Surgery and was involved in the experimental design of the Osaka discovery sample set, data analysis/interpretation and unblinding of data. HM was the head of surgery (for CRC population, Chiba) responsible for the patient enrolment and selection for the Chiba samples. FN was the group leader at Chiba overseeing the entire project, including protocol design and approvals, data analysis and unblinding. DBG was the President and CEO of Phenomenome Discoveries Inc, and oversaw most of the efforts at PDI, was integrally involved in the interpretation of MS/MS data, the development of FTICR methodology, the experimental designs and was also a significant contributor to the format and direction of the manuscript.

Competing interests

The following authors are full-time employees and have received salaries from Phenomenome Discoveries Inc, Saskatoon, Canada: Shawn A Ritchie, Pearson W K Ahiahonu, Dushmanthi Jayasinghe, Doug Heath, Jun Liu, Yingshen Lu, Wei Jin, Amir Kavianpour, Yasuyo Yamazaki, Amin M. Khan. Mohammad Hossain, Khine Khine Su-Myat and Paul L Wood. Dayan B Goodenowe is the co-founder, President and CEO, of Phenomenome Discoveries, Inc. Only Dayan B Goodenowe owns shares in the company. Kevin Krenitsky, Ichiro Takemasa, Masakazu Miyake, Mitsugo Sekimoto, Morito Monden, Hisahiro Matsubara and Fumio Numura have no competing financial interests. None of the authors have non-financial competing interests. Phenomenome Discoveries Inc is financing the article processing fees for the manuscript. Shawn A Ritchie and Dayan B Goodenowe are named inventors on submitted patent applications relating to the discoveries disclosed within the manuscript and have both received a salary from Phenomenome Discoveries Inc (the organization named in the patents).

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References

- Roy HK, Backman V, Goldberg MJ: Colon cancer screening: the good, the bad, and the ugly. Arch Intern Med 2006, 166:2177-2179.
- Ouyang DL, Chen JJ, Getzenberg RH, Schoen RE: Noninvasive testing for colorectal cancer: a review. Am J Gastroenterol 2005, 100:1393-1403.
- Davies RJ, Miller R, Coleman N: Colorectal cancer screening: prospects for molecular stool analysis. Nat Rev Cancer 2005, 5:199-209.
- Kleivi K, Lind GE, Diep CB, Meling GI, Brandal LT, Nesland JM, Myklebost O, Rognum TO, Giercksky KE, Skotheim RI, Lothe RA: Gene expression profiles of primary colorectal carcinomas, liver metastases, and carcinomatoses. Mol Cancer 2007, 6:2.
- Solmi R, Ugolini G, Rosati G, Zanotti S, Lauriola M, Montroni I, del Governatore M, Caira A, Taffurelli M, Santini D, Coppola D, Guidotti L, Carinci P, Strippoli P: Microarray-based identification and RT-PCR test screening for epithelial-specific mRNAs in peripheral blood of patients with colon cancer. BMC Cancer 2006, 6:250.
- Komori T, Takemasa I, Higuchi H, Yamasaki M, Ikeda M, Yamamoto H,
 Ohue M, Nakamori S, Sekimoto M, Matsubara K, Monden M: Identification
 of differentially expressed genes involved in colorectal carcinogenesis
 using a cDNA microarray. J Exp Clin Cancer Res 2004, 23:521-527.
- Hegde P, Qi R, Gaspard R, Abernathy K, Dharap S, Earle-Hughes J, Gay C, Nwokekeh NU, Chen T, Saeed AI, Sharov V, Lee NH, Yeatman TJ, Quackenbush J: Identification of tumor markers in models of human colorectal cancer using a 19,200-element complementary DNA microarray. Cancer Res 2001, 61:7792-7797.
- Kitahara O, Furukawa Y, Tanaka T, Kihara C, Ono K, Yanagawa R, Nita ME, Takagi T, Nakarnura Y, Tsunoda T: Alterations of gene expression during colorectal carcinogenesis revealed by cDNA microarrays after lasercapture microdissection of tumor tissues and normal epithelia. Cancer Res 2001, 61:3544-3549.
- Notterman DA, Alon U, Sierk AJ, Levine AJ: Transcriptional gene expression profiles of colorectal adenoma, adenocarcinoma, and normal tissue examined by oligonucleotide arrays. Cancer Res 2001, 61:3124-3130.
- Takemasa I, Higuchi H, Yarnarnoto H, Sekimoto M, Tomita N, Nakamori S, Matoba R, Monden M, Matsubara K: Construction of preferential cDNA microarray specialized for human colorectal carcinoma: molecular sketch of colorectal cancer. Biochem Biophys Res Commun 2001, 285:1244-1249.
- Backert S, Gelos M, Kobalz U, Hanski ML, Bohm C, Mann B, Lovin N, Gratchev A, Mansmann U, Moyer MP, Riecken EO, Hanski C: Differential

- gene expression in colon carcinoma cells and tissues detected with a cDNA array. Int J Cancer 1999, 82:868-874.
- Mori Y, Cai K, Cheng Y, Wang S, Paun B, Harnilton JP, Jin Z, Sato F, Berki AT, Kan T, Ito T, Mantzur C, Abraham JM, Meltzer SJ: A genome-wide search identifies epigenetic silencing of somatostatin, tachykinin-1, and 5 other genes in colon cancer. Gastroenterology 2006, 131:797-808.
- Chen WD, Han ZJ, Skoletsky J, Olson J, Sah J, Myeroff L, Platzer P, Lu S, Dawson D, Willis J, Pretlow TP, Lutterbaugh J, Kasturi L, Willson JK, Rao JS, Shuber A, Markowitz SD: Detection in fecal DNA of colon cancer-specific methylation of the nonexpressed vimentin gene. J Natl Cancer Inst 2005, 97:1124-1132.
- Leung WK, To KF, Man EP, Chan MW, Bai AH, Hui AJ, Chan FK, Sung JJ: Quantitative detection of promoter hypermethylation in multiple genes in the serum of patients with colorectal cancer. Am J Gastroenterol 2005, 100:2274-2279.
- Ward DG, Suggett N, Cheng Y, Wei W, Johnson H, Billingham LJ, Ismail T, Wakelam MJ, Johnson PJ, Martin A: Identification of serum biomarkers for colon cancer by proteomic analysis. Br J Cancer 2006, 94:1898-1905.
- Lou J, Fatima N, Xiao Z, Stauffer S, Smythers G, Greenwald P, Ali IU: Proteomic profiling identifies cyclooxygenase-2-independent global proteomic changes by celecoxib in colorectal cancer cells. Cancer Epidemiol Biomarkers Prev 2006, 15:1598-1606.
- Mazzanti R, Solazzo M, Fantappie O, Elfering S, Pantaleo P, Bechi P, Cianchi F, Ettl A, Giulivi C: Differential expression proteomics of human colon cancer. Am J Physiol Gastrointest Liver Physiol 2006, 290:G1329-1338.
- Roblick UJ, Hirschberg D, Habermann JK, Palmberg C, Becker S, Kruger S, Gustafsson M, Bruch HP, Franzen B, Ried T, Bergmann T, Auer G, Jornvall H: Sequential proteome alterations during genesis and progression of colon cancer. Cell Mol Life Sci 2004, 61:1246-1255.
- de la Chapelle A: Genetic predisposition to colorectal cancer. Nat Rev Cancer 2004, 4:769-780.
- Marshall JR: Prevention of colorectal cancer: diet, chemoprevention, and lifestyle. Gastroenteral Clin North Am 2008, 37:73-82.
- Fearnhead NS, Wilding JL, Bodmer WF: Genetics of colorectal cancer: hereditary aspects and overview of colorectal tumorigenesis. Br Med Bull 2002. 64:27-43.
- McGarr SE, Ridlon JM, Hylemon PB: Diet, anaerobic bacterial metabolism, and colon cancer: a review of the literature. J Clin Gastroenterol 2005, 39:98-109
- Aharoni A, Ric de Vos CH, Verhoeven HA, Maliepaard CA, Kruppa G, Bino R, Goodenowe DB: Nontargeted metabolome analysis by use of Fourier Transform Ion Cyclotron Mass Spectrometry. Omics 2002, 6:217-234.
- Dettmer K, Aronov PA, Hammock BD: Mass spectrometry-based metabolomics. Mass Spectrom Rev 2007, 26:51-78.
- Want EJ, Nordstrom A, Morita H, Siuzdak G: From exogenous to endogenous: the inevitable imprint of mass spectrometry in metabolomics. J Proteome Res 2007, 6:459-468.
- Pinto DM, Boyd RK, Volmer DA: Ultra-high resolution for mass spectrometric analysis of complex and low-abundance mixtures - the emergence of FTICR-MS as an essential analytical tool. Anal Bioanal Chem 2002, 373:378-389.
- Breitling R, Ritchie S, Goodenowe D, Stewart ML, Barrett MP: Ab initio prediction of metabolic networks using Fourier transform mass spectrometry data. *Metabolomics* 2006, 2:155-164.
- Żytkovicz TH, Fitzgerald EF, Marsden D, Larson CA, Shih VE, Johnson DM, Strauss AW, Comeau AM, Eaton RB, Grady GF: Tandem mass spectrometric analysis for amino, organic, and fatty acid disorders in newborn dried blood spots: a two-year summary from the New England Newborn Screening Program. Clin Chem 2001, 47:1945-1955.
- Hong S, Gronert K, Devchand PR, Moussignac RL, Serhan CN: Novel docosatrienes and 17S-resolvins generated from docosahexaenoic acid in murine brain, human blood, and glial cells. Autacoids in antiinflammation. J Biol Chem 2003, 278:14677-14687.
- Hong S, Lu Y, Yang R, Gotlinger KH, Petasis NA, Serhan CN: Resolvin D1, protectin D1, and related docosahexaenoic acid-derived products: Analysis via electrospray/low energy tandem mass spectrometry based on spectra and fragmentation mechanisms. J Am Soc Mass Spectrom 2007, 18:128-144.
- Serhan CN, Hong S, Gronert K, Colgan SP, Devchand PR, Mirick G, Moussignac RL: Resolvins: a family of bioactive products of omega-3

- fatty acid transformation circuits initiated by aspirin treatment that counter proinflammation signals. *J Exp Med* 2002, 196:1025-1037.
- Lu Y, Hong S, Yang R, Uddin J, Gotlinger KH, Petasis NA, Serhan CN: Identification of endogenous resolvin E1 and other lipid mediators derived from eicosapentaenoic acid via electrospray low-energy tandem mass spectrometry: spectra and fragmentation mechanisms. Rapid Commun Mass Spectrom 2007, 21:7-22.
- Murphy RC, Fiedler J, Hevko J: Analysis of nonvolatile lipids by mass spectrometry. Chem Rev 2001, 101:479-526.
- Poulos A, Beckman K, Johnson DW, Paton BC, Robinson BS, Sharp P, Usher S, Singh H: Very long-chain fatty acids in peroxisomal disease. Adv Exp Med Biol 1992, 318:331-340.
- Johnson DW, Trinh MU: Analysis of isomeric long-chain hydroxy fatty acids by tandern mass spectrometry: application to the diagnosis of long-chain 3-hydroxyacyl CoA dehydrogenase deficiency. Rapid Commun Mass Spectrom 2003, 17:171-175.
- Lim JY, Cho JY, Paik YH, Chang YS, Kim HG: Diagnostic application of serum proteomic patterns in gastric cancer patients by ProteinChip surface-enhanced laser desorption/ionization time-of-flight mass spectrometry. Int J Biol Markers 2007, 22:281-286.
- Su Y, Shen J, Qian H, Ma H, Ji J, Ma L, Zhang W, Meng L, Li Z, Wu J, Jin G, Zhang J, Shou C: Diagnosis of gastric cancer using decision tree classification of mass spectral data. Cancer Sci 2007, 98:37-43.
- Chen YD, Zheng S, Yu JK, Hu X: Artificial neural networks analysis of surface-enhanced laser desorption/ionization mass spectra of serum protein pattern distinguishes colorectal cancer from healthy population. Clin Cancer Res 2004, 10:8380-8385.
- 39. Ringner M, Peterson C, Khan J: Analyzing array data using supervised methods. *Pharmacogenomics* 2002, **3**:403-415.
- Baggerly KA, Morris JS, Coombes KR: Reproducibility of SELDI-TOF protein patterns in serum: comparing datasets from different experiments. *Bioinformatics* 2004, 20:777-785.
- 41. LV H: Meta-Analysis. Journal of Educational Statistics 1992, 17:279-296.
- 42. Fisher RA: Statistical methods for research workers London: Oliver & Boyd, 4
- Marinangeli CP, Kassis AN, Jain D, Ebine N, Cunnane SC, Jones PJ: Comparison of composition and absorption of sugarcane policosanols. Br J Nutr 2007, 97:381-388.
- Wang MF, Lian HZ, Mao L, Zhou JP, Gong HJ, Qian BY, Fang Y, Li J: Comparison of various extraction methods for policosanol from rice bran wax and establishment of chromatographic fingerprint of policosanol. J Agric Food Chem 2007, 55:5552-5558.
- Collins JF, Lieberman DA, Durbin TE, Weiss DG: Accuracy of screening for fecal occult blood on a single stool sample obtained by digital rectal examination: a comparison with recommended sampling practice. Ann Intern Med 2005, 142:81-85.
- Das UN: Essential fatty acids: biochemistry, physiology and pathology. Biotechnol J 2006, 1:420-439.
- Das UN: Folic acid and polyunsaturated fatty acids improve cognitive function and prevent depression, dementia, and Alzheimer's disease– but how and why?. Prostaglandins Leukot Essent Fatty Acids 2008, 78:11-19.
- Arita M, Yoshida M, Hong S, Tjonahen E, Glickman JN, Petasis NA, Blumberg RS, Serhan CN: Resolvin E1, an endogenous lipid mediator derived from omega-3 eicosapentaenoic acid, protects against 2,4,6trinitrobenzene sulfonic acid-induced colitis. Proc Natl Acad Sci USA 2005, 102:7671-7676.
- Goh J, Baird AW, O'Keane C, Watson RW, Cottell D, Bernasconi G, Petasis NA, Godson C, Brady HR, MacMathuna P: Lipoxin A(4) and aspirintriggered 15-epi-lipoxin A(4) antagonize TNF-alpha-stimulated neutrophil-enterocyte interactions in vitro and attenuate TNF-alphainduced chemokine release and colonocyte apoptosis in human intestinal mucosa ex vivo. J Immunol 2001, 167:2772-2780.
- Gewirtz AT, Collier-Hyams LS, Young AN, Kucharzik T, Guilford WJ, Parkinson JF, Williams IR, Neish AS, Madara JL: Lipoxin a4 analogs attenuate induction of intestinal epithelial proinflammatory gene expression and reduce the severity of dextran sodium sulfate-induced colitis. J Immunol 2002, 168:5260-5267.
- Serhan CN: Controlling the resolution of acute inflammation: a new genus of dual anti-inflammatory and proresolving mediators. J Periodontal 2008, 79:1520-1526.

- Schwab JM, Chiang N, Arita M, Serhan CN: Resolvin E1 and protectin D1 activate inflammation-resolution programmes. Nature 2007, 447:869-874.
- Serhan CN, Gotlinger K, Hong S, Lu Y, Siegelman J, Baer T, Yang R, Colgan SP, Petasis NA: Anti-inflammatory actions of neuroprotectin D1/ protectin D1 and its natural stereoisomers: assignments of dihydroxycontaining docosatrienes. J Immunol 2006, 176:1848-1859.
- Serhan CN: Novel chemical mediators in the resolution of inflammation: resolvins and protectins. Anesthesiol Clin 2006, 24:341-364.
- Schwab JM, Serhan CN: Lipoxins and new lipid mediators in the resolution of inflammation. Curr Opin Pharmacol 2006, 6:414-420.

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