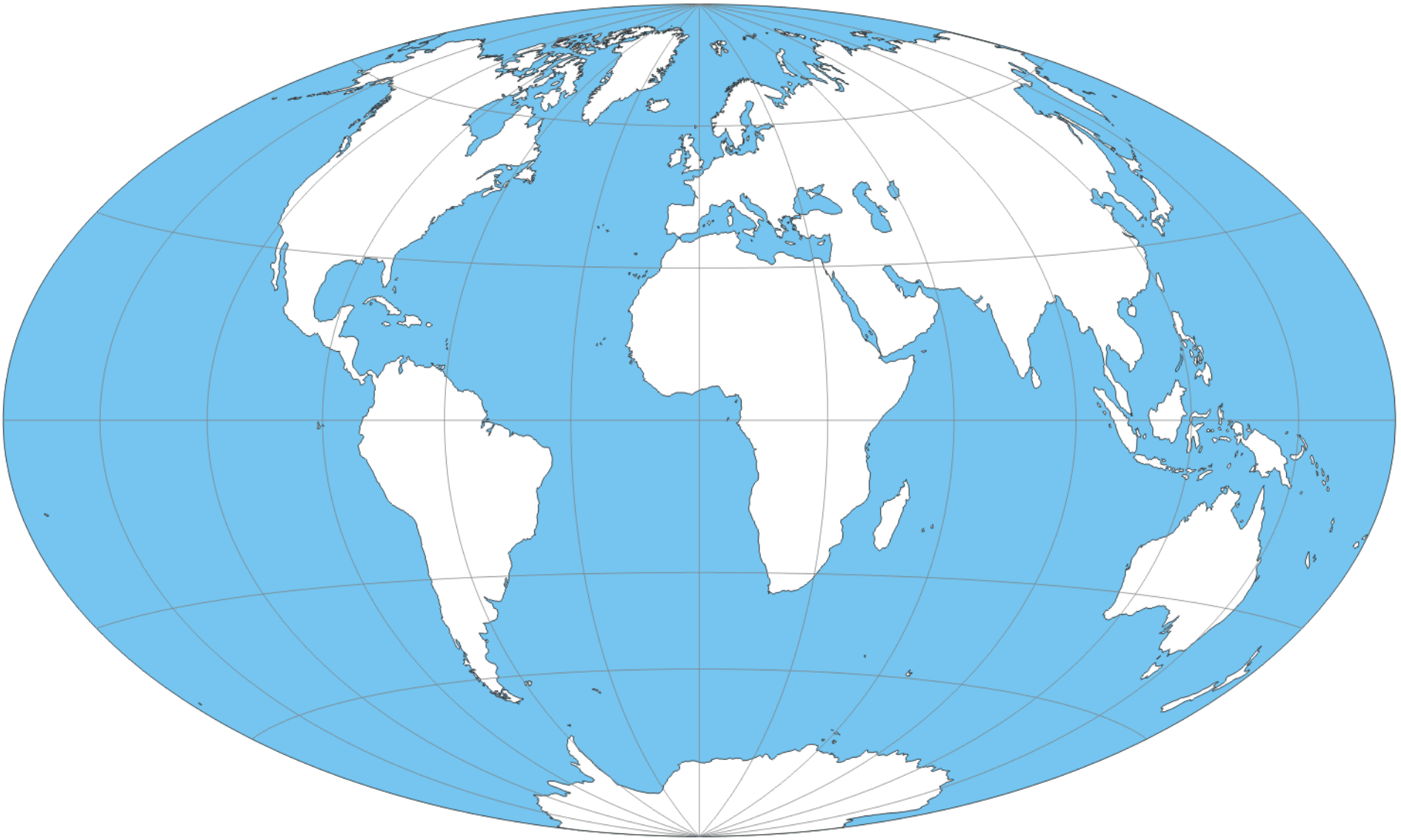
NordiQC

Workshop in Diagnostic Immunohistochemistry
Aalborg University Hospital, September 19th – 21st 2016

Welcome To Aalborg

Søren Nielsen
Project coordinator & Scheme Manager NordiQC
Aalborg University Hospital, Denmark

IHC – NordiQC workshop 2016



IHC – NordiQC workshop 2016

IHC – NordiQC workshop 2016

Workshop in Diagnostic Immunohistochemistry
Aalborg University Hospital, September 19th – 21st 2016

56 participants - 12 countries

Workshop frames:

- Approximately 18 lecture hours
- Focus on technical parameters influencing IHC results
- Review on diagnostic / clinical use of IHC

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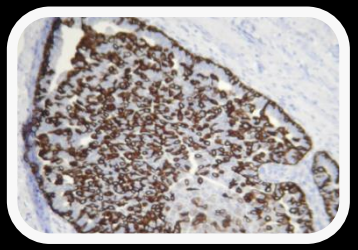
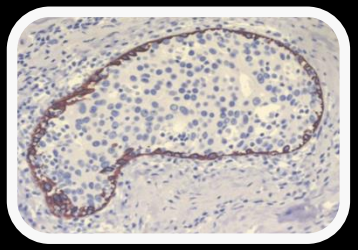
Hyperplasia or In-situ

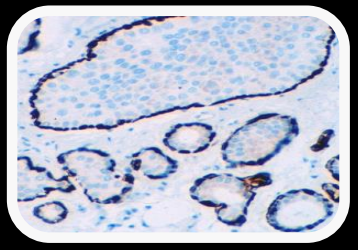
CK5, CK14, Heavy chain myosin, p63

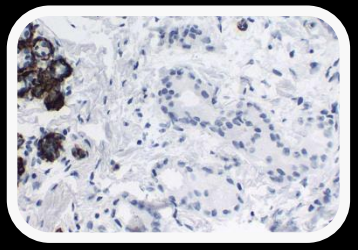




In-situ or invasive

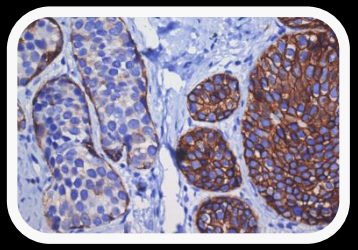
CK5, CK14, Heavy chain myosin, p63

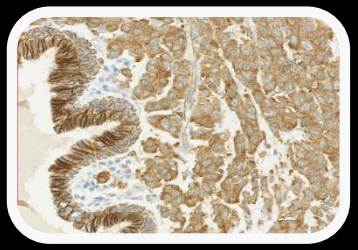




Lobular or ductal lesion

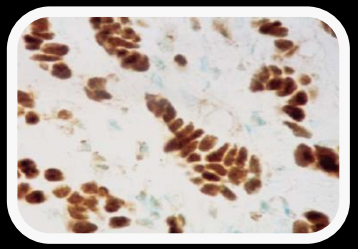
E-cadherin, p120

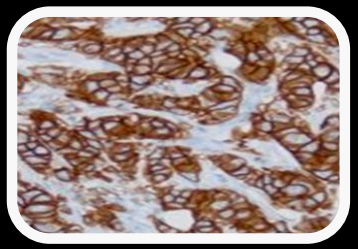




Predictive - Prognostic

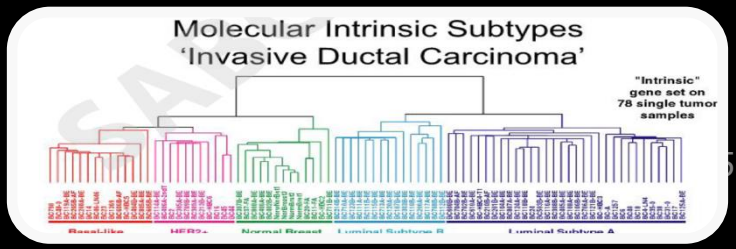
ER, PR, HER2, Ki67





Intrinsic subtype

PAM50 – *ER, PR, HER2, Ki67, CK5*



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Original nomenclature and grouping of IHC tests:

- 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, SOX10, CDX2, p40 etc

- Class II 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, PR, HER2, CD117 etc .

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 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]

CME/SAM

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Class II (Class III, US), IHC companion diagnostics (CDx):

IHC test	Demonstration	Application
ER	Estrogen receptor protein	Breast cancer
HER2	Overexpression of HER2 protein	Breast cancer, gastric cancer
CD117	Protein second to gene mutation	GIST
EGFR	Overexpression of HER1 protein	Colorectal cancer
ALK	Fusion protein second to gene rearrangement	NSCLC
PD-L1	PD-L1 protein expression	NSCLC, Melanoma,….
…….		

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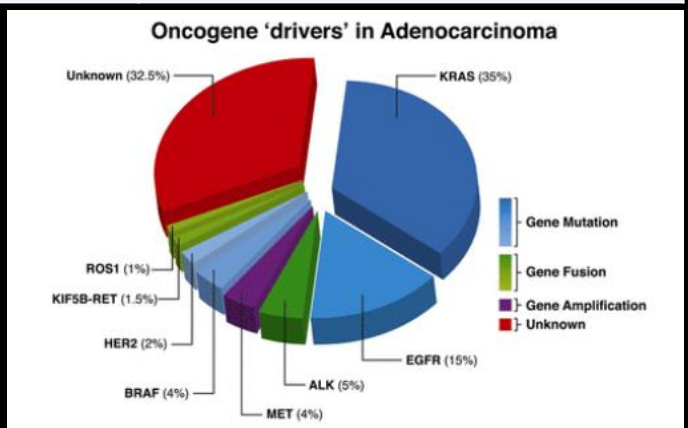
In practice more and more IHC tests become Class II tests: Directly indicated

	Area	Class I	Class II	Comment
CD20	Lymphoma	B-cell origin	Mabthera	Evaluation of theraphy
CD30	Lymphoma	HL, ALCL	Brentuximab	
CD56	Carcinoma	Neuroendo.	Lorvotuzumab	Class II: Lung SCLC
ALK	Lymphoma	ALCL	Crizotinib	Class II: Lung NSCLC

Indirectly indicated typically due to personalized treatment e.g.

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



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… 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

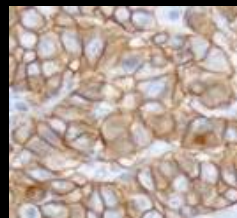
Development
Sensitivity,
Localization

Controlment

Post-analytic

Quantification
Reporting

Interpretation
Localization
Positive/Negative - cut-off level



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- 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

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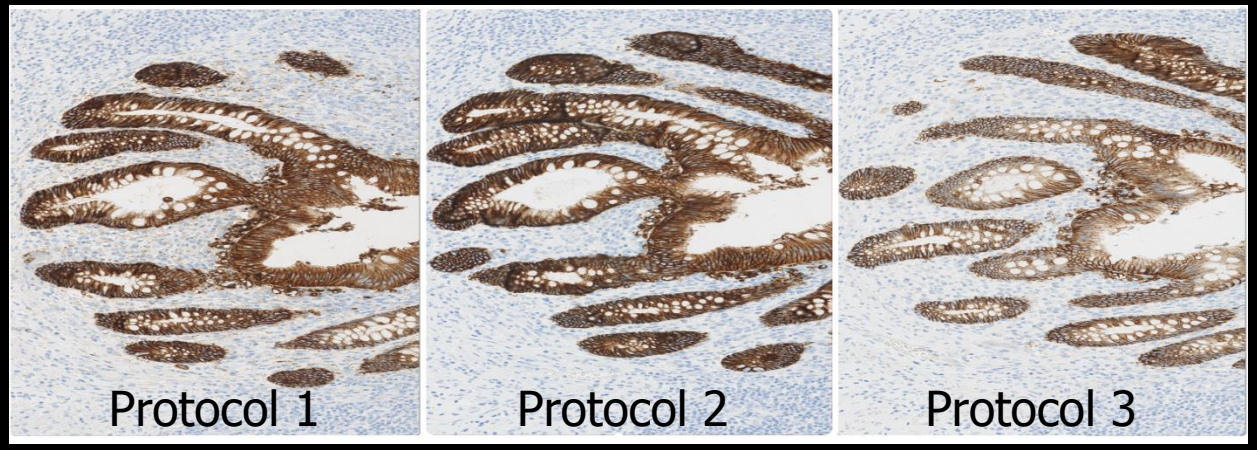
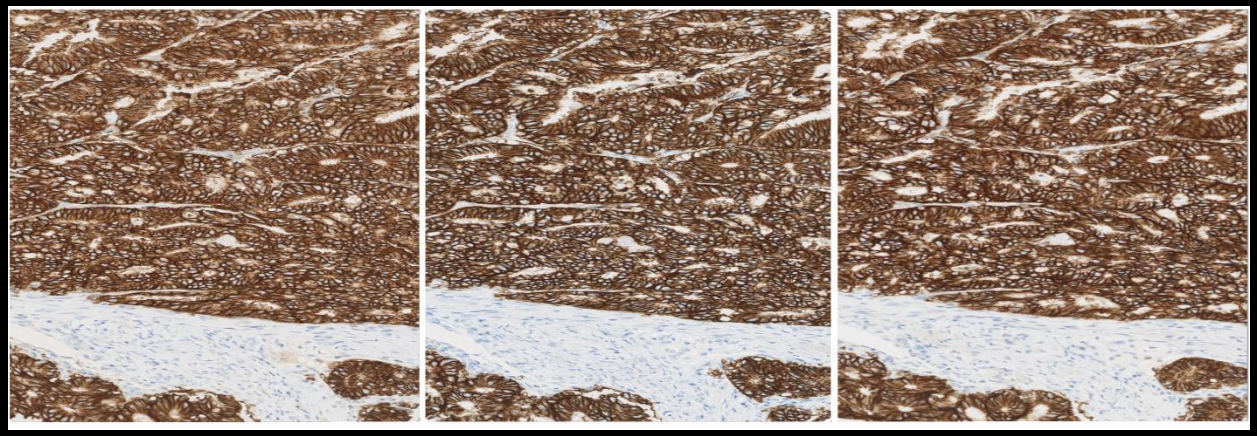
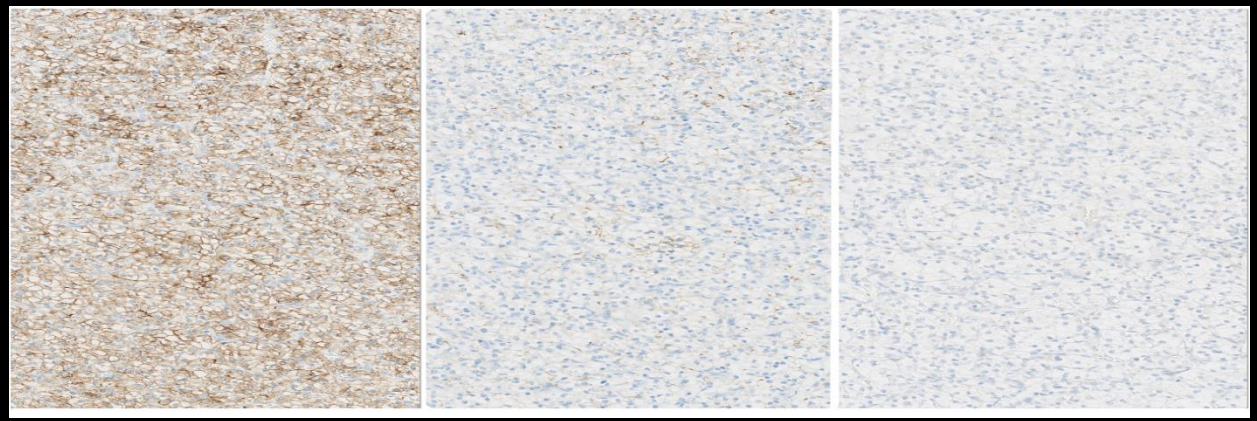


EPCAM calibration & validation challenge

Normal colon mucosa



Colon adenocarcinoma



Renal clear cell carc.

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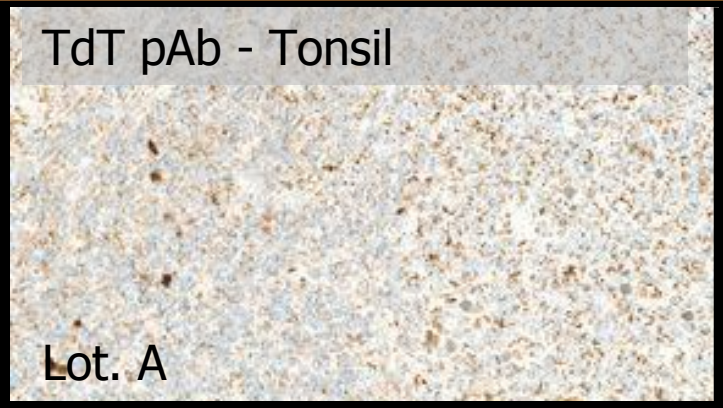

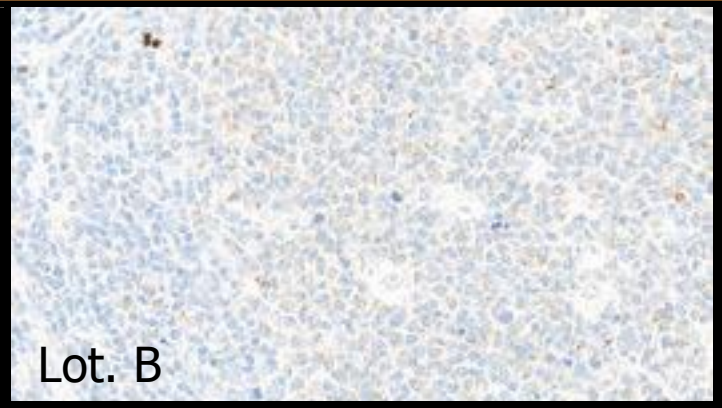

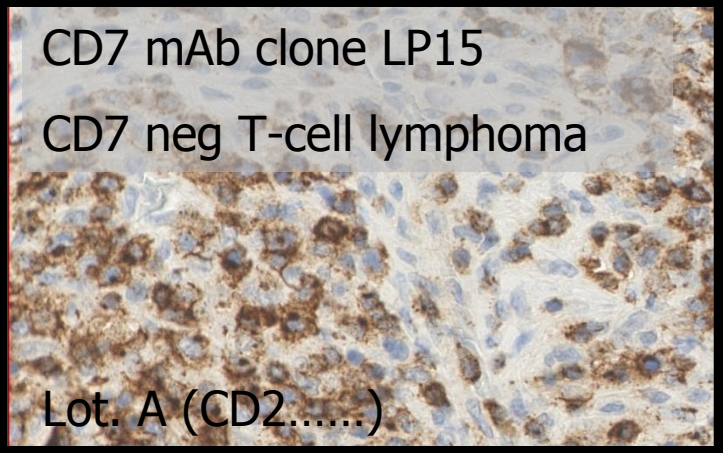

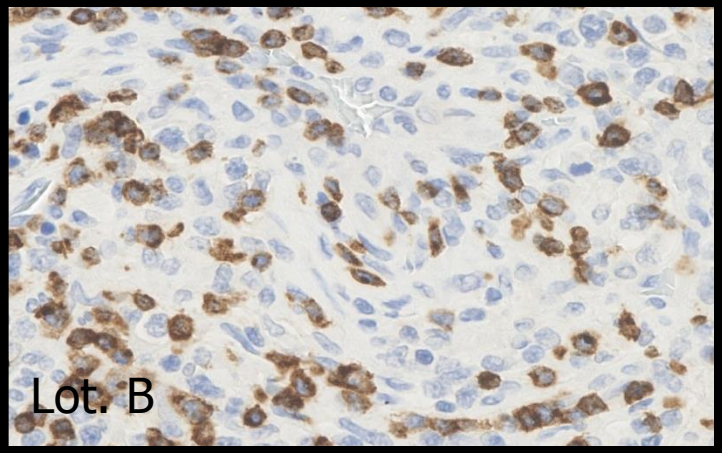

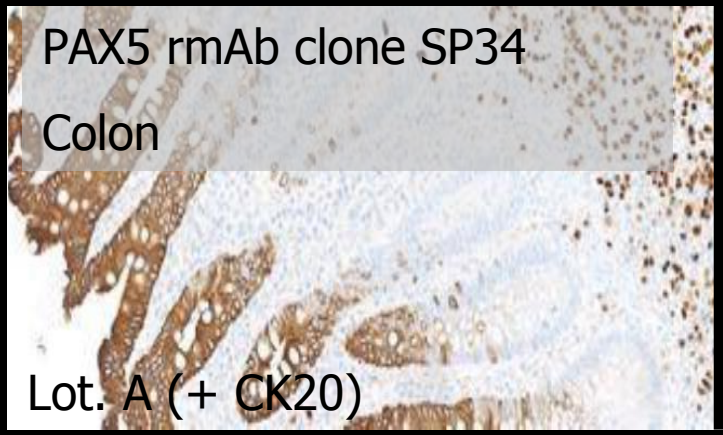

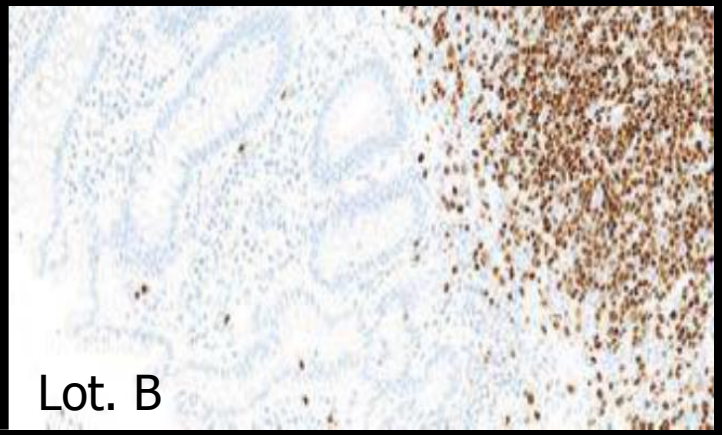

FP staining reactions

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”

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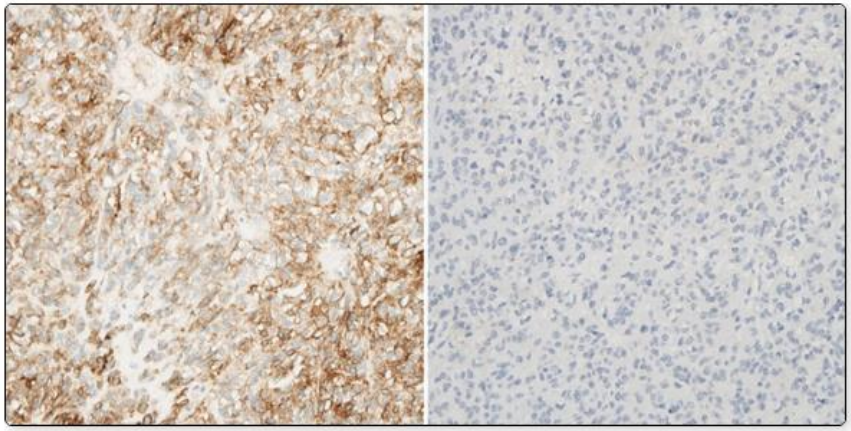
NordiQC

Info ▾ Modules ▾ Assessments Protocols Controls Events ▾ Login



Results general module - run 47

11-Jul-2016

The results from general module - run 47 are now available. Individual scores will be mailed to participants. Click to see a summary.

Figure: Serial sections of GIST stained for CD117 in two labs. Left: optimal, right: false negative due to an insufficient protocol.

All news

Events

NordiQC Workshop in Diagnostic Immunohistochemistry
19-21 Sep 2016: Aalborg, Denmark

NordiQC Academy of Immunohistochemistry
12-14 Oct 2016: Krakow, Poland

Important dates

Run 48, B22, H10
Protocol submission deadline
10 Sep 2016
Slide circulation
18 Sep 2016
Slide return deadline
11 Oct 2016
Publication of results
9 Dec 2016

Questions

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

Google™ Custom Search Search

BIOCARE MEDICAL · CELL MARQUE · Dako Agilent Pathology Solutions · horizon · Leica Biosystems · Roche · ThermoFisher SCIENTIFIC · VISIOPHARM®

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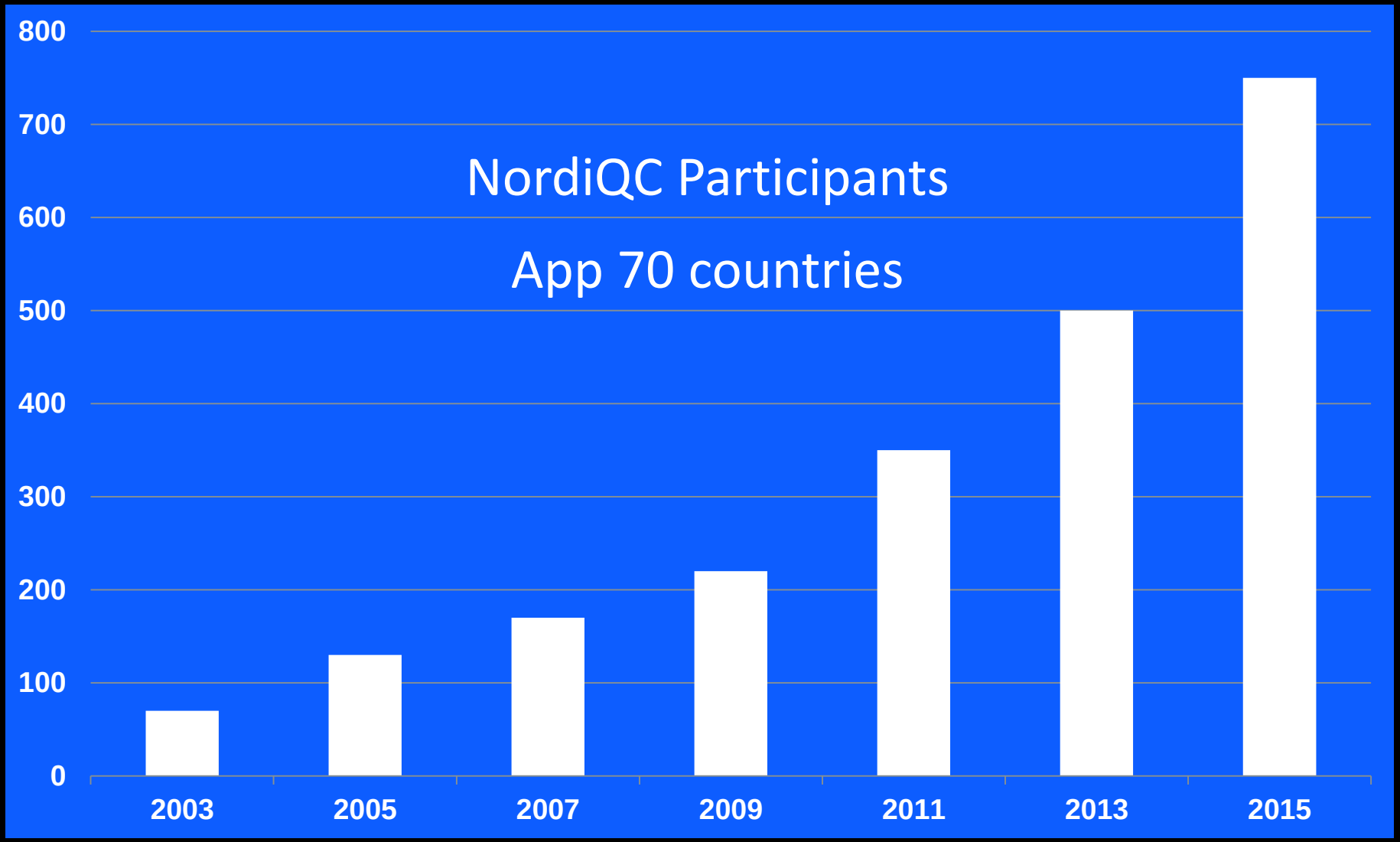

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Central assessment with consensus between experienced pathologists and histotechnologists

- 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

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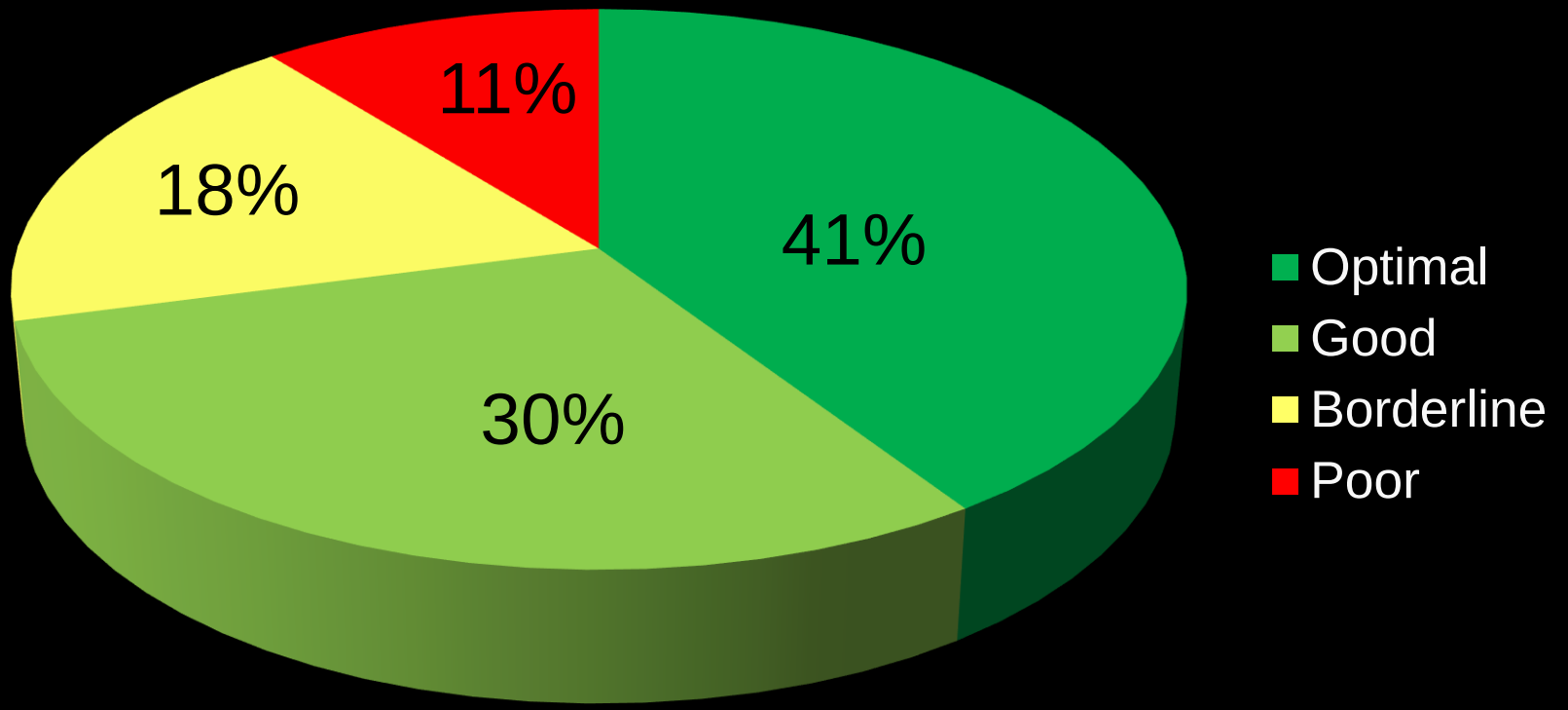
2003 - 2013
Total ~ 27,000 slides (~ 135,000 core sections)



90% of insufficient results characterized by weak or false negative results

Only focusing on the analytical IHC method

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Common causes of insufficient stains in ~ 27,000 slides

1. Inappropriate reagents used
2. Inappropriate protocol used

   A: Inadequately validated and calibrated by laboratory

   B: Imprecise information provided by vendor of the reagents / system

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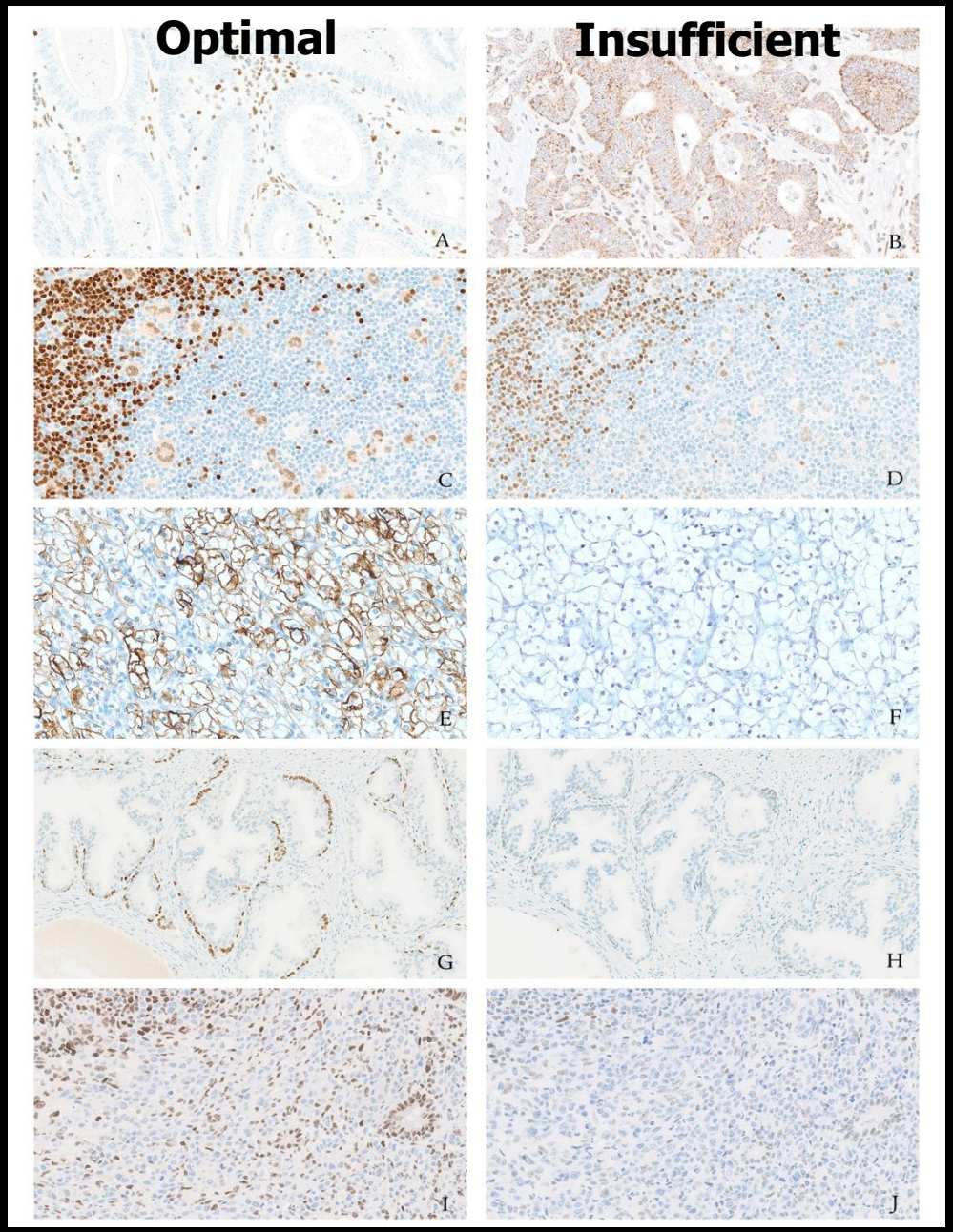

MSH2 — Poor signal-to-noise

PAX5 — False negative

CK-LMW — False negative

P63 — False negative

MLH1 — False negative

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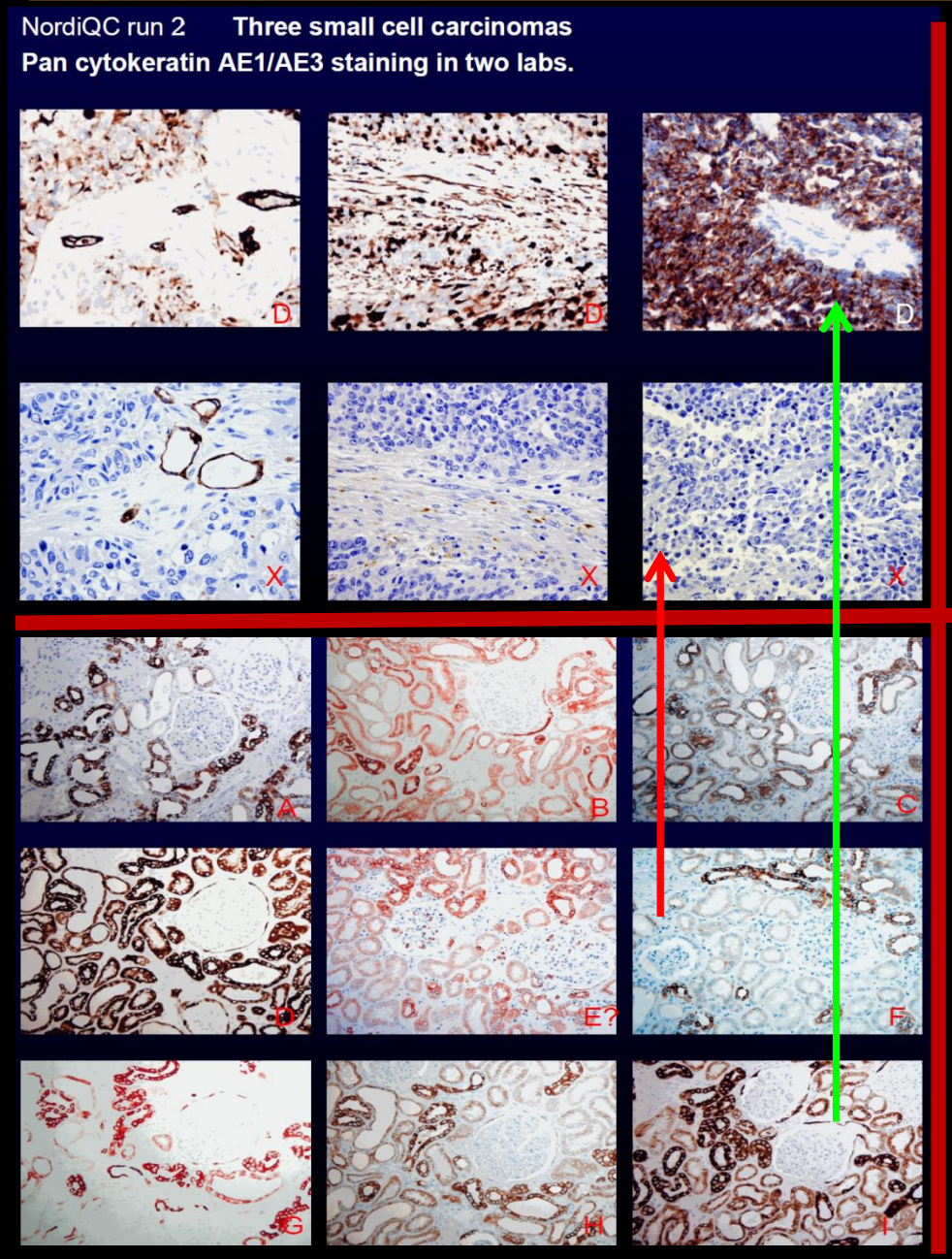

Protocol settings +

Identification of appropriate tissue control to evaluate the level of calibration

CK-PAN

A)

Protease 1
AE1/AE3* 1:50 (½h)
Ventana SAB (8 min)
* DAKO

B)

Tris/EDTA
KL1 1:800 (½h)
Dako SAB (½h)

C)

Ci + Proteinase K
MNF116 1:300 (½h)
Dako SAB (½h)

D)

EDTA
AE1/AE3* 1:50 (½h)
Dako EnV+ (½h)
* Signet

E)

Protease XXVII
Zymed poly 1:150
DAKO SAB (½h)

F)

Protease 1
MNF116 1:100 (½h)
Ventana SAB (8 min)

G)

Ci + Proteinase K
AE1/AE3* 1:3.000
(¾h)
Dako SAB (½h)
* DAKO

H)

Ci
AE1/AE3* 1:1.000
(½h)
Ventana SAB (?)
* Boeh.Mann.

I)

Tris/EDTA
AE1/AE3* 1:250 (2h)
EnV+ (½h)
* DAKO

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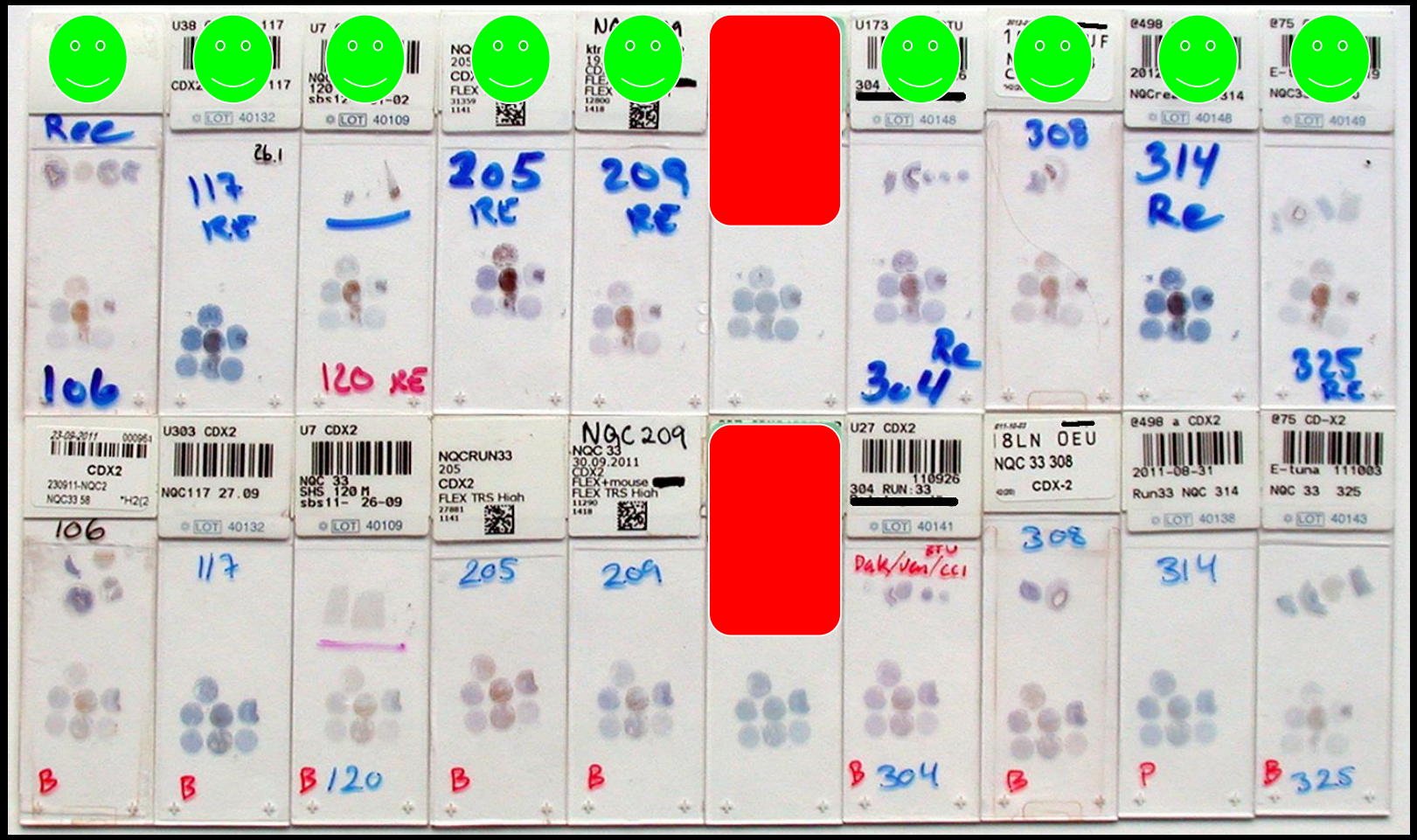
Reassessment slides for CDX2 - 9 of 10 labs improved the score to a sufficient result



Insuffient staining results from 10 laboratories for CDX2, run 33 2011

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Aim for Workshop 2016 is to focus on knowledge sharing

3 main lecturers

Ole Nielsen, Odense University Hospital
Michael Bzorek, Næstved Hospital
Søren Nielsen, Aalborg University Hospital

All NordiQC coworkers with primary focus to analyze and summarize assessment data

5 pathologists focusing on IHC in different subspecialties

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Program

Monday, September 19th

09:30 – 10:00		*Arrival, coffee*	
10:00 – 10:15	**15**	Welcome and introduction	SN
10:15 – 11:00	**45**	Immunohistochemical principles: The technical test approach – pre-analytical phase I	ON
11:05 – 11:50	**45**	Immunohistochemical principles: The technical test approach – pre-analytical phase II	ON
12:00 – 12:45	**45**	Immunohistochemical principles: The technical test approach - analytical phase I	MB
12:45 – 13:30	**45**	*Lunch*	
13:30 – 14:15	**45**	Immunohistochemical principles: The technical test approach - analytical phase II	MB
14:20 – 15:05	**45**	Immunohistochemical principles: The technical test approach - post-analytical phase I	SN
15:05 – 15.25	**20**	*Coffee*	
15:25 – 16:10	**45**	Immunohistochemical principles: The technical test approach - post-analytical phase II	SN
16:15 – 17:00	**45**	Immunohistochemical classification of breast tumours	AVL
17.00 – 19.00		Social arrangement (optional) – Keglespil (Skittles)	

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Tuesday, September 20th			
08:15 – 09:00	**45**	Optim… contr… …otocols and	SN
09:00 – 09:45	**45**	Imm… unkn… …of the	MV
09:50 – 10:10	**20**	*Coffe…*	
10:10 – 10:40	**30**	Optim… contr… …otocols and …art I	SN
10:45 – 11:30	**45**	Immunohistochemical classification of the unknown primary tumour – part II	MV
11:35 – 12:05	**30**	Optimization of antibodies, selection, controls – unknown primary tumours	
12:10 – 13:00	**50**	*Lunch*	
13:00 – 13:45	**45**	Immunohistochemical classificati… tumours - Lung cancer, diagnosis… Notes	
13:50 – 14:20	**30**	Optimization of antibodies, selection, controls – lung tumours	
14.25 – 14:45	**20**	*Coffee*	
14:45 – 15:30	**45**	Immunohistochemical classification of haematolymphoid tumours	SH
15:35 – 16:20	**45**	Optimization of antibodies, selection, protocols and controls – haematolymphoid tumours	MB
16:25 – 16:40	**15**	Discussion	
19:00 –		*Workshop Dinner at Restaurant Søgaards Bryghus, C.W. Obels Plads*	

The challenging day…….

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Wednesday, September 21st			
08:45 – 09:30	**45**	Immunohistochemical double stainings – overview, considerations and applications	MB
09:35 – 10:05	**30**	Immunocytochemistry and immunohistochemistry on frozen sections – overview, considerations and applications	ON
10:05 – 10:25	**20**	*Coffee*	
10:25 – 10:55	**30**	Immunohistochemical stainers – overview, pro- and cons	SN
11:00 – 11:45	**45**	Image analysis in IHC - overview, considerations and applications	RR
11:45 – 12:00	**15**	Discussion and evaluation	SN
12:00 – 12:50		*Lunch and departure*	

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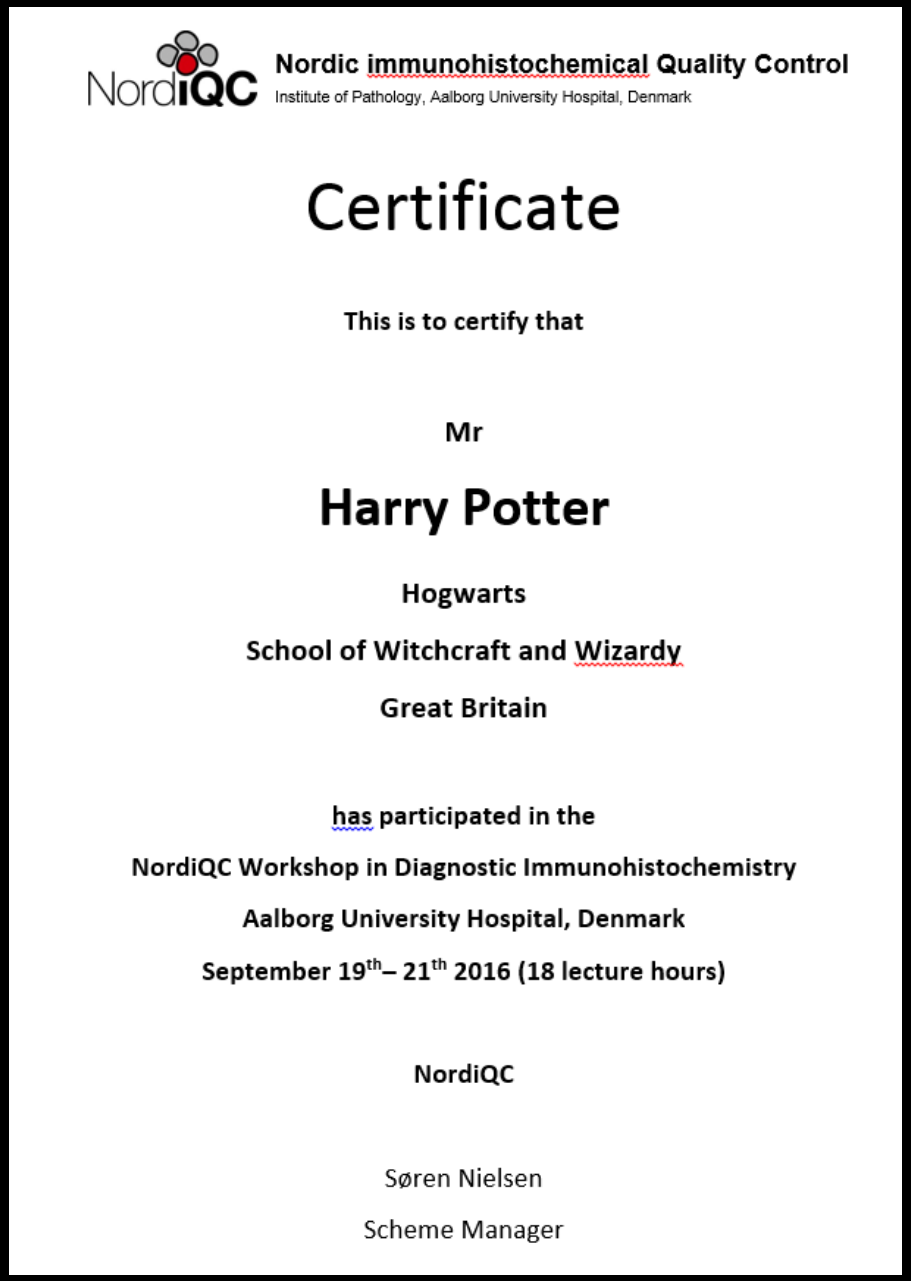

Nordic immunohistochemical Quality Control
Institute of Pathology, Aalborg University Hospital, Denmark

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 19th– 21th 2016 (18 lecture hours)

NordiQC

Søren Nielsen

Scheme Manager

Will be e-mailed

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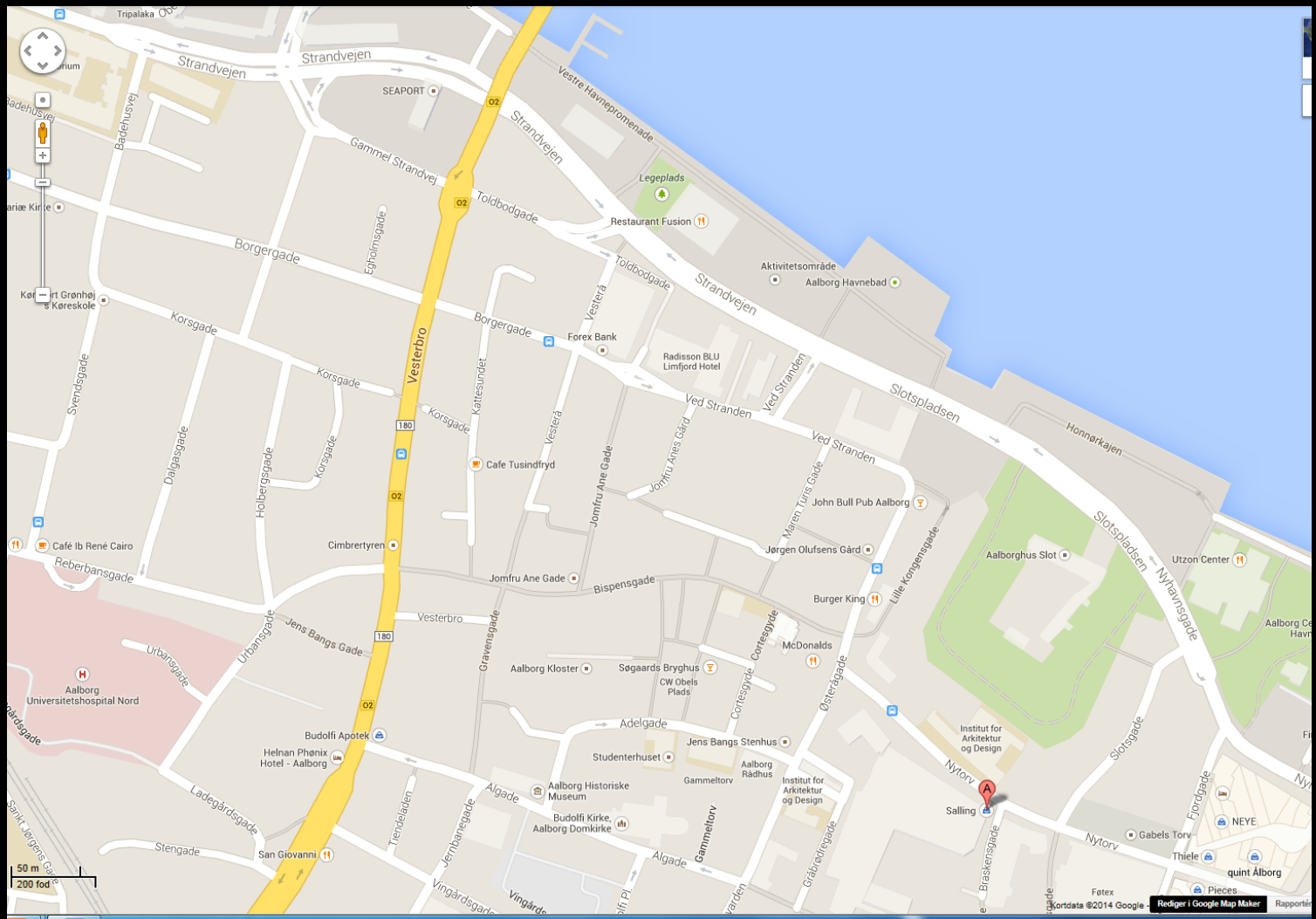
Shops open till 17.30
Salling (warehouse) till 20.00



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Wifi:

All final presentations will be available on www.nordiqc.org and also on the USB-stick in the hand-out material.

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

Lunch served in the restaurant downstairs.

Toilets – just outside.