

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

GENEOSCOPY, INC.,
Petitioner,

v.

EXACT SCIENCES CORPORATION,
Patent Owner.

U.S. Patent 11,634,781

DECLARATION OF BRENDAN T. JONES

1. I am an attorney at Foley Hoag LLP, and counsel of record for Geneoscopy, Inc. in the above-captioned matter. I am registered to practice before the United States Patent and Trademark Office.

2. Attached as EX1004 is a true and correct copy of Konstanze Lenhard et al., “Analysis of Promoter Methylation in Stool: A Novel Method for the Detection of Colorectal Cancer,” *Clinical Gastroenterology and Hepatology*, 3:142-149 (2005).

3. Attached as Ex. 1005 is a true and correct copy of Alex Vilkin et al., “Performance Characteristics and Evaluation of an Automated-Developed and Quantitative, Immunochemical Fecal Occult Blood Screening Test,” *American Journal of Gastroenterology*, 100:2519-2525 (2005).

4. Attached as Ex. 1006 is a true and correct copy of Steven Itzkowitz et al., “Improved Fecal DNA Test for Colorectal Cancer Screening,” *Clinical Gastroenterology and Hepatology*, 5:111-117 (2007).

5. Attached as Ex. 1008 is a true and correct copy of Sarah Derks et al., “Promoter Methylation Precedes Chromosomal Alterations in Colorectal Cancer Development,” *Cellular Oncology*, 28:247-257 (2006).

6. Attached as Ex. 1010 is a true and correct copy of Lydia Guittet et al., “Comparison of A Guaiac Based And An Immunochemical Faecal Occult Blood Test In Screening For Colorectal Cancer In A General Average Risk Population,” *Gut*, 56:210-214 (2007).

7. Attached as Ex. 1011 is a true and correct copy of Takashi Nishikawa et al., “A Simple Method Of Detecting K-Ras Point Mutations in Stool Samples for Colorectal Cancer Screening Using One-Step Polymerase Chain Reaction/Restriction Fragment Length Polymorphism Analysis,” *Clinica Chimica Acta*, 318 107–112 (2002).

8. Attached as Ex. 1012 is a true and correct copy of Nadie Kutzner et al., “Non-Invasive Detection of Colorectal Tumours by the Combined Application Of Molecular Diagnosis and the Faecal Occult Blood Test,” *Cancer Letters*, 229:33-41 (2005).

9. Attached as Ex. 1013 is a true and correct copy of Bernard Levin et al., “Screening and Surveillance for the Early Detection of Colorectal Cancer and Adenomatous Polyps, a Joint Guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology,” *Gastroenterology*, 134:1570–1595 (2008).

10. Attached as Ex. 1016 is a true and correct copy of the LinkedIn profile of Dr. Joost Louwagie as obtained from <https://www.linkedin.com/in/joost-louwagie/?originalSubdomain=ch> on January 10, 2024.

11. Attached as Ex. 1024 is a true and correct copy of GP Young et al., “New Stool Screening Tests for Colorectal Cancer,” *Digestion*, 76:26-33 (2007).

12. Attached as Ex. 1025 is a true and correct copy of Jeff Olson et al., “DNA Stabilization is Critical for Maximizing Performance of Fecal DNA-Based Colorectal Cancer Tests,” *Diagnostic Molecular Pathology*, 3:183-191 (2005).

13. Attached as Ex. 1026 is a true and correct copy of Dorothy Melvin and Marion Brooke, “Laboratory Procedures for the Diagnosis of Intestinal Parasites”, *U.S. Department of Health and Human Services Centers for Disease Control* (1982).

14. Attached as Ex. 1029 is a true and correct copy of N. Hoepffner et al., “Comparative Evaluation of a New Bedside Faecal Occult Blood Test in a Prospective Multicentre Study,” *Alimentary Pharmacology & Therapeutics*, 23:145-154 (2006).

15. Attached as Ex. 1030 is a true and correct copy of Jordan Nechvatal et al., “Fecal Collection, Ambient Preservation, and DNA Extraction for PCR Amplification of Bacterial And Human Markers from Human Feces,” *Journal of Microbiological Methods*, 72(2):124-32 (2008).

16. Attached as Ex. 1033 is a true and correct copy of JB Simon, “Occult Blood Screening for Colorectal Carcinoma: A Critical Review,” *Gastroenterology*, 88:820-837 (1985).

17. Attached as Ex. 1035 is a true and accurate copy of D. Sidransky, “Identification of Ras Oncogene Mutations in the Stool of Patients with Curable Colorectal Tumors,” *Science*, 256:102–105 (1992).
18. Attached as Ex. 1037 is a true and correct copy of Hannes Müller et al., “Methylation Changes in Faecal DNA: A Marker for Colorectal Cancer Screening?” *Lancet*, 63:1283-1285 (2004).
19. Attached as Ex. 1038 is a true and correct copy of Kornel Schuebel et al., “Comparing the DNA Hypermethylome with Gene Mutations in Human Colorectal Cancer,” *PLoS Genet.* 3:1709–1723 (2007).
20. Attached as Ex. 1039 is a true and correct copy of Lanlan Shen, et al., “Integrated Genetic and Epigenetic Analysis Identifies Three Different Subclasses of Colon Cancer,” *Proc Natl. Acad. Sci. U.S.A.* 104(47): 18654–18659 (2007).
21. Attached as Ex. 1040 is a true and correct copy of Tagore, K.S., et al., “Review Article: the Evolution to Stool DNA Testing for Colorectal Cancer,” *Aliment Pharmacol. Ther.* 19: 1225-1233 (2004).
22. Attached as Ex. 1041 is a true and correct copy of the abstract of Sarah Derks et al., “Promoter Methylation Precedes Chromosomal Alterations in Colorectal Cancer Development,” *Cellular Oncology*, 28:247-257 (2006), obtained from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4618222/> on January 9, 2024.

23. Attached as Ex. 1043 is a true and correct copy of Thomas Imperiale et al., “Fecal DNA Versus Fecal Occult Blood for Colorectal-Cancer Screening in an Average-Risk Population,” *New England Journal Medicine*, 351(26): 2704-2714 (2004).

24. Attached as Ex. 1044 is a true and correct copy of David Ahlquist et al., “Stool DNA and Occult Blood Testing for Screen Detection of Colorectal Neoplasia,” *Annals of Internal Medicine*, 149(7): 441–W81 (2008).

25. Attached as Ex. 1045 is a true and correct copy of Rennert et al., “Detecting K-Ras Mutations in Stool from Fecal Occult Blood Test Cards in Multiphasic Screening for Colorectal Cancer,” *Cancer Letters*, 253: 258-264 (2007).

26. Attached as Ex. 1047 is a true and correct copy of Karl, et al., “Improved Diagnosis of Colorectal Cancer Using a Combination of Fecal Occult Blood and Novel Fecal Protein Markers,” *Clinical Gastroenterology and Hepatology*, 6:1122–1128 (2008).

27. Attached as Ex. 1048 is a true and correct copy of Donald Ostrow, “Tests for Fecal Occult Blood, in Clinical Methods: The History, Physical, and Laboratory Examinations.” Boston: Butterworths; Chapter 98 (1990).

28. Attached as Ex. 1050 is a true and correct copy of Charles Kahi et al., “Screening, Surveillance, and Primary Prevention for Colorectal Cancer: A Review of the Recent Literature,” *Gastroenterology*, 135: 380-399 (2008).

29. Attached as Ex. 1051 is a true and correct copy of Victoria White and Richard Miller, “Colorectal Cancer: Prevention and Early Diagnosis,” *Medicine*, 35(6) 297-301 (2007).

30. Attached as Ex. 1052 is a true and correct copy of H Zou et al., “Highly Methylated Genes in Colorectal Neoplasia: Implications for Screening,” *Cancer Epidemiol Biomarkers Preview*, 16(12):2686-96 (2007).

31. Attached as Ex. 1053 is a true and correct copy of Susumu Eguchi et al., “Mutations of the P53 Gene in Stool of Patients with Resectable Colorectal Cancer,” *Cancer*, 77:1707–1710 (1996).

32. Attached as Ex. 1054 is a true and correct copy of E. Villa, et al., “Identification of Subjects at Risk for Colorectal Carcinoma through a Test Based on K-Ras Determination in the Stool,” *Gastroenterology*, 110:1346–1353 (1996).

33. Attached as Ex. 1055 is a true and correct copy of Steven Itzkowitz, “A Simplified, Noninvasive Stool DNA Test for Colorectal Cancer Detection,” *American Journal of Gastroenterology*, 103: 2862-2870 (2008).

34. Attached as Ex. 1056 is a true and correct copy of Boynton et al., “DNA Integrity as a Potential Marker for Stool-based Detection of Colorectal Cancer,” *Clinical Chemistry*, 49:7 1058–1065 (2003).

35. Attached as Ex. 1057 is a true and correct copy of J. Milburn Jessup et al., “Diagnosing Colorectal Carcinoma: Clinical and Molecular Approaches,” *A Cancer Journal for Clinicians*, 47(2):70-92 (1997).

36. Attached as Ex. 1058 is a true and correct copy of WD Chen et al., “Detection in Fecal DNA of Colon Cancer-Specific Methylation of the Nonexpressed Vimentin Gene.” *Journal of National Cancer Institute*, 97:1124-1132 (2005).

37. Attached as Ex. 1059 is a true and correct copy of L-C Li and R. Dahiya, “MethPrimer: Designing Primers for Methylation Pcrs,” *Bioinformatics*, 18(11): 1427-1431 (2002).

38. Attached as Ex. 1061 is a true and correct copy of Shigeru Kanaoka et al., “Potential Usefulness of Detecting Cyclooxygenase 2 Messenger RNA in Feces for Colorectal Cancer Screening,” *Gastroenterology*, 127:422-427 (2004).

39. Attached as Ex. 1062 is a true and correct copy of Y. Matsumura and D. Tarin, “Significance of CD44 Gene Products for Cancer Diagnosis and Disease Evaluation,” *Lancet*, 340: 1053-1058 (1992).

40. Attached as Ex. 1063 is a true and correct copy of Y Mastumura et al., “Non-Invasive Detection of Malignancy by Identification of Unusual CD44 Gene Activity in Exfoliated Cancer Cells,” *BMJ*, 308:619-624 (1994).

41. Attached as Ex. 1064 is Wai Leung et al., “Detection of Hypermethylated DNA or Cyclooxygenase-2 Messenger RNA in Fecal Samples of Patients with Colorectal Cancer or Polyps,” *American Journal Gastroenterology*, 102: 1070-1076 (2007).

42. Attached as Ex. 1065 is a true and correct copy of D.A. Ahlquist et al., “Colorectal Cancer Screening by Detection of Altered Human DNA in Stool: Feasibility of a Multitarget Assay Panel,” *Gastroenterology*, 119(5):1219-1227 (2000).

43. Attached as Ex. 1066 is a true and correct copy of D.A. Ahlquist et al., “Molecular Stool Screening for Colorectal Cancer. Using DNA Markers May Be Beneficial, But Large Scale Evaluation is Needed.” *BMJ*, 29;321(7256):254-5 (2000).

44. Attached as Ex. 1068 is a true and correct copy of Suzanne Mahon, “Prevention and Screening of Gastrointestinal Cancers,” *Seminars in Oncology Nursing*, 25(1): 15-31 (2009).

45. Attached as Ex. 1069 is a true and correct copy of G.P. Young, “Fecal Immunochemical Tests (FIT) vs. Office-Based Guaiac Fecal Occult Blood Test (FOBT),” *Practical Gastroenterology* (2004).

46. Attached as Ex. 1071 is a true and correct copy of I Hirata et al., “Usefulness of Fecal Lactoferrin and Hemoglobin in Diagnosis of Colorectal Diseases,” *World Journal of Gastroenterology*, 14;13(10):1569-74 (2007).

47. Attached as Ex. 1072 is a true and correct D.A. Ahlquist et al., “A Stool Collection Device: The First Step in Occult Blood Testing,” *Annals of Internal Medicine*, (108)4:609-612 (1988).

48. Attached as Ex. 1073 is a true and accurate copy of the online version of Konstanze Lenhard et al., “Analysis of Promoter Methylation in Stool: A Novel Method for the Detection of Colorectal Cancer,” *Clinical Gastroenterology and Hepatology*, 3:142-149 (2005), obtained from [https://www.cghjournal.org/article/S1542-3565\(04\)00624-X/fulltext](https://www.cghjournal.org/article/S1542-3565(04)00624-X/fulltext), on January 9, 2024.

49. Attached as Ex. 1074 is a true and accurate copy of Farid Ahmed et al., “Transcriptomic Molecular Markers for Screening Human Colon Cancer in Stool and Tissue,” *Cancer Genomics and Proteomics* 4:1-20 (2007).

50. Attached as Ex. 1076 is a true and accurate copy of the online version of Steven Itzkowitz et al., “Improved Fecal DNA Test for Colorectal Cancer

Screening,” *Clinical Gastroenterology and Hepatology*, 5:111-117 (2007), as obtained from [https://www.cghjournal.org/article/S1542-3565\(06\)01044-5/fulltext](https://www.cghjournal.org/article/S1542-3565(06)01044-5/fulltext), on January 9, 2024.

51. Attached Ex. 1077 is a true and accurate copy of a December 13, 2006 press release obtained from <https://www.sciencedaily.com/releases/2006/12/061213104115.htm#> on January 9, 2024.

I declare, under penalty of perjury under the laws of the United States, that the foregoing is true and accurate.

Dated: January 11, 2024

/Brendan T. Jones/
Brendan T. Jones