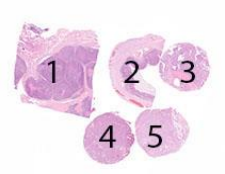
Assessment Run 71 2024

Mismatch repair protein PMS2 (PMS2)

Purpose
Evaluation of the technical performance and level of analytical sensitivity and specificity of IHC tests among NordiQC participants for PMS2 status in solid tumours as e.g. colon adenocarcinomas. Loss of PMS2 function due to gene mutation or epigenetic changes is characterized by absence of nuclear expression in neoplastic cells,whereas intact nuclear PMS2 expression indicates normal PMS2 function and no gene mutations.

Material
The slide to be stained for PMS2 comprised:

1. Tonsil, 2. Appendix, 3. Colon adenocarcinoma with normal PMS2 expression, 4-5. Colon adenocarcinomas with loss of PMS2 expression.



All tissues were fixed in 10% neutral buffered formalin.

Criteria for assessing PMS2 staining as optimal included:

- An at least weak to moderate, distinct nuclear staining reaction of virtually all cells in the appendix
- An at least weak to moderate, distinct nuclear staining reaction of virtually all mantle zone B-cells and a moderate to strong, distinct nuclear staining reaction of the germinal centre B-cells in the tonsil
- A moderate to strong, distinct nuclear staining reaction of virtually all neoplastic and stromal cells in the colon adenocarcinoma no. 3
- No nuclear staining reaction of the neoplastic cells in the colon adenocarcinomas no. 4 and 5, but an at least weak to moderate distinct nuclear staining reaction in the vast majority of other cells (stromal cells, lymphocytes etc.).

A general weak cytoplasmic staining reaction was accepted.

KEY POINTS FOR PMS2 IMMUNO ASSAYS
- The widely used rmAb clone **EP51** is recommendable both as concentrate and RTU.
- 3-step detection systems are mandatory for optimal performance.
- The Ventana/Roche RTU system based on clone **A16-4** gave an inferior performance.
- Tonsil and colon with adenocarcinoma with PMS2 loss are recommendable positive and negative tissue controls.

Participation

Number of laboratories registered for PMS2, run 71	405
Number of laboratories returning slides	380 (94%)

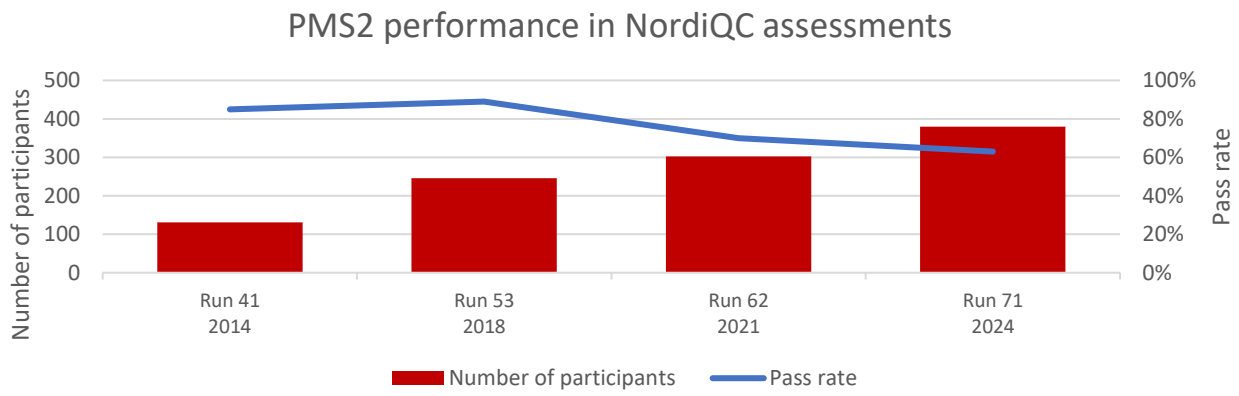
Results
At the date of assessment, 94% of the participants had returned the circulated NordiQC slides. All slides returned after the assessment were assessed and laboratories received advice if the result was insufficient, but the data were not included in this report.

380 laboratories participated in this assessment. 238 (63%) of these achieved a sufficient mark (optimal or good). Table 1a-c summarizes antibodies (Abs) used and assessment marks (see page 3-4).

The most frequent causes of insufficient staining were:
- Less successful performance of the Ventana/Roche RTU system based on mAb clone A16-4
- General reproducibility challenges with the tyramide amplification kit on Ventana/Roche platforms
- Use of detection systems with too low sensitivity

Performance history
This was the fourth NordiQC assessment of PMS2. A pass rate of 63% was observed, which was lower compared to the previous run 62, 2021.

Graph 1. **Proportion of sufficient results for PMS2 in the four NordiQC runs performed**



Controls
Tonsil is recommendable as positive tissue control for PMS2. Virtually all mantle zone B-cells must show an at least weak to moderate, distinct nuclear staining reaction, while a moderate to strong, distinct nuclear staining reaction must be seen in proliferating germinal centre B-cells. Tumour tissue, e.g. colon adenocarcinoma with loss of PMS2 expression must be used as negative tissue control, in which no nuclear staining reaction of the neoplastic cells must be seen. Stromal cells within the tumour tissue must exhibit a distinct nuclear staining reaction serving as internal positive tissue control.

Conclusion
Optimal staining results could be obtained with the rabbit monoclonal Ab (rmAb) clones **EP51** and **EPR3947** and the mouse monoclonal Ab (mAb) clone **A16-4.** Irrespective of the clone applied, efficient HIER (Heat Induced Epitope Retrieval) in an alkaline buffer, use of a sensitive polymer/multimer based detection system and careful calibration of the primary Ab were the most important prerequisites for an optimal staining result. The concentrated (conc.) format of the rmAb clone EP51 provided a high proportion of optimal staining results on all four main stainer platforms - Omnis (Dako/Agilent), Autostainer (Dako/Agilent), Bond (Leica Biosystems) and BenchMark (Ventana/Roche). Corresponding Ready-To-Use (RTU) systems based on rmAb clone EP51 from e.g. Dako/Agilent and Leica Biosystems also provided a high pass rate and proportion of optimal results. Contrary to these, the Ventana/Roche RTU system based on mAb clone A16-4 showed an inferior performance.

Table 1a. **Overall results for PMS2, run 71**

	n	Optimal	Good	Borderline	Poor	Suff.[1]	OR[2]
Concentrated antibodies	56	29	14	8	5	77%	52%
Ready-To-Use antibodies	324	104	91	95	34	60%	32%
Total	380	133	105	103	39		
Proportion		35%	28%	27%	10%	63%	

1) Proportion of sufficient stains (optimal or good).
2) Proportion of Optimal Results.

Table 1b. **Concentrated antibodies and assessment marks for PMS2, run 71**

Concentrated antibodies	n	Vendor	Optimal	Good	Borderline	Poor	Suff.[1]	OR[2]
rmAb clone **EP51**	28 6 3 2 1	Dako/Agilent Epitomics Bio SB Cell Marque Master Diagnostica	22	11	4	3	83%	55%
mAb clone **A16-4**	3 2 1	BD Biosciences Zytomed Biocare	3	2	-	1	83%	50%
rmAb clone **EPR3947**	3	Abcam	2	-	1	-	-	-
rmAb clone **ZR317**	1	Zeta Corporation	-	-	1	-	-	-
rmAb clone **BP6116**	1	Biolynx Biotechnology	1	-	-	-	-	-
rmAb clone **QR009**	1	Quartett	-	1	-	-	-	-
mAb clone **MOR4G**	3	Leica Biosystems	-	-	2	1	-	-
mAb clone **2E7-C3**	1	Wondfo	1	-	-	-	-	-
Total	56		29	14	8	5		
Proportion			52%	25%	14%	9%	77%	

1) Proportion of sufficient stains (optimal or good) (≥5 assessed protocols).
2) Proportion of Optimal Results (≥5 assessed protocols).

Table 1c. **Ready-To-Use antibodies and assessment marks for PMS2, run 71**

Ready-To-Use antibodies	n	Vendor	Optimal	Good	Borderline	Poor	Suff.[1]	OR[2]
mAb clone **A16-4 790-5094 (VRPS)[3]**	50	Ventana/Roche	2	14	24	10	32%	4%
mAb clone **A16-4 790-5094 (LMPS)[4]**	84	Ventana/Roche	6	14	48	16	24%	7%
rmAb clone **EPR3947 760-4531[5]**	1	Ventana/Roche	-	-	1	-	-	-
rmAb clone **EP51 IR087 (VRPS)[3]**	3	Dako/Agilent	2	-	-	1	-	-
rmAb clone **EP51 IR087 (LMPS)[4]**	58	Dako/Agilent	31	16	7	4	81%	53%
rmAb clone **EP51 GA087 (VRPS)[3]**	45	Dako/Agilent	32	12	1	-	98%	71%
rmAb clone **EP51 GA087 (LMPS)[4]**	27	Dako/Agilent	16	8	3	-	89%	59%
rmAb clone **EP51 PA0991 (VRPS)[3]**	12	Leica Biosystems	4	8	-	-	100%	33%
rmAb clone **EP51 PA0991 (LMPS)[4]**	15	Leica Biosystems	3	8	4	-	73%	20%
rmAb clone **EP51 8328-C010**	3	Sakura Finetek	-	3	-	-	-	-
mAb clone **MRQ-28 288M-18**	3	Cell Marque	-	2	1	-	-	-
rmAb clone **EPR3947 288R-10/17/18**	8	Cell Marque	4	1	3	-	63%	50%
mAb clone **A16-4 PM344AA**	4	BioCare Medical	1	2	1	-	-	-
rmAb clone **EP51 MAD-000681QD**	3	Master Diagnostica	1	-	-	2	-	-
rmAb clone **EP51 BSB2121**	1	Bio SB	-	1	-	-	-	-
rmAb clone **EP51 AN844-10M**	1	Biogenex	-	-	-	1	-	-
rmAb clone **EP51 GT215907**	1	Gene Tech	1	-	-	-	-	-
mAb clone **DA101 RMB1A080**	1	Dartmon Biotechnology	-	1	-	-	-	-
rmAb clone **EPR3947 Ab214442**	1	Abcam	-	-	1	-	-	-
Ab clone **MXR019 RMA-1051**	1	Fuzhou Maixin	-	1	-	-	-	-
Ab clone **157G1F5 PA243**	1	Abcarta	1	-	-	-	-	-
Ab clone **BY161 BFM-0483**	1	Bioin Biotechnology	-	-	1	-	-	-
Total	324		104	91	95	34		
Proportion			32%	28%	29%	11%	60%	

1) Proportion of sufficient stains (optimal or good) (≥5 assessed protocols).
2) Proportion of Optimal Results (≥5 assessed protocols).
3) Vendor Recommended Protocol Settings (VRPS) to a specific RTU product applied on the vendor recommended platform(s) (≥5 assessed protocols).
4) Laboratory Modified Protocol Settings (LMPS) to a specific RTU product (≥5 assessed protocols).
5) Terminated from vendor.

Detailed analysis of PMS2, Run 71
The following protocol parameters were central to obtain optimal staining:

Concentrated antibodies
rmAb clone **EP51**: Protocols with optimal results were all based on HIER using Bond Epitope Retrieval Solution 2 (BERS2; Leica Biosystems) (6/10), Cell Conditioning Solution 1 (CC1, Ventana/Roche) (13/25), Target Retrieval Solution (TRS) High pH (Dako/Agilent) (1/2) or TRS HiGH pH 9 3-1 (Dako/Agilent) (2/3) as retrieval buffer. The rmAb was typically diluted in the range of 1:20-1:100 depending on the total sensitivity of the protocol employed. Using these protocol settings, 30 of 37 (81%) laboratories produced a sufficient staining result.
* (number of optimal results/number of laboratories using this HIER buffer)

mAb clone **A16-4**: Protocols with optimal results were all based on HIER using BERS2 (Leica Biosystems) (3/4)* as retrieval buffer. The mAb was diluted in the range of 1:50-1:300 depending on the total sensitivity of the protocol employed. Using these protocol settings, 4 of 4 (100%) laboratories produced a sufficient staining result.

Table 2. **Proportion of optimal results for PMS2 for the most commonly used antibodies as concentrate on the four main IHC systems***

Concentrated antibody	**Dako/Agilent Autostainer[1]**		**Dako/Agilent Omnis**		**Ventana/Roche BenchMark[2]**		**Leica Biosystems Bond[3]**	
	TRS pH 9.0	TRS pH 6.1	TRS pH 9.0	TRS pH 6.1	CC1 pH 8.5	CC2 pH 6.0	BERS2 pH 9.0	BERS1 pH 6.0
rmAb clone **EP51**	2/3	-	1/2	-	13/25 (52%)	-	6/10 (60%)	-
mAb clone **A16-4**	-	-	-	-	-	-	3/4	-

* Antibody concentration applied as listed above, HIER buffers and detection kits used as provided by the vendors of the respective systems.
** Number of optimal results/number of laboratories using this buffer.
1) Autostainer Classical, Link 48.
2) BenchMark GX, XT, Ultra, Ultra plus.
3) Bond III, MAX, Prime.

Ready-To-Use antibodies and corresponding systems
mAb clone **A16-4**, product no. **790-5094**, Ventana/Roche, Ventana Benchmark:
Protocols with optimal results were typically based on HIER in CC1 (efficient heating time for 64-92 min. at 100°C), 32-64 min. incubation at 36°C of the primary Ab and OptiView (760-700) with OptiView Amplification Kit (760-099 / 860-099) as detection system. Using these protocol settings, 25 of 83 (30%) laboratories produced a sufficient staining result (optimal or good).

rmAb clone **EP51**, product no. **IR087**, Dako/Agilent, Autostainer:
Protocols with optimal results were typically based on HIER in PT-Link using TRS High pH (3-in-1) (efficient heating time 10-30 min. at 95-98°C), 20-40 min. incubation of the primary Ab and EnVision FLEX/FLEX+ (K8000/K8002) as detection system. Using these protocol settings, 21 of 23 (91%) laboratories produced a sufficient staining result (optimal or good).
31 laboratories used product no. IR087 on other platforms. These were not included in the description above.

rmAb clone **EP51**, product no. **GA087**, Dako/Agilent, Omnis:
Protocols with optimal results were typically based on HIER using TRS High pH (efficient heating time 30 min.), 20 min. incubation of the primary Ab and EnVision FLEX+/FLEX++ (GV8000/GV823/GV809/GV821) as detection system. Using these protocol settings, 55 of 57 (97%) laboratories produced a sufficient staining result (optimal or good).
5 laboratories used product no. GA087 on other platforms. These were not included in the description above.

rmAb clone **EP51**, product no. **PA0991**, Leica Biosystems, Bond:
Protocols with optimal results were based on HIER using BERS2 for 20-30 min., 15-20 min. incubation of the primary Ab and Bond Refine (DS9800) as detection system. Using these protocol settings, 17 of 20 (85%) laboratories produced a sufficient staining result (optimal or good).
1 laboratory used product no. PA0991 on other platforms. This was not included in the description above.

Table 3 summarizes the proportion of sufficient and optimal marks for the most commonly used RTU systems. The performance was evaluated both as "true" plug-and-play systems performed strictly accordingly to the vendor recommendations and by laboratory modified systems changing basal protocol settings. Only protocols performed on the intended IHC stainer device are included.

Table 3. **Proportion of sufficient and optimal results for PMS2 for the most commonly used RTU IHC systems**

RTU systems	**Recommended protocol settings***		**Laboratory modified protocol settings****	
	Sufficient	Optimal	Sufficient	Optimal
VMS mAb clone **A16-4, 790-5094**	16/50 (32%)	2/50 (4%)	20/84 (24%)	6/84 (7%)
Dako AS rmAb clone **EP51, IR087**	2/3	2/3	23/27 (85%)	14/27 (52%)
Dako Omnis rmAb clone **EP51, GA087**	44/45 (98%)	32/45 (71%)	19/22 (86%)	0/22 (0%)
Leica Bond rmAb clone **EP51, PA0991**	12/12 (100%)	4/12 (33%)	10/14 (71%)	2/14 (14%)

* Protocol settings recommended by vendor – Retrieval method and duration, Ab incubation times, detection kit, IHC stainer/equipment.
** Significant modifications: retrieval method, retrieval duration and Ab incubation time altered, detection kit – only protocols performed on the specified vendor IHC stainer integrated.

Comments

In this assessment the prevalent feature of an insufficient staining result was a poor signal-to-noise ratio and/or an excessive background staining often combined with granular staining reaction complicating the interpretation. This pattern was seen in 73% (104 of 142) of the insufficient results. In 24% (34 of 142) of the insufficient results, too weak or completely false negative staining reactions were seen. In the remaining 3% a false positive nuclear staining reaction in tumors with loss of PMS2 expression (tissue cores no. 4 and 5) was observed.

15% (56 of 380) of the laboratories used Abs as conc. format within laboratory developed (LD) assays for PMS2. Optimal staining results could be obtained with the mAb clones A16-4, 2E7-C3 and the rmAb clones EP51, EPR3947 and BP6116 (see Table 1b). Irrespective of the clone applied, careful calibration of the titre and efficient HIER with an alkaline buffer were the main protocol prerequisites for optimal results. Only 3-step polymer/multimer based detection systems could be used to provide an optimal result for conc. Abs and were used in total in 96% (54 of 56) of the protocols assessed.

The rmAb clone EP51 was the most widely used conc. Ab for demonstration of PMS2 and provided a high proportion of sufficient and optimal staining results. The Ab was mostly used on the BenchMark and Bond platforms, but optimal results could be obtained on all four main IHC systems from Dako/Agilent, Leica Biosystems and Ventana/Roche (see Table 2).

85% (324 of 380) of the laboratories used Abs in RTU formats. The use of RTUs for PMS2 has increased from 63% in 2014, 72% in 2018 to 80% 2021. In this period more RTU products has been released from vendors both as true RTU systems and LD formats. All three main IHC system providers (Dako/Agilent, Leica Biosystems and Ventana/Roche) have RTU systems available for PMS2.

The most widely used RTU system for PMS2, was the Ventana/Roche **790-5094** system based on mAb clone A16-4, being used by 35% of all participants with intended use on the BenchMark systems, providing a pass rate of 32% if using the vendor recommended protocol settings and 24% if modifying the protocol (see Table 3). The majority of insufficient results were caused by a poor signal-to-noise ratio and/or excessive cytoplasmic staining reaction combined with a granular staining pattern complicating the interpretation (see Figs 1b-4b). Of the 134 laboratories submitting protocols using the 790-5094 product 87% used OptiView with tyramide amplification (VPRS protocol) with a total of 97 protocols producing either granular staining reaction and/or excessive background. In addition to this observation with extensive disturbing granular precipitations for the PMS2 RTU system, it was noted that similar aberrant staining patterns was seen for other markers as BAP1 assessed in run 71 when OptiView with Amplification Kit (760-099/860-099) was applied.

At present no conclusive root cause(s) for this aberrant pattern have been identified. However as similar results and challenges also were observed in run 62, 2021 for the Ventana RTU system based on clone A16-4 with a low pass rate of 40%, these data indicate a challenge to get reproducible results with clone A16-4 on the BenchMark platforms and especially in combination with the tyramide amplification kit.

Compiled data shown in Table 4 display a significant lower pass-rate when using the mAb clone A16-4 with the Ventana system (27% in total for both RTU and conc.), whereas the rmAb clones provide a higher passrate (72% in total). Using the rmAb clones 50 of 57 laboratories were still using the amplification kit, but only 12% (7 of 57) were producing granular staining or excessive background indicating that robust antibodies carefully calibrated can be used with the amplification system.

Table 4. **Antibodies and assessment marks for PMS2 strictly on the Ventana Benchmark platform. Concentrates and prediluted Abs are pooled together.**

RTU/conc	n	Optimal	Good	Borderline	Poor	Suff.[1]	OR[2]
mAb clone **A16-4 790-5094 (VRPS)**[3]	50	2	14	24	10	32%	4%
mAb clone **A16-4**	85	6	14	49	16	24%	7%
rmAb clone **EP51**	46	26	9	5	6	76%	56%
rmAb clone **EPR3947**	11	5	1	5	-	55%	46%
Total	192	39	38	83	32	40%	

1) Proportion of sufficient stains (optimal or good) (≥5 assessed protocols).
2) Proportion of Optimal Results (≥5 assessed protocols).
3) Vendor Recommended Protocol Settings (VRPS) to a specific RTU product applied on the vendor recommended platform(s) (≥5 assessed protocols).

In previous runs the RTU systems from Ventana/Roche also included the rmAb clone EPR3947 which is now terminated from vendor, but as an alternative Cell Marque offers the **288R-10/17/18** prediluted (RTU) antibody. In this assessment 7 laboratories applied the Cell Marque RTU product to the Ventana platform with a pass-rate of 57%. Optimal results were achieved by using OptiView with amplification as detection system and CC1 for 64 min with an antibody incubation time between 16-32 min. The rmAb clone EPR3947 is also available as a concentrate from Abcam (see Table 1b) also achieving optimal results on the Ventana platform.

The RTU system **GA087** from Dako/Agilent, based on rmAb clone EP51 with intended use on the Dako Omnis system, gave a pass rate of 98% when following the vendor recommended protocol settings with dual linker. Modifying the protocol provided a pass-rate of 86% (see Table 3). The main prevalent feature of less successful staining where poor-signal-to-noise or excessive background.

The **IR087** RTU system from Dako/Agilent based on rmAb EP51, with the intended use on the Dako Autostainer systems were only used by 3 laboratories in compliance with vendor recommended protocol settings including application on the specified IHC stainer platform, but typically (n=58) by a modified protocol giving an overall pass rate of 81%. The protocols were most frequently adjusted by prolonging incubation time of primary Ab and/or using EnVision Flex+ as detection system. A total of 61 laboratories used the IR087 product but only half of the participants used it on the intended Autostainer platform. 31 laboratories applied the RTU product to other platforms with a pass-rate of 77% (24 of 31).

The RTU system **PA0991** from Leica Biosystems based on rmAb clone EP51, intended use on the Bond systems, achieved an overall pass rate of 100%. If following the recommended protocol settings, 4 of 12 obtained an optimal result, and if modifying the protocol settings (prolonging efficient HIER time) 2 of 14 results were assessed as optimal. The main issue for a relative low proportion of optimal results was a mixture of both excessive background and/or too weak staining reaction. No obvious reason was found to explain the low level of optimal results, however it should be noted that when a rmAb clone is applied on the Bond platform together with Bond Refine detection system this will perform as a 2-layer detection system due to the absence of a mouse anti-rabbit linker. For the rmAb clone EP51 it was crucial for achieving optimal results on the other platforms to use detections systems with a high sensitivity as the EnVision Flex+(+) (Dako/Agilent Autostainer/Omnis) or OptiView +/- amplification (Ventana/Roche BenchMark). The conc. format of mAb clone **A16-4** was used by 4 laboratories on the Bond platforms with a 100% pass-rate, 3 of them being optimal.

This was the fourth assessment of PMS2 in NordiQC (see Graph 1). The number of participants increased from 302 laboratories in 2021 to 380 in the current assessment. The decrease in the pass rate was most likely caused by a less succesfull performance of the Venana/Roche RTU system based on the mAb clone A16-4 (790-5094). In this context it was observed that, the Ventana RTU system based on rmAb clone EPR3947 (760-4531) in run 53 gave a pass rate of 88%.

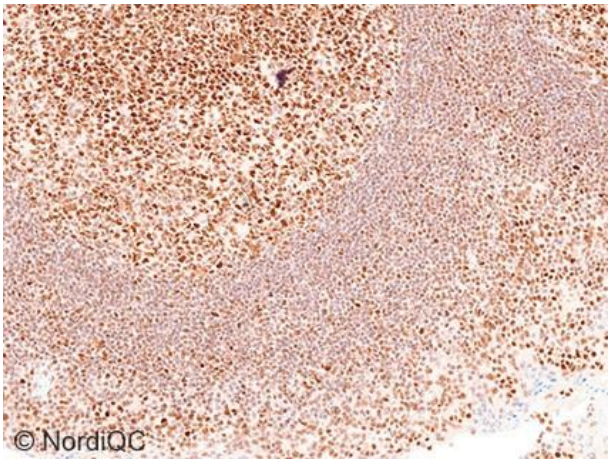


Fig. 1a (x100)
Optimal PMS2 staining reaction of the tonsil using the GA087 RTU system for the Dako Omnis platform based on rmAb clone EP51, following the recommended protocol settings using dual linker. Virtually all mantle zone B-cells show a moderate and distinct nuclear staining reaction, while the germinal centre B-cells show a strong nuclear staining reaction. Also compare with Figs. 2a - 4a, same protocol.

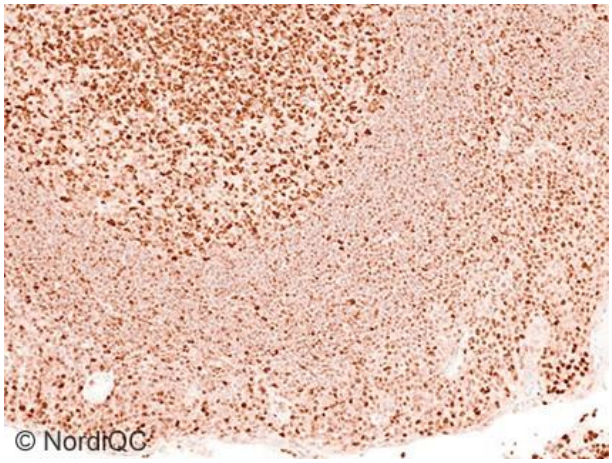


Fig. 1b (x100)
Insufficient PMS2 staining reaction of the tonsil using the mAb clone A16-4 on the Ventana Benchmark platform following the vendor recommended protocol settings with tyramide amplification same field as in Fig. 1a.
Virtually all mantle zone B-cells show a moderate but granulated staining reaction of both nuclei and cytoplasm, while the germinal centre B-cells show a strong nuclear staining reaction.
Also compare with Figs. 2b – 4b, same protocol.

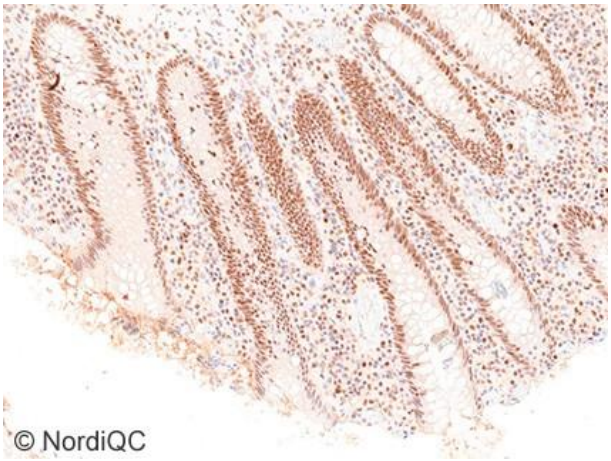


Fig. 2a (x100)
Optimal PMS2 staining reaction of the appendix using same protocol as in Fig. 1a. Virtually all cells show an at least weak distinct nuclear staining reaction. Also compare with Figs. 3a - 4a, same protocol.

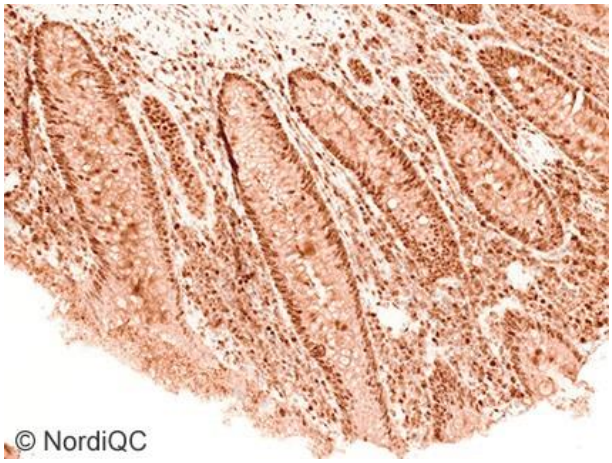


Fig. 2b (x100)
Insufficient PMS2 staining reaction of the appendix using same protocol as in Fig. 1b – same field as in Fig. 2a. An excessive background reaction is seen, giving a cytoplasmic staining reaction especially in the epithelial cells. Also compare with Figs. 3b – 4b, same protocol.

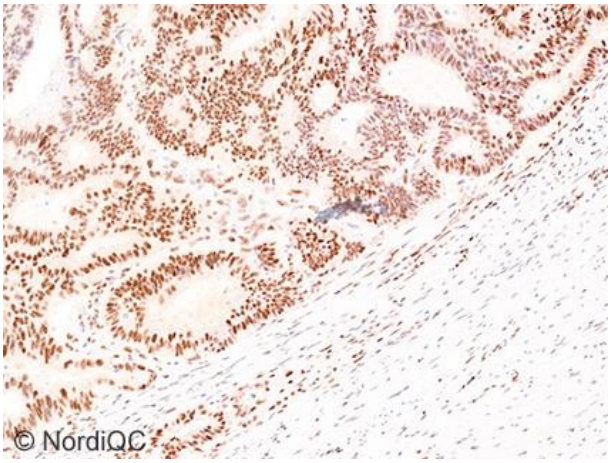


Fig. 3a (x100)
Optimal PMS2 staining reaction of the colon adenocarcinoma, tissue core no. 3, with normal PMS2 expression using same protocol as in Figs. 1a – 2a. Virtually all neoplastic cells show a moderate to strong nuclear staining reaction with only faint cytoplasmic staining.

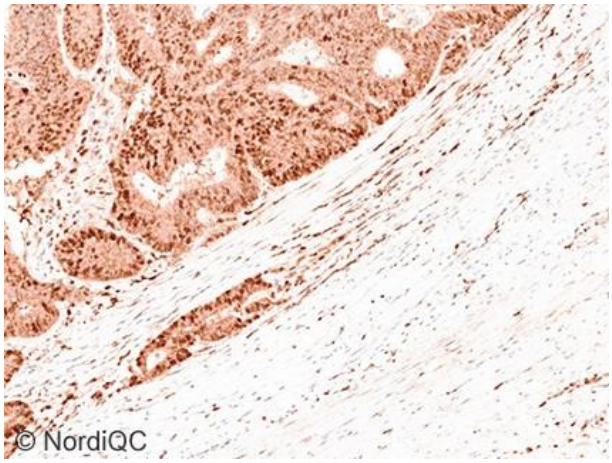


Fig. 3b (x100)
Insufficient PMS2 staining reaction for of the colon adenocarcinoma, tissue core no. 3, using same protocol as in Figs. 1b – 2b, same field as in Fig. 3a. An excessive background reaction is seen, giving a cytoplasmic staining reaction especially in the epithelial cells and muscle cells. Also compare with Fig. 4b, same protocol.

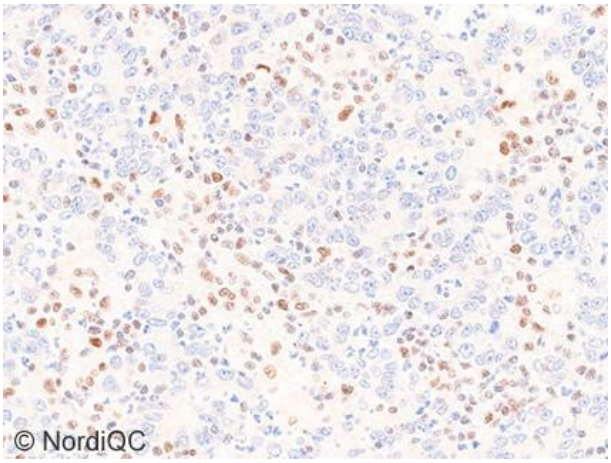


Fig. 4a (x200)
Optimal PMS2 staining reaction of the colon adenocarcinoma, tissue core no. 5, with loss of PMS2 expression using same protocol as in Figs. 1a – 3a. The neoplastic cells are negative, while stromal cells show a distinct nuclear staining reaction serving as internal positive tissue control.

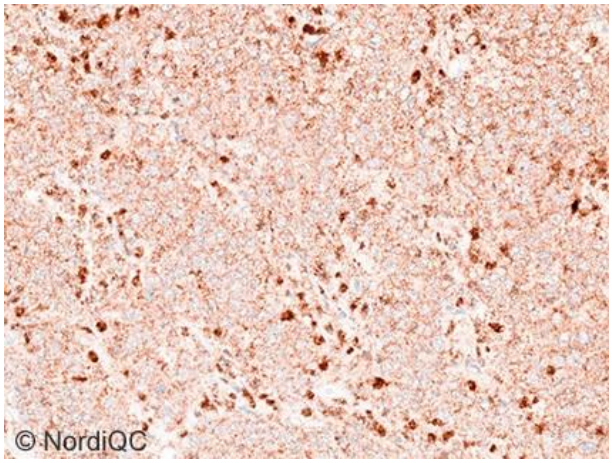


Fig. 4b (x200)
Insufficient PMS2 staining reaction of the colon adenocarcinoma, tissue core no. 5, with loss of PMS2 expression using same protocol as in Figs. 1b – 3b, same field as in Fig. 4a. A diffuse granular staining reaction is seen in both the cytoplasmic and nuclear compartment complicating the interpretation of the neoplastic cells expected to be negative.

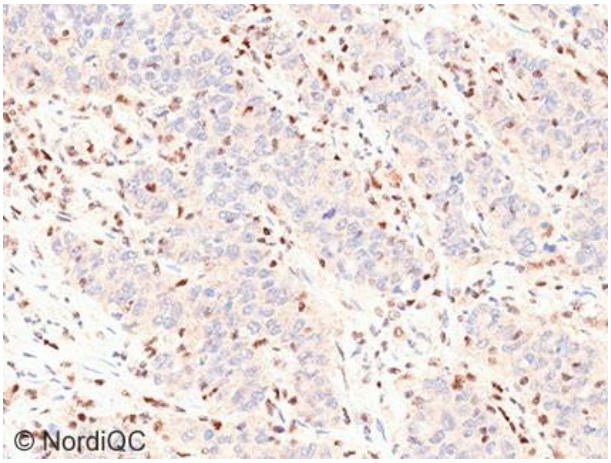


Fig. 5a (x100)
Sufficient PMS2 staining reaction of the colon adenocarcinoma, tissue core no. 5, with loss of PMS2 using the same protocol settings as Figs 1a-4a but within a different laboratory.
A generel background hue was observed in all tissue cores most likely due to problems with the EnVision Flex detections system and/or less successful wahing steps. The result was assessed as good, as the result could be interpreted with confidence.

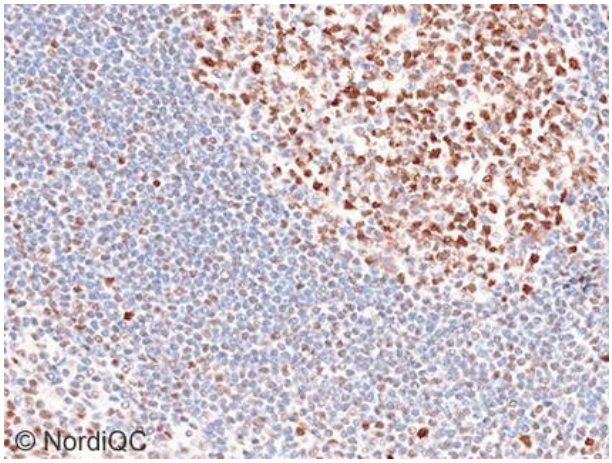


Fig. 5b (x100)
Insufficient PMS2 staining reaction of the tonsil, using a protocol giving a low level of analytical sensitivity. Only the germinal centre B-cells are distinctively demonstrated, while mantle zone B-cells expressing low levels of PMS2 are virtually unstained.

TJ/LE/SN 19.06.24