

**Supplementary Table 1**

**Search strategy for PubMed (3 December 2018)**

[Mesh] = Medical subject headings

[tiab] = words in title OR abstract

Search	Query	Items found
#5	#4 NOT (animals[mh] NOT humans[mh])	2,194
#4	#1 AND #2 AND #3	2,393
#3	"Blood"[Mesh] OR "blood" [Subheading] OR plasma*[tiab] OR "Hematologic Tests"[Mesh] OR hematolog*[tiab] OR haematolog*[tiab] OR blood[tiab] OR serum*[tiab] OR seral*[tiab]	4,431,122
#2	"DNA Methylation"[Mesh] OR "DNA Copy Number Variations"[Mesh] OR (("DNA"[Mesh] OR dna[tiab] OR dnas[tiab] OR kras[tiab] OR braf[tiab] OR sept9[tiab] OR "sept 9"[tiab] OR cdkn2a[tiab] OR p16[tiab] OR hltf[tiab] OR alx4[tiab] OR alex4[tiab] OR bcat1[tiab] OR ikzf1[tiab] OR vim[tiab] OR pik3ca[tiab] OR tp53[tiab] OR "tp 53"[tiab] OR apc[tiab] OR cfdna*[tiab] OR ccdna*[tiab] OR ctdna*[tiab] OR ftdna*[tiab] OR fcdna*[tiab] OR cpdna*[tiab]) AND ("Methylation"[Mesh] OR "Mutation"[Mesh] OR methylati*[tiab] OR mutation*[tiab] OR (copy number*[tiab] AND (variation*[tiab] OR variant*[tiab] OR change*[tiab])) OR abberati*[tiab] OR alterati*[tiab] OR amplificati*[tiab] OR gain*[tiab] OR loss*[tiab] OR deleti*[tiab]))	451,201
#1	"Colorectal Neoplasms"[Mesh] OR "Appendiceal Neoplasms"[Mesh] OR ((carcinoma*[tiab] OR neoplas*[tiab] OR tumour*[tiab] OR adenocar*[tiab] OR adenoid*[tiab] OR tumor[tiab] OR tumora*[tiab] OR tumorb*[tiab] OR tumorc*[tiab] OR tumord*[tiab] OR tumore*[tiab] OR tumorf*[tiab] OR tumorg*[tiab] OR tumorh*[tiab] OR tumori*[tiab] OR tumorj*[tiab] OR tumork*[tiab] OR tumorl*[tiab] OR tumorm*[tiab] OR tumorn*[tiab] OR tumoro*[tiab] OR tumorp*[tiab] OR tumorq*[tiab] OR tumorr*[tiab] OR tumors*[tiab] OR tumort*[tiab] OR tumoru*[tiab] OR tumorv*[tiab] OR tumorw*[tiab] OR tumorx*[tiab] OR tumory*[tiab] OR tumorz*[tiab] OR cancer*[tiab] OR malignan*[tiab]) AND ("Intestine, Large"[Mesh:NoExp] OR "Cecum"[Mesh] OR "Colon"[Mesh] OR "Rectum"[Mesh] OR colorectal*[tiab] OR colon*[tiab] OR rectal*[tiab] OR appendi*[tiab] OR cecum*[tiab] OR coecum*[tiab] OR caecum*[tiab] OR cecal*[tiab] OR coecal*[tiab] OR caecal*[tiab] OR sigmoid*[tiab]))	323,289

**Search strategy for Embase.com (3 December 2018)**

/exp = EMtree keyword with explosion

/de = EMtree keyword without explosion

/mj = EMtree keyword as major subject

:ti,ab = words in title or abstract

Search	Query	Items found
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#5	#4 NOT ('animal cell'/de OR 'animal experiment'/de OR 'animal model'/de OR 'animal tissue'/de OR 'cancer cell culture'/de OR 'case report'/de OR 'human cell'/de OR 'in vitro study'/de OR 'nonhuman'/de)	3,221
#4	#1 AND #2 AND #3	5,462
#3	'blood'/exp OR 'blood examination'/exp OR plasma*:ab,ti,kw OR hematolog*:ab,ti,kw OR haematolog*:ab,ti,kw OR blood:ab,ti,kw OR serum*:ab,ti,kw OR seral*:ab,ti,kw	5,379,508
#2	'dna methylation'/exp OR 'dna methylation assay'/exp OR 'copy number variation'/exp OR (('dna'/exp OR dna:ti,ab,kw OR dnas:ti,ab,kw OR kras:ti,ab,kw OR braf:ti,ab,kw OR sept9:ti,ab,kw OR 'sept 9':ti,ab,kw OR cdkn2a:ti,ab,kw OR p16:ti,ab,kw OR hltf:ti,ab,kw OR alx4:ti,ab,kw OR alex4:ti,ab,kw OR bcat1:ti,ab,kw OR ikzf1:ti,ab,kw OR vim:ti,ab,kw OR pik3ca:ti,ab,kw OR tp53:ti,ab,kw OR 'tp 53':ti,ab,kw OR apc:ti,ab,kw OR cfdna*:ti,ab,kw OR ccdna*:ti,ab,kw OR ctdna*:ti,ab,kw OR ftdna*:ti,ab,kw OR fcdna*:ti,ab,kw OR cpdna*:ti,ab,kw) AND ('mutation'/exp OR 'methylation'/exp OR methylati*:ti,ab,kw OR mutation*:ti,ab,kw OR (('copy number*' NEAR/3 (variation* OR variant* OR change*)):ti,ab,kw) OR abberati*:ti,ab,kw OR alterati*:ti,ab,kw OR amplificati*:ti,ab,kw OR gain*:ti,ab,kw OR loss*:ti,ab,kw OR deleti*:ti,ab,kw))	568,751
#1	'colon tumor'/de OR 'colon cancer'/exp OR 'colorectal tumor'/exp OR 'large intestine tumor'/de OR 'appendix tumor'/exp OR 'cecum tumor'/exp OR 'large intestine cancer'/exp OR 'rectum tumor'/exp OR ((carcinoma*:ab,ti OR neoplas*:ab,ti OR tumour*:ab,ti OR adenocar*:ab,ti OR adenoid*:ab,ti OR tumor*:ab,ti OR cancer*:ab,ti OR malignan*:ab,ti) AND ('large intestine'/de OR 'cecum'/exp OR 'colon'/exp OR 'rectum'/exp OR colorectal*:ab,ti OR colon*:ab,ti OR rectal*:ab,ti OR appendi*:ab,ti OR cecum*:ab,ti OR coecum*:ab,ti OR caecum*:ab,ti OR cecal*:ab,ti OR coecal*:ab,ti OR caecal*:ab,ti OR sigmoid*:ab,ti))	486,547

### Search strategy for Clarivate Analytics/Web of Science Core Collection (3 December 2018)

Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=All years

TOPIC = words in title, abstract or author keywords

NEAR/x = words near to each other, x places apart

Search	Query	Items found
#5	#4 AND #3 AND #2 AND #1	3,063
#4	TOPIC: (plasma* OR hematolog* OR haematolog* OR blood OR serum* OR seral*)	3,582,437
#3	TOPIC: (methylati* OR mutation* OR ("copy number*" AND (variation* OR variant* OR change*)) OR abberati* OR alterati* OR amplificati* OR gain* OR loss* OR deleti*)	3,332,539
#2	TOPIC: (dna OR dnas OR kras OR braf OR sept9 OR "sept 9" OR cdkn2a OR p16 OR hltf OR alx4 OR alex4 OR bcat1 OR ikzf1 OR vim OR pik3ca OR tp53 OR "tp 53" OR apc OR cfdna* OR ccdna* OR ctdna* OR ftdna* OR fcdna* OR cpdna*)	1,381,156
#1	TOPIC: (((carcinoma* OR neoplas* OR tumour* OR adenocar* OR adenoid* OR tumor* OR cancer* OR malignan*) NEAR/3 (colorectal* OR colon* OR rectal* OR appendi* OR cecum* OR coecum* OR caecum* OR cecal* OR coecal* OR caecal* OR sigmoid*)))	289,433

**Supplementary Figure 1a**

Risk of bias assessment according to the QUADAS-2 for all 134 initially included studies.



## Supplementary Figure 1b

A detailed overview of the risk of bias assessment according to the QUADAS-2 for each study.

	Risk of Bias				Applicability Concerns				Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard		Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Ahliquist Clin Gastroenterol Hepatol. 2012	High	Low	Low	Low	Low	Low	Low	Ito Jpn J Cancer Res. 2002	Unclear	High	Low	Low	Low	Low	Low
Alizadeh Asian Pac J Cancer Prev. 2018	Unclear	High	Low	Low	Low	Low	Low	Ito Oncol Rep. 2003	Low	Unclear	Low	Low	Low	Low	Low
Anker Gastroenterology. 1997	High	High	Unclear	Unclear	Low	Low	Unclear	Jin J Gastroenterol Hepatol. 2015	Low	Low	Low	Low	Low	Low	Low
Bartak Epigenetics. 2017	High	High	Low	High	Low	Low	Low	Johnson PLoS One. 2014	Low	Unclear	Low	Unclear	Low	Low	Low
Baumgartner Ann Surg Oncol. 2018	Low	High	Low	High	High	Low	Low	Kawasaki Personalized Medicine Universe. 2013	Unclear	High	Low	Low	Low	Low	Low
Bazan Ann Oncol. 2018	High	High	Low	Low	Unclear	Low	Low	Kidess Oncotarget. 2015	Unclear	Low	Low	Low	Low	Low	Low
Bedin Int J Cancer. 2017	Unclear	High	Low	Low	Low	Low	Low	Kim Clin Lab. 2018	Low	High	Low	Low	Low	Low	Low
Beranek Acta Medica (Hradec Kralove). 2016	Unclear	Low	Low	Unclear	Low	Low	Low	Kim Oncol Rep. 2011	Unclear	Low	Low	Low	Low	Low	Low
Bergheim Br J Cancer. 2018	Low	High	Low	Low	Low	Low	Low	Kim Oncotarget. 2015	Unclear	Low	Low	Low	Low	Low	Low
Bettegowda Sci Transl Med. 2014	Unclear	High	Low	Low	Low	Low	Low	Kloten Oncotarget. 2017	Unclear	Low	Low	Low	Low	Low	Low
Boeckx Clin Colorectal Cancer. 2018	Unclear	High	Low	Low	Low	Low	Low	Kondratov Biopolym. Cell. 2014	Unclear	Low	Low	Low	Low	Low	Low
Chen J Clin Lab Anal. 2017	Low	Low	Low	Low	Low	Low	Low	Kottorou Oncotarget. 2018	Unclear	Low	Low	High	Low	Low	Low
Church Gut. 2014	High	Low	Low	Low	Low	Low	Low	Kuo Clin Chim Acta. 2014	Unclear	Low	Low	Low	Low	Low	Low
Danese Br J Cancer. 2013	Low	Low	Low	Low	Low	Low	Low	Lee Clin Cancer Res. 2009	Unclear	Low	Low	Low	Low	Low	Low
Danese PLoS One. 2015	Low	Low	Low	Low	Low	Low	Low	Leung Am J Gastroenterol. 2005	Unclear	High	Low	Low	Low	Low	Low
de Kok Scand J Clin Lab Invest. 1997	Unclear	High	Low	Low	Low	Low	Low	Lilleberg Ann N Y Acad Sci. 2004	Unclear	Low	Low	Low	Low	Low	Low
deVos Clin Chem. 2009	Unclear	High	Low	Unclear	Low	Low	Low	Li Mol Oncol. 2017	Low	Low	Low	Low	Low	Low	Low
Diehl Gastroenterology. 2008	Unclear	High	Low	Low	Low	Low	Low	Lin Ann Surg Oncol. 2014	Unclear	Unclear	Low	Low	Low	Low	Low
Diehl Proc Natl Acad Sci U S A. 2005	Low	High	Low	Low	Low	Low	Low	Lin Ann Surg Oncol. 2015	High	Low	Low	Unclear	Low	Low	Low
Ebert Gastroenterology. 2006	High	Low	Low	Low	Low	Low	Low	Li Nat Biotechnol. 2009	Unclear	Low	Low	Low	Low	Low	Low
Erdem Turk J Gastroenterol. 2014	Unclear	Unclear	Low	Low	Low	Low	Low	Lindfors Anticancer Res. 2005	Unclear	High	Low	Low	Low	Low	Low
Fratini Cancer Lett. 2008	Unclear	Unclear	Low	Low	Low	Low	Low	Li Theranostics. 2018	Unclear	Low	Low	Low	Low	Low	Low
Fu Dis Markers. 2018	Unclear	Low	Low	Low	Low	Low	Low	Liu Biomarkers. 2013	Unclear	High	Low	Low	Low	Low	Low
Furuki Eur J Surg Oncol. 2018	Unclear	High	Low	Low	Low	Low	Low	Liu Clin Chim Acta. 2010	Unclear	Unclear	Low	Low	Low	Low	Low
Grady Cancer Res. 2001	Unclear	Unclear	Low	Low	Low	Low	Low	Liu Exp Ther Med. 2012	Unclear	Unclear	Low	Low	Low	Low	Low
Grutzmann PLoS One. 2008	Unclear	High	Low	High	Low	Low	Low	Lofton-Day Clin Chem. 2008	Unclear	Low	Low	Low	Low	Low	Low
He Cancer Genet Cytogenet. 2010	Unclear	Low	Low	Low	Low	Low	Low	Loree J Natl Cancer Inst. 2018	Unclear	High	Low	Low	Low	Low	Low
Herbst Am J Gastroenterol. 2011	Unclear	High	Low	Low	Low	Low	Low	Matthaios Oncol Lett. 2016	Unclear	Unclear	Low	Low	Low	Low	Low
Herbst Eur J Gastroenterol Hepatol. 2009	Unclear	Low	Low	Low	Low	Low	Low	Melson Int J Cancer. 2014	Unclear	High	Low	Low	Low	Low	Low
Herbst Int J Cancer. 2017	Unclear	Low	Low	Low	Low	Low	Low	Miotto Cancer Res. 2004	Unclear	Unclear	Low	Low	Low	Low	Low
Hibi Anticancer Res. 2012	Unclear	Low	Low	Low	Low	Low	Low	Mitchell Genes (Basel). 2016	Unclear	Low	Low	Low	Low	Low	Low
Hibi Cancer Lett. 2011	Unclear	Low	Low	Low	Low	Low	Low	Miyano Exp Ther Med. 2012	Unclear	High	Low	Low	Low	Low	Low
Hibi Cancer Res. 1998	Unclear	High	Low	High	Low	Low	Low	Molparia PLoS One. 2018	Unclear	Low	Low	Low	Low	Low	Low
Hsieh Am Surg. 2005	Unclear	Unclear	Low	Low	Low	Low	Low	Nagai Oncotarget. 2017	Low	High	Low	Low	Low	Low	Low

● High      ? Unclear      ● Low

● High      ? Unclear      ● Low



### Supplementary Figure 1b (continued)

	Risk of Bias				Applicability Concerns				Risk of Bias				Applicability Concerns				
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard		Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard		
Nakayama Anticancer Res. 2007	?	●	●	●	●	●	●		Song Biomark Med 2018	?	●	●	●	●	●	●	●
Nakayama Anticancer Res. 2011	?	●	●	●	●	●	●		Song Epigenomics. 2017	●	●	●	●	●	●	●	●
Nakayama Cancer Lett. 2002	?	●	●	●	●	●	●		Song J Cancer Res Clin Oncol. 2017	●	●	●	●	●	●	●	●
Nishio Anticancer Res. 2010	?	●	●	●	●	●	●		Sun Oncol Lett. 2018	●	●	●	●	●	●	●	●
Nunes Cancers (Basel). 2018	●	●	●	●	●	●	●		Symonds Clin Epigenetics. 2018	?	●	●	●	●	●	●	●
Oh J Mol Diagn. 2013	?	●	●	●	●	●	●		Symonds Clin Transl Gastroenterol. 2016	●	●	●	●	●	●	●	●
Olmedillas Int J Mol Sci. 2016	●	?	●	●	●	●	●		Taback Ann N Y Acad Sci. 2006	?	●	●	●	●	●	●	●
Ono Mol Oncol. 2017	?	●	●	●	●	●	●		Tanzer PLoS One. 2010	?	●	●	●	●	●	●	●
Orntoft BMC Cancer. 2015	●	●	●	●	●	●	●		Thomsen Cancer Med. 2017	●	●	●	●	●	●	●	●
Pack Int J Colorectal Dis. 2013	●	●	●	●	●	●	●		Tian Int J Biol Markers. 2017	●	●	●	●	●	●	●	●
Pedersen BMC Cancer. 2015	●	●	●	●	●	●	●		Toledo Oncotarget 2017	?	●	●	●	●	●	●	●
Perrone Tumori. 2014	?	?	●	●	●	●	●		Toth PLoS One. 2012	?	●	●	●	●	●	●	●
Phallen Sci Transl Med. 2017	●	●	●	●	●	●	●		Toth PLoS One. 2014	?	●	●	●	●	●	●	●
Philipp BMC Cancer. 2014	?	●	●	●	●	●	●		Wallner Clin Cancer Res. 2006	?	●	●	?	●	●	●	●
Philipp Int J Cancer. 2012	?	●	●	●	●	●	●		Wang World J Surg. 2004	?	?	●	●	●	●	●	●
Potter Clin Chem. 2014	?	●	●	●	●	●	●		Warren BMC Med. 2011	?	●	●	●	●	●	●	●
Pu Oncol Lett. 2013	?	?	●	●	●	●	●		Wu Chin J Cancer Res. 2011	?	?	●	●	●	●	●	●
Rachiglio Oncotarget. 2016	?	●	●	●	●	●	●		Wu J Mol Diagn. 2016	●	●	●	?	●	●	●	●
Rasmussen PLoS One. 2017	?	●	●	●	●	●	●		Xiao Oncol Lett. 2015	?	?	●	?	●	●	●	●
Rezvani Oncol Lett. 2017	?	●	●	●	●	●	●		Xie Front Oncol. 2018	?	●	●	●	●	●	●	●
Riviere Mol Cancer Ther. 2018	●	●	●	?	●	●	●		Xue Oncotarget. 2017	?	?	?	?	●	●	●	●
Roperch BMC Cancer. 2013	?	●	●	●	●	●	●		Xu J Dig Dist 2018	●	●	●	●	●	●	●	●
Ryan Gut. 2003	?	●	●	●	●	●	●		Yamada Cancer Sci. 2016	?	●	●	●	●	●	●	●
Sabbioni Mol Diagn. 2003	?	?	?	?	●	●	●		Yamashita PLoS One. 2014	?	●	●	●	●	●	●	●
Sakai PLoS One. 2015	?	?	●	●	●	●	●		Yamauchi Int J Cancer. 2018	●	●	●	●	●	●	●	●
Sakamoto Cancer Epidemiol. 2010	?	?	●	●	●	●	●		Yang Biosci Rep. 2018	?	●	●	●	●	●	●	●
Salehi Adv Biomed Res. 2015	?	?	●	●	●	●	●		Yan World J Gastroenterol. 2014	●	?	●	●	●	●	●	●
Sclafani Sci Rep. 2018	●	●	●	●	●	●	●		Yuan Transl Cancer Res 2016	?	?	●	●	●	●	●	●
Sefrioui Clin Biochem. 2017	●	●	●	●	●	●	●		Zeng Mol Diagn Ther. 2017	?	●	●	●	●	●	●	●
Shalaby Gene. 2018	?	●	●	●	●	●	●		Zhang World J Gastroenterol. 2015	?	●	●	●	●	●	●	●
Shen Lab Med. 2010	?	●	?	?	●	●	●		Zheng Hepatogastroenterology. 2011	?	?	●	●	●	●	●	●
Shin PLoS One. 2017	●	●	●	●	●	●	●		Zou Clin Cancer Res. 2002	?	?	●	●	●	●	●	●
Shirahata Anticancer Res. 2010	?	?	●	●	●	●	●										
Shirahata Anticancer Res. 2014	?	●	●	●	●	●	●										

● High      ? Unclear      ● Low