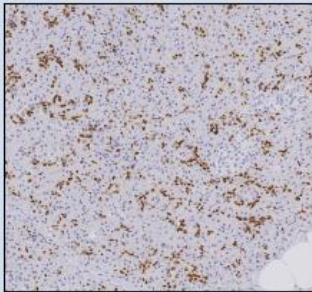
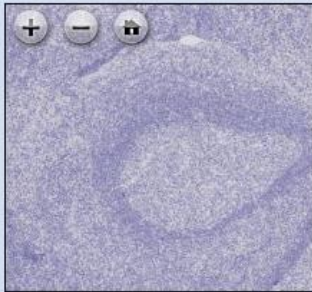
Recommended controls



Search:

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

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	<p>All epithelial cells must show a strong nuclear staining reaction.</p> <p><i>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.</i></p>	<p>The vast majority of epithelial cells of intercalated ducts must show a weak to moderate nuclear staining reaction.</p>	<p>No staining reaction should be seen.</p> <p><i>Note, dispersed lymphocytes can show a faint nuclear staining reaction.</i></p>
Example	 <p>Click to enlarge</p>	 <p>Click to enlarge</p>	 <p>Click to enlarge</p>

Back

Available for NordiQC participants

Tissues

Purpose

Reaction patterns

Online scans accessible

IHC – NordiQC workshop 2021

Aim for Workshop 2021 is to focus on knowledge sharing

Scientists

Heidi
Tanya
Michael
Donald
Søren



Pathologists

Rasmus
Steve
Anne Vibeke
Henrik



PROGRAM

Wednesday, September 29nd

09:15 – 10:00		<i>Arrival and registration, coffee</i>	
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	<i>Lunch</i>	
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	<i>Coffee</i>	
15:35 – 16:20	45	Validation and verification process for IHC – what, how and why? (pre-recorded / virtual)	DVH
16:20 – 16:30	15	Discussion and summary of lecture	
16:30 – 18:00		<i>Social arrangement (optional)</i>	

IHC – NordiQC workshop 2021

Thursday, September 30th

08:30 – 09:15	45	The u
09:25 – 09:50	25	Nordi
09:50 – 10:10	20	Coffee
10:10 – 10:55	45	Lung c
11:05 – 11:30	25	Nordi
11:30 – 11:45	15	Discus
11:45 – 12:30	45	Breast cancer: IHC for diagnostic use
12:30 – 13:30	60	Lunch
13:30 – 13:55	25	NordiQC data: Antibody selection, p
14:10 – 14:55	45	Hematolymphoid neoplasms IHC for
14:55 – 15:10	20	Coffee
15:10 – 15:35	25	NordiQC data: Antibody selection, p
15:40 – 16:05	25	"The antibody graveyard"; Goodbye
16:10 – 16:30	20	Discussion and summary of lectures
18:00 –		Workshop dinner – Mortens Kro



diagnostic use	RR
ocols and controls	TJ
	HH
ocols and controls	HLK
	AVL



The challenging day.....

IHC – NordiQC workshop 2021

Friday, October 1th

08:30 – 09:15	45	IHC double stains – overview, considerations and applications	MB
09:20 – 10:00	30	Immunocytochemistry – overview, considerations and applications	SN
10:00 – 10:20	20	<i>Coffee</i>	
10:20 – 10:45	25	IHC stainers – overview, pros and cons	SN
10:50 – 11:35	45	In Situ Hybridization – novel techniques	MB
11:45 – 12.30	45	IHC in the time of molecular era – Predictive, diagnostic and prognostic markers	HH
12:30 – 12.45	15	Discussion and evaluation	
12:45 –		<i>Lunch (on-site or to-go), departure</i>	





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

September 29-1st October 2021 (16 lecture hours)


NordiQC

Søren Nielsen
Scheme Director

Will be e-mailed

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

Will Martin 

© Feb. 6, 2016, 8:05 AM  312,207

BUSINESS
INSIDER

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.



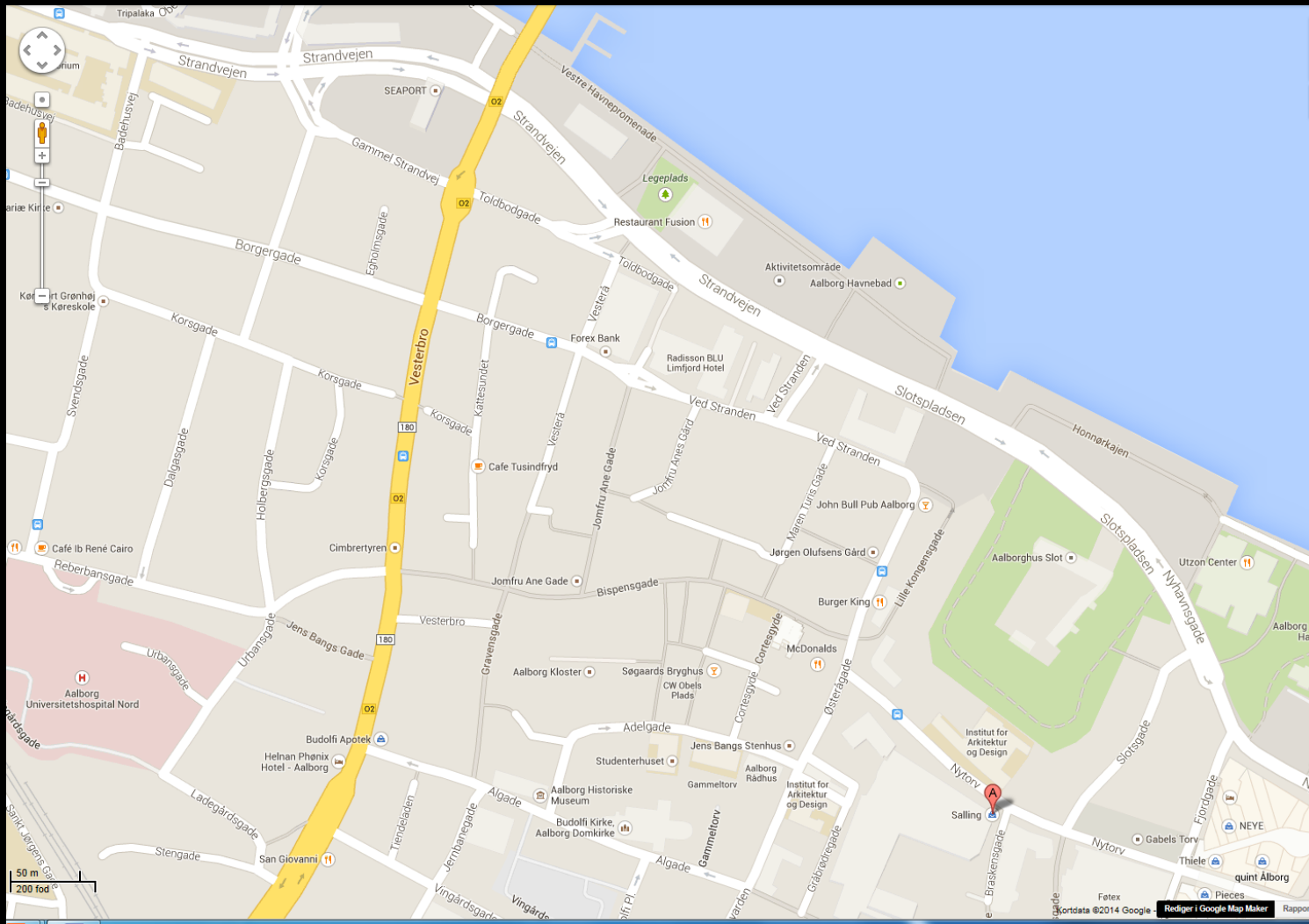
IHC – NordiQC workshop 2021



IHC – NordiQC workshop 2021

Shops open till 17.30

Salling (warehouse) till 20.00



Wifi: network; AKKC Guest password; kongres2021

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.