BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Mason, Joel B.	Professor and Senior Scientist
eRA COMMONS USER NAME (credential, e.g., agency login) JMASON	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
University of Illinois, Urbana, IL	BS	1977	
University of Chicago, Chicago, IL	MD	1981	Medicine
University of Iowa Hospitals and Clinics, Iowa City, IA	Internship & Residency	1981-1984	Internal Medicine
University of Chicago Hospitals and Clinics, Chicago, IL	Fellowship	1984-1987	Gastroenterology/Nutrition

A. Personal Statement

From 1990 through 2009 my primary research focus was the relationship between the intake of 1-carbon nutrients (eg: folate, vitamins B2, B6 and B12, and methionine) and the risk of developing cancer of the colorectum. It was my laboratory that took what was merely an epidemiological association in the late 1980s and proved, within the framework of an animal model, a true cause and effect relationship between inadequate folate intake and increased colorectal tumorigenesis. In the ensuing years we built extensively upon this initial foundation, pursuing the mechanistic pathways through which the availability of 1-carbon nutrients modulate carcinogenesis. We were the first to identify, and confirm, how mild inadequacies of these nutrients activate an important pro-transformational cell-signaling pathway in colon, the *Wnt* cascade. Our mechanistic work has also examined a variety of other co-determinants such as age, ethanol consumption, gene variants and availability of the other 1-carbon vitamins in determining the effects of folate status on colorectal carcinogenesis, Over the years, we have emphasized translational and other types of clinical studies as well in order to determine the relevance of our mechanistic observations in animal models to human cancer biology: in this pursuit we have successfully conducted 3 studies within the colonoscopy suite at Tufts Medical Center.

Over the past three years my laboratory has devoted an increasingly larger portion of its efforts towards examining the mechanistic link between obesity and colon carcinogenesis, and this now constitutes the majority effort of my laboratory. We are busily engaged in mechanistic studies in animal models aimed at identifying the biochemical and molecular pathways by which obesity exerts its impact on cancer risk, and we have recently completed a translational study of obese and lean individuals undergoing routine colonoscopic screening.

I have been studying the nutritional modulation of colon carcinogenesis in both animal models and humans for over 20 years, with funding as P.I. from the NCI, NIEHS, AICR, International Life Science Institute, Agricultural Research Service and U.S.D.A. and therefore have both the scientific expertise and management skills necessary to conduct the studies proposed in this application.

B. Positions and Honors

Positions and Employment

1987-1988 Res Associate, JM USDA Human Nutrition Research Center on Aging at Tufts University (HNRCA)
1988-1989 Scientist III, HNRCA
1988-1997 Assistant Professor, Tufts University, Schools of Medicine & Nutrition
1989-1996 Scientist II, HNRCA
1996-2010 Scientist I, HNRCA
1996-present Chief, Vitamins and Carcinogenesis Laboratory, HNRCA
1996-2009 Associate Professor, Tufts University Schools of Medicine & Nutrition

1997-2002 Chief, Division of Clinical Nutrition, Tufts University, School of Medicine
2001 *ad-hoc* member, NCI Scientific Review Group, Subcommittee G
2003-2008 Member, NCI Scientific Review Group, Subcommittee J
2009, '10 *ad hoc* member, NCI Scientific Review Group, CDP
2010, '11 Chair, NIH Special Emphasis Panel, The Role of Microbial Metabolites in Cancer Prevention and Etiology, PAR-10-208
2005-present Associate Director, Tufts Cancer Center
2010-present Professor, Tufts University Schools of Medicine & Nutrition
2011-present Senior Scientist (=Professor), HNRCA

Honors

1976 Phi Beta Kappa, Univ. of Illinois-Urbana,
1981 Kraftco Fellowship Award for Clinical Nutrition Research, University of Chicago,
1990 International Life Science Institute: Future Leader in Nutrition Award
1991 SmithKline/Beecham Award for Clinical Research, American Gastroenterological Association
2004-7 Most highly cited paper in the *Journal of Nutrition* four years in a row (Choi SW, Mason JB. J Nutr 2000;130:129-32)
2007 Most highly cited paper in *Cancer Epidemiol Biomarkers and Prevention* (Mason JB et al. CEBP 2007;16:1-5)
2009 Invited expert on folate and cancer risk, European Union Food Safety Authority, Meeting on "Folic Acid: an update on scientific development," Uppsala, Sweden
2010 Mary Swartz Rose Senior Investigator Award, American Society for Nutrition
2010 Fellow, American Gastroenterological Association
2014 E.V. McCullom Award, American Society for Nutrition

C. Selected Peer-reviewed Publications

Most relevant to the current application

1. Liu Z, Brooks RS, Ciappio ED, Kim SJ, Crott JW, Bennett G, Greenberg AS, and **Mason JB**. Diet-induced obesity elevates TNF-α in mice and is accompanied by an activation of *Wnt* signaling: a mechanism for obesity-associated colorectal cancer. J Nutr Biochem. 2012;23: 1207-13. PMCID in process.
2. Protiva P, **Mason JB**, Liu Z, Hopkins ME, Nelson C, Lambrecht RW, Pendyala S, Marshall JR, Kopelovich L, Kim M, Kleinstein S, Laird PW, Lipkin M, Holt PR. Altered folate availability modifies the molecular environment of the human colon: implications for colorectal carcinogenesis. Cancer Prev Res 2011;4: 530-43. PMCID 21321062
3. Flood A, **Mason JB**, Zhenhua L, Cash BD, Schatzkin A, Schoenfeld PS, Cross AJ. Concentration of folate in colorectal tissue biopsies predicts prevalence of adenomatous polyps. Gut. 2011;60: 66-72. PMCID 21068136
4. Liu Z, Ciappio E, Crott J, Brooks R, Nesvet J, Smith D, Choi SW, **Mason JB**. Combined inadequacies of multiple B-vitamins amplify colonic *Wnt*-signaling and promote intestinal tumorigenesis in *BAT-LacZ×Apc1638N* mice. FASEB J. 2011;25: 313-46. PMCID: PMC3157689
5. Kim Y-I, Baik H, Fawaz K, Knox T, Lee Y-M, Norton R, Libby E, **Mason JB**. Effects of folate supplementation on two provisional molecular markers of colon cancer: a prospective, randomized trial. Am J Gastro 2001;96: 184-95.

Additional recent publications of importance to the field

1. Byun AJ, Hung KE, Fleet JC, Bronson RT, **Mason JB**, Garcia PE, Crott JW. Colon-specific tumorigenesis in mice driven by Cre-mediated inactivation of Apc and activation of mutant Kras. Cancer Letters March 2014 (epub ahead of print). PMID 24632531.
2. Selhub J, Byun A, Liu Z, **Mason JB**, Bronson RT, Crott JW. Dietary vitamin B6 intake modulates colonic inflammation in the IL10-/- model of inflammatory bowel disease. J Nutr Biochem. 2013;24: 2138-43. PMID: 24183308.
3. Ciappio E, Liu Z, Brooks R, **Mason JB**, Bronson R, Crott J. Maternal B-vitamin supplementation from preconception through weaning suppresses intestinal tumorigenesis in *Apc*$^{+/1638N}$ mouse offspring. GUT. 2011;60: 1695-702. PMID: 21659408.

4. Tao MH, **Mason JB**, Marian C, McCann SE, Platek ME, Millen A, Ambrosone C, Edge SB, Krishnan SS, Trevisan M, Shields PG, Freudenheim JL. Promoter methylation of E-cadherin, p16, and RAR-β(2) genes in breast tumors and dietary intake of nutrients important in one-carbon metabolism. Nutr Cancer. 2011;63: 1143-50.
5. Tomaszewski JJ, Cummings JL, Parwani AV, Dhir R, **Mason JB**, Nelson JB, Bacich DJ, O'Keefe DS. Increased cancer cell proliferation in prostate cancer patients with high levels of serum folate. Prostate 2011;71: 1287-93. PMCID: PMC3120927
6. Marian C, Tao M, **Mason JB**, Goerlitz DS, Nie J, Chanson A, Freudenheim JL, Shields PG. Single nucleotide polymorphisms in uracil-processing genes, intake of one-carbon nutrients and breast cancer risk. Eur J Clin Nutr. 2011;65: 683-9. Epub 2011 Mar 23. PMID: 21427733
7. Chanson A, Parnell LD, Ciappio ED, Liu Z, Crott JW, Tucker KL, **Mason JB**. Polymorphisms in uracil-processing genes, but not one-carbon nutrients, are associated with altered DNA uracil concentrations in an urban Puerto Rican population. Am J Clin Nutr 2009;89:1927-36. PMCID: PMC2683003.
8. **Mason JB**, Dickstein A, Jacques P, Haggarty P, Selhub J, Dallal G, Rosenberg IH. A temporal association between folic acid fortification and a rise in colorectal cancer rates may be illuminating important biological principles: a hypothesis. Cancer Epidemiol Biomarkers Prevent 2007;16: 1-5
9. van den Donk M, Pellis L, Crott J, van Engeland M, Friederich P, Vallei Ede G, Y. de Boer S, Nagengast F, **Mason JB**, Kok F, Keijer J, Kampman E. Supplementation with folic acid in combination with vitamin B-12 does not favorably influence uracil incorporation and promotor methylation in rectal mucosa DNA among those with previous colorectal adenomas. J Nutr 2007;137: 2114-20.
10. Gabriel HE, Crott JW, Ghandour H, Dallal GE, Choi SW, Keyes MK, Jang H, Liu Z, Nadeau M, Johnston A, Mager D, **Mason JB**. Chronic cigarette smoking is associated with diminished folate status, altered folate form distribution and increased genetic damage in the buccal mucosa of healthy adults. Am J Clin Nutr 2006;83: 835-41.

D. Research Support

Ongoing

1950-5100-074-01S (PI: Mason JB) 10/01/09-09/30/14
USDA/ARS (10/1/15-9/30/20 renewal pending)
Nutrition and Cancer Prevention
This cooperative agreement provides the core support for the Vitamins and Carcinogenesis Laboratory, the major goals of which are to elucidate the means by which: 1) obesity and 2) 1-carbon nutrients modulate the risk of cancer development and to translate such knowledge into tools for cancer chemoprevention.

Prevent Cancer Foundation (PI: Mason JB) 02/01/13-1/31/15
The major goals of these studies in mice are to define the relative contributions of IL-1β and TNF-α in mediating the promotional effects of diet-induced obesity on colon carcinogenesis.

R01 CA13844404-04 (PI: O'Keefe DS) 02/01/10-01/31/15
NIH/NCI
Folate and PSMA Interact to Regulate DNA Methylation and Prostate Carcinogenesis
The studies use an animal model to examine how a prostate protein, PSMA, acts as a folate transporter in the prostate, and how the level of dietary folate impacts on DNA methylation in prostate cancer development.
Role: Co-Investigator

R01 DK073321-05 (PI: Lichtenstein AH) 09/01/07-08/31/13 (NCE)
NIH/NIDDK
Evaluation of Glycemic Index to Assess Diet-Associated Chronic Disease Risk
The objective is to assess the validly of using glycemic index and glycemic load as criterion with which to make chronic disease (obesity, heart disease, diabetes) risk reduction recommendations.
Role: Study Physician

HNRCA Pilot Program (PI: Mason JB) 04/01/11-09/30/14 (NCE)
Translational study of TNF-α-mediated *Wnt*-signaling as a molecular mechanism for obesity-associated colorectal carcinogenesis

The objective of this project is to determine whether the concept of obesity-induced inflammation as a promoter of colorectal carcinogenesis is an operable pathway in the human.

Completed

R21 CA150118-02 (PI: Mason JB) 02/01/11-01/31/14 (NCE)
NIH/NCI
Defining the promoting effect of folate on colorectal cancer in a novel animal model
This proposal will utilize a novel animal mouse model of colorectal carcinogenesis to monitor the development of colonic neoplasms *in vivo* in order to determine whether the many sources of folic acid that supplement the quantities naturally present in foods are collectively sufficient to produce the cancer-promoting effect of folate.

R21 ES019102 (PI: Mason JB) 09/30/09-03/31/12
NIH/NCI
The MTHFR C677T SNP exerts bipolar effects on colorectal cancer risk through the Wnt pathway
The purpose of this proposed animal study is to define the mechanistic basis for the interaction between the common genetic variant, C677T, and the availability of folate and other related B-vitamins in determining the risk of colon cancer.

R01 AG025834-05 (PI: Choi SW) 03/01/07-02/28/13 (NCE)
NIH/NIA
Effects of aging and folate on colonic carcinogenesis
A series of rodent studies will be performed to define how elder age and folate metabolism interact mechanistically to determine the risk of colorectal cancer.
Role: Co-Investigator

2009-35200-05016 (PI: Mason JB) 12/01/08-11/30/10
USDA
Interaction between one-carbon nutrient status and polymorphisms in uracil repair genes in determining DNA stability
The goal of this project is to determine whether folate and other one-carbon nutrient status affects levels of uracil in the human genome, and how relatively common polymorphisms in uracil-repair genes modify these associations. This project will also aim to determine whether uracil levels in blood DNA may be used as a surrogate measure of uracil levels in breast DNA.