

Appendix A. Search Strategy for MEDLINE®

1. exp Colorectal Neoplasms/
2. ((colorectal or colon\$ or rectal or Sigmoid) adj3 (neoplasm\$ or cancer\$ or carcino\$ or tumo?r\$)).tw.
3. 1 or 2
4. Gene Expression Profiling/
5. (gene expression adj (profil\$ or monitor\$ or pattern\$ or signature\$ or predictor\$ or test\$ or chip\$ or regulation)).tw.
6. transcript\$ expression analys\$.tw.
7. transcriptom\$.tw.
8. ((DNA or cDNA or tissue) adj (fingerprint\$ or microarray\$)).tw.
9. ((mrna or mirna or Microarray or MicroRNA) adj2 (profil\$ or expression or signature\$)).tw.
10. array sequence analysis.tw.
11. oncotype dx.tw.
12. Affymetrix.tw.
13. Coloprint.tw.
14. (Mismatch repair deficiency status or dmmr).tw.
15. microsatellite instability/
16. Microsatellite Repeats/
17. replication error phenotype\$.tw.
18. or/4-17
19. recurrence/
20. (recur\$ or relaps\$).tw.
21. exp treatment outcome/
22. (respons\$ or outcome\$ or react\$ or eligibl\$).tw.
23. Chemotherapy, Adjuvant/
24. (adjuvant or chemotherap\$).tw.
25. or/19-24
26. incidence/
27. exp mortality/
28. follow up studies/
29. prognos\$.tw.
30. predict\$.tw.
31. course\$.tw.
32. or/26-31
33. and/3,18,25,32
34. (animals not humans).sh.
35. 33 not 34

Appendix B. Elements Abstracted from Included Articles

For all articles:

- Article (details regarding author(s), institutions, funding)
- Which test(s) were used?
 - Type(s) of tissue used (e.g., fresh tissue)
 - Time for analysis (turnaround time)
- Inclusion and exclusion criteria
 - Was only a subset of patients with stage II disease used? If so, which one?
 - For adjuvant chemotherapy, which regimens were used?
 - Sample size (number of patients/specimens)
 - If samples are from previous studies, which studies?
 - Is there information to assess the completeness of sampling from previous studies?

For articles that describe analytic validity:

- Was information provided about preanalytic factors (e.g., handling of specimens)?
- What aspects of analytic validity were measured (e.g., accuracy, reproducibility)?
- Does it provide narrative summary of results related to analytic validity?

For articles that describe clinical validity and clinical utility:

- What outcomes were measured, for example, recurrence rates, response to adjuvant chemotherapy (regimen specific), avoidance of chemotherapy (with reduction in medication side effects), et cetera?
- What was the study design?
 - Prospective, retrospective, or prospective-retrospective
 - Randomized trial, controlled trial, cohort study, or case (convenience) series
 - Derivation and/or validation (For validation, when was the method of analysis and interpretation determined?)
- Was a reclassification analysis performed (to determine if the GEP test results provide new (additional) information when compared with that obtained with usual predictors)?
- Was MSI (MMR) status determined?
 - If so, by which method?
- Was MSI (MMR) status considered in the overall analysis?
 - If so, how?
- Was the GEP performed (analysis, calculation, interpretation) as described in initial studies for derivation and/or studies of analytic validity?
- Does the final classification provide discrimination among groups of patients; that is, are the patients grouped into a specific category that is distinct and different from other categories? (In addition, when the GEP predicts risk groups, how were the cut-points for various groups determined?)
- Do the authors comment on factors such as race and ethnic background that could impact the generalizability of the findings?

- For blinding, were determinations of the outcomes and the GEP result made independently, that is, did those assessing outcomes know the results of GEP testing?

The following additional information will be obtained from these articles (related to the validity of the outcomes):

- For recurrence of disease, how was it measured (duration of followup, biopsy result, imaging finding, level of carcinoembryonic antigen, etc.)?
- For response to adjuvant chemotherapy, how was it measured?
- For disease-free survival, how was it determined?

Note: Study results will NOT be abstracted.

Appendix C. Publications that Did Not Provide Specific Results for Stage II Colon Cancer

1. Ågesen TH, Sveen A, Merok MA, et al. ColoGuideEx: a robust gene classifier specific for stage II colorectal cancer prognosis. *Gut*. 2012 Jan 2 PMID: 22213796.
2. Antonacopoulou AG, Grivas PD, Skarlas L, et al. POLR2F, ATP6V0A1 and PRNP expression in colorectal cancer: new molecules with prognostic significance? *Anticancer Research*. 2008 Mar-Apr;28(2B):1221-7. PMID: 18505059.
3. Barrier A, Boelle P-Y, Lemoine A, et al. Gene expression profiling of nonneoplastic mucosa may predict clinical outcome of colon cancer patients. *Diseases of the Colon & Rectum*. 2005 Dec;48(12):2238-48. PMID: 16228831.
4. Barrier A, Lemoine A, Boelle P-Y, et al. Colon cancer prognosis prediction by gene expression profiling. *Oncogene*. 2005 Sep 8;24(40):6155-64. PMID: 16091735.
5. Camus M, Tosolini M, Mlecnik B, et al. Coordination of intratumoral immune reaction and human colorectal cancer recurrence. *Cancer Research*. 2009 Mar 15;69(6):2685-93. PMID: 19258510.
6. Coppola D, Nebozhyn M, Khalil F, et al. Unique ectopic lymph node-like structures present in human primary colorectal carcinoma are identified by immune gene array profiling. *American Journal of Pathology*. 2011 Jul;179(1):37-45. PMID: 21703392.
7. Deves C, Renck D, Garicochea B, et al. Analysis of select members of the E26 (ETS) transcription factors family in colorectal cancer. *Virchows Archiv*. 2011 Apr;458(4):421-30. PMID: 21318373.
8. Fritzmann J, Morkel M, Besser D, et al. A colorectal cancer expression profile that includes transforming growth factor beta inhibitor BAMBI predicts metastatic potential. *Gastroenterology*. 2009 Jul;137(1):165-75. PMID: 19328798.
9. Gröene J, Mansmann U, Meister R, et al. Transcriptional census of 36 microdissected colorectal cancers yields a gene signature to distinguish UICC II and III.[Erratum appears in *Int J Cancer*. 2007 Jul 15;121(2):466]. *International Journal of Cancer*. 2006 Oct 15;119(8):1829-36. PMID: 16721809.
10. Kammula US, Kuntz EJ, Francone TD, et al. Molecular co-expression of the c-Met oncogene and hepatocyte growth factor in primary colon cancer predicts tumor stage and clinical outcome. *Cancer Letters*. 2007 Apr 18;248(2):219-28. PMID: 16945480.
11. Kornmann M, Schwabe W, Sander S, et al. Thymidylate synthase and dihydropyrimidine dehydrogenase mRNA expression levels: predictors for survival in colorectal cancer patients receiving adjuvant 5-fluorouracil. *Clinical Cancer Research*. 2003 Sep 15;9(11):4116-24. PMID: 14519634.
12. Lassmann S, Hennig M, Rosenberg R, et al. Thymidine phosphorylase, dihydropyrimidine dehydrogenase and thymidylate synthase mRNA expression in primary colorectal tumors-correlation to tumor histopathology and clinical follow-up. *International Journal of Colorectal Disease*. 2006 Apr;21(3):238-47. PMID: 16132996.
13. Lin Y-H, Friederichs J, Black MA, et al. Multiple gene expression classifiers from different array platforms predict poor prognosis of colorectal cancer. *Clinical Cancer Research*. 2007 Jan 15;13(2 Pt 1):498-507. PMID: 17255271.
14. Merlos-Suarez A, Barriga FM, Jung P, et al. The intestinal stem cell signature identifies colorectal cancer stem cells and predicts disease relapse. *Cell Stem Cell*. 2011 May 6;8(5):511-24. PMID: 21419747.
15. Pogue-Geile KL, Yothers GA, Gavin P, et al. Use of a prognostic (prog) gene index and nodal status to identify a subset of stage II and III colon cancer patients (pts) who may not need oxaliplatin (ox)-containing adjuvant chemotherapy. *Journal of Clinical Oncology*. Conference. 2010;28(15 SUPPL. 1) PMID: 70259000.
16. Salazar R, Roepman P, Capella G, et al. Gene expression signature to improve prognosis prediction of stage II and III colorectal cancer. *Journal of Clinical Oncology*. 2011 Jan 1;29(1):17-24. PMID: 21098318.

17. Staub E, Groene J, Heinze M, et al. An expression module of WIPF1-coexpressed genes identifies patients with favorable prognosis in three tumor types. *Journal of Molecular Medicine*. 2009 Jun;87(6):633-44. PMID: 19399471.
18. Vendrell E, Ribas M, Valls J, et al. Genomic and transcriptomic prognostic factors in R0 Dukes B and C colorectal cancer patients. *International Journal of Oncology*. 2007 May;30(5):1099-107. PMID: 17390011.
19. Yamasaki M, Takemasa I, Komori T, et al. The gene expression profile represents the molecular nature of liver metastasis in colorectal cancer. *International Journal of Oncology*. 2007 Jan;30(1):129-38. PMID: 17143521.