North Central Region Canola Research Program
Application Cover Page
(Must fit on one page)

Project Title: Canola oil reduces breast cancer risk

Lead Principal Investigator and Institution: Chung Park, North Dakota State University

Co-Principal Investigator(s):

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Funds Requested for 2007: $31,900

Project Status: New __X__ Renewal _____

Does this project involve recombinant DNA, human subjects or vertebrate animals?
__X__ Yes _____ No
If yes, please complete a CSREES Assurance Statement Form 2008 or a Research & Related Other Project Information Form that is available as part of the new application kit through Grants.gov.

Does this project involve the sale of goods or services? _____ Yes __X__ No
If yes, please indicate the nature of the sale in this space:

By signing this proposal, the applicant certifies that the information contained herein is true and complete to the best of their knowledge and accepts as to any award the obligation to comply with the terms and conditions of the Cooperative State Research, Education and Extension Service in effect at the time of the award.

C. S. Park
PI Signature

Dept. Chair/REC Director signature
(applies only to NDSU applicants)

Authorized Organizational Representative
(applies only to non-NDSU applicants)

RESEARCH & RELATED Other Project Information

1. * Are Human Subjects Involved? ☐ Yes ☑ No

1.a If YES to Human Subjects

Is the IRB review Pending? ☐ Yes ☐ No

IRB Approval Date:

Exemption Number: ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6

Human Subject Assurance Number:

2. * Are Vertebrate Animals Used? ☑ Yes ☐ No

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ☑ Yes ☐ No

IACUC Approval Date:

Animal Welfare Assurance Number A3244-01

3. * Is proprietary/privileged information included in the application? ☐ Yes ☑ No

4.a. * Does this project have an actual or potential impact on the environment? ☐ Yes ☑ No

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ☐ Yes ☐ No

4.d. If yes, please explain:

5.a. * Does this project involve activities outside the U.S. or partnership with International Collaborators? ☐ Yes ☑ No

5.b. If yes, identify countries:

5.c. Optional Explanation:

6. * Project Summary/Abstract Add Attachment | Delete Attachment | View Attachment

7. * Project Narrative Add Attachment | Delete Attachment | View Attachment

8. Bibliography & References Cited Add Attachment | Delete Attachment | View Attachment

9. Facilities & Other Resources Add Attachment | Delete Attachment | View Attachment

10. Equipment Add Attachment | Delete Attachment | View Attachment

11. Other Attachments Add Attachments | Delete Attachments | View Attachments ☐

OMB Number: 4040-0001

Expiration Date: 04/30/2008

PROJECT NARRATIVE

Canola Oil Reduces Breast Cancer Risk

A. OBJECTIVES:

We hypothesize that canola oil, due to its uniquely balanced fatty acid composition (i.e., high oleic acid concentration and low omega-6 to omega-3 fatty acid ratio), may reduce breast tumor incidence by enhancing anticancer immune cell proliferation and cytotoxicity resulting in increased cell death (apoptosis). Specific objectives are to determine the extent to which dietary canola oil supplementation affects: 1) the susceptibility to mammary carcinogenesis, and 2) the in vitro proliferative response of immune cells to mitogens.

B. PROCEDURES:

(1) Experimental Protocol

Animal and Diet. All animal procedures and techniques will be approved by the North Dakota State University Institutional Animal Care and Use Committee. Thirty female Sprague-Dawley rats (approximately 3 weeks of age) will be purchased from Harlan (Indianapolis, IN). Rats will be individually housed in polyethylene cages and acclimated to the experimental environment of approximately 25°C and 50% relative humidity. During the 1-week acclimation period rats will be given ad libitum access to water and a standard control diet (AIN-76). Rats will then be assigned randomly to the control diet (AIN-76) or a diet supplemented with canola oil (treatment) for the duration of the experiment (**Table 1**). The treatment diet will be formulated to replace carbohydrate energy with canola oil. The control diet will be formulated to have 18.4% protein and 3.84 Kcal/g of energy based on the AIN-76 diet, while the canola diet will have 18.9% protein and 4.15 Kcal/g of energy. Rats will have ad libitum access to respective diets and water, and will be weighed twice weekly. At 50 days of age, all rats will be subjected to mammary tumor induction (**Figure 1**).

Table 1. Composition of the experimental diets[a]

Item	Control	Canola
	------- % -------	
Casein	20	20
DL-methionine	0.3	0.3
Sucrose	50	44.3
Corn starch	15	15
Cellulose (fiber)	5	5
Choline	0.2	0.2
AIN-76 mineral mixture	3.5	3.5
AIN-76 vitamin mixture	1	1
Corn oil	5	--
Canola oil	--	10.7
Ethoxyquin	0.001	0.001

[a]Modified from AIN-76 and Benyon et al., 1997 (3).

(2) Experimental Procedure

<u>Specific Objective 1</u>. To determine if dietary canola oil reduces the susceptibility of rats to chemically induced mammary tumorigenesis.

<u>Mammary Tumor Induction</u>. At 50 days of age, all rats will be injected s.c. with 50 mg of nitrosomethylurea (NMU) per kg of body weight as described previously (17). At weekly intervals, beginning 4 weeks after NMU injection, rats will be palpated for mammary tumors. Upon detection, the position and date of appearance (latency and number) of mammary tumors will be recorded. Twelve weeks after NMU injection, mammary tumor sizes will be determined weekly by Vernier caliper measurements; tumor volumes will be calculated as described previously (17). A minimum of two rats per treatment will be sacrificed by CO_2 inhalation overdose followed by thoracotomy at 49 days of age and approximately 4, 10, and 20 weeks after NMU administration for collection of spleens. Sixty days after initial tumor detection, remaining rats will be sacrificed.

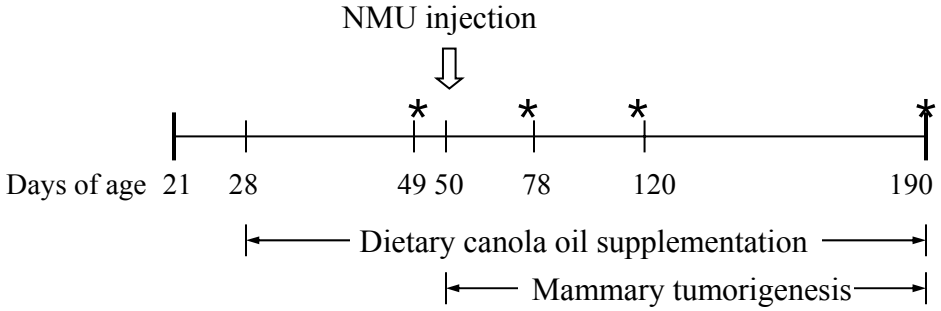

Figure 1. Experimental protocol. At 28 days of age, rats will be assigned to control or dietary canola oil supplementation groups for the duration of the trial. At 50 days of age, all rats will be injected with nitrosomethylurea (NMU). *Two rats per treatment will be killed for the in vitro cell culture study (proliferative response of immune cells to mitogens).

<u>Specific Objective 2</u>. To examine if canola oil affects the in vitro proliferative response of immune cells to mitogens.

<u>Immune Cell Culture and Cell Proliferation by the CellTiter 96 AQueous One Solution Assay.</u> Two rats per treatment will be sacrificed by CO_2 inhalation overdose followed by thoracotomy at 49 days of age and 4, 10, and 20 weeks after NMU administration for collection of spleens. Splenocytes (immune cells) will be harvested from the spleens and cultured (1×10^6 cells/mL) in a 5% CO_2-humidified atmosphere at 37^oC in a basal medium (IMDM, Gibco Invitrogen Corp., Carlsbad, CA) supplemented with 10% heat-inactivated fetal bovine serum, 100 U/mL penicillin, 100 μg/mL streptomycin, and 5×10^{-5} M 2-mercaptoethanol (Sigma, St. Louis, MO), with the mitogens Concanavalin A (Con A; Sigma) or lipopolysaccharide (LPS; Sigma). After 5 days of culture, cell proliferation will be determined using the CellTiter 96 AQueous One Solution Reagent (Promega, Madison, WI) according to the manufacturer's instructions.

(3) Statistical Analyses

The number of rats to be used will be the minimum number required to detect a statistical difference at $P = 0.05$ and power of 0.78 of one-half the standard deviation between treatments. Data on tumorigenesis and immune cell proliferation will be analyzed by one-way analysis of variance with repeated measures. Comparisons of cancer latency with tumorigenesis data will be based on cancer-free times using the Mantel-Haenszel life table (12). Differences in tumor numbers will be evaluated after square root transformation (12). Comparisons of tumor volumes will be conducted with a nonparameter Kruskal-Wallis test. Means will be separated using Student's *t*-test and Tukey's procedure (26). Correlation and regression will be performed as appropriate. All data will be analyzed with SAS statistical package (SAS Institute, Cary, NC).

(4) Anticipated Results and Future Studies

We expect that dietary canola oil supplementation may increase the tumor latency period, and decrease mammary tumor number and volume by increasing the resistance to chemical carcinogenic stimuli. In addition, we expect to show an increase in the in vitro proliferative response of anticancer immune cells from canola oil-supplemented rats to mitogens. If the proposed study demonstrates a decrease in cancer incidence, we may further investigate immune status and cancer as it relates to dietary canola oil supplementation by assessing in vitro cytotoxic T lymphocyte (CTL) cytotoxicity and target cancer cell death.

(5) Pitfalls and Limitations

We have experience in the dietary use of canola oil in the production of an anticancer agent (conjugated linoleic acid) in milk of dairy cows. Also, we have used the rat NMU mammary carcinogenesis model previously (7). Immune cell proliferation will be measured by a colorimetric procedure. If this assay is not sensitive enough, then an alternative [^{3}H] thymidine incorporation assay will be used.

C. JUSTIFICATION:

Breast cancer is the most common malignancy amongst women worldwide, constituting 10% of all cancers (4), with the United States having the highest incidence (101 cases per 100,000 people) (2). Epidemiological studies indicate that women consuming high-fat diets have a risk of breast cancer that can be five-fold higher than that of women consuming low-fat diets (16). However, there is increasing evidence that it is not the quantity of lipid but the type of lipid intake that influences cancer risk (5). Oils rich in omega-3 polyunsaturated fatty acids (9), docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA) (31), as well as those rich in oleic acid (4) are receiving attention because of their potential health benefits. A case-control study by Maillard et al. (13) suggested that the anticancer effect of omega-3 fatty acids depends on the corresponding levels of omega-6 polyunsaturated fatty acids. The omega-6 to omega-3 fatty acid ratio can modulate membrane activity both in normal and cancer cells (27). A balanced omega-6 to omega-3 fatty acid ratio has been shown to be beneficial in decreasing the risk of cancer, including breast cancer (13, 25).

Diets in Western societies have been characterized as high in omega-6 fatty acids and low in omega-3 fatty acids, with a 10 to 20:1 omega-6 to omega-3 fatty acid ratio (20). A workshop on the Essentiality of and Recommended Dietary Intakes for Omega-6 and Omega-3 Fatty Acids recommended a 2:1 ratio of omega-6 to omega-3 fatty acids for human consumption (24). This recommendation was supported in a review by Simopoulos (25) who indicated that a ratio of 2.5:1 reduces rectal cell proliferation in patients with colorectal cancer and was also associated with a decrease in breast cancer risk. The omega-6 to omega-3 ratio is also vital for immune cell proliferation as polyunsaturated fatty acids are potent modulators of the immune response (29).

Canola seed is a crop that originated in Canada through genetic modification of rapeseed by conventional breeding and emerged in the 1970s as a viable oilseed for both human and animal consumption (28). Currently, the United States is the seventh largest canola producer and processor in the world. North Dakota produces about 90% of this, with smaller amounts grown in Minnesota and a few other states (1). Canola oil has the lowest concentration of saturated fatty acids (7%) of all eight major vegetable oils, it is high in monounsaturated fatty acids (61%), and it has a favorable omega-6 (21%) to omega-3 (11%) fatty acid ratio (1.9:1) [10]. Considering the recommended 1 to 2:1 omega-6 to omega-3 fatty acid ratio for the reduction of breast cancer, and the involvement of monounsaturated fatty acids, particularly oleic acid, in the down-regulation of cancer-related oncogenes, canola oil has a uniquely balanced fatty acid composition and may be beneficial in enhancing anticancer immune cell proliferation, especially cancer killing T cells, and subsequently in reducing breast cancer incidence.

In summary, breast cancer is the second leading cause of cancer death in women. Data on dietary canola oil supplementation and the susceptibility to mammary carcinogenesis obtained from the proposed studies could be useful in the development of improved diets that may prevent and reduce breast cancer in humans. Comparative studies of breast development in women and rodents indicate that there are similarities between them and validate the extrapolation of findings from the experimental model to humans (21, 22). Further, for a new crop to be successful, markets must be established; and given the fact that the marketing system for canola is still young (30), showing that canola oil may reduce breast cancer risk may positively influence the market as well as increase the demand for canola oil, thereby benefiting the whole canola industry.

D. LITERATURE REVIEW:

Oleic acid is the most abundant monounsaturated fatty acid found in animal and vegetable oils (4). Studies have shown that feeding vegetable oils high in monounsaturated fatty acids appears to have an inhibitory effect on breast cancer (6). The consumption of olive oil, high in oleic acid, may have a potential role in lowering the risk of breast, stomach, ovarian, colon, and endometrial cancers (16). A population-based case-control study from Spain examined the role of dietary fat and vegetable oils in breast cancer etiology and found that a higher consumption of olive oil is significantly related to a lower risk of breast cancer (14). The strongest evidence that monounsaturated fatty acids may influence breast cancer risk comes from studies of southern European populations, where intake of oleic acid, particularly olive oil, appears protective (23). An Italian case-control study on women with breast cancer and control women in hospital with acute, non-neoplastic diseases found that high intakes of polyunsaturated

and unsaturated fatty acids (i.e., polyunsaturated fatty acids plus oleic acid) are associated with a decreased risk of breast cancer (8).

Although some studies have shown no association between breast cancer incidence and the consumption of omega-3 fatty acids (4), in the laboratory, omega-3 fatty acids have consistently been shown to inhibit the growth of human breast cancer cells both in culture and in explants in immunosuppressed mice (27). Omega-3 fatty acids inhibit the proliferation of breast and prostate cell lines in vitro and reduce the risk and progression of these tumors in animal models (18). Some studies report that diets high in saturated or omega-6 fatty acids increase the risk of breast cancer while others have shown no effect (4). Interestingly, positional isomers of omega-6 fatty acids such as γ-linolenic acid may slow tumor growth by exerting selective cytotoxic effects on cancer cells without affecting normal cells (15, 18).

Several molecular mechanisms whereby omega-3 fatty acids potentially affect carcinogenesis have been proposed. These mechanisms include the suppression of arachidonic acid-derived eicosanoid biosynthesis, which results in altered immune response to cancer cells and modulation of inflammation, cell proliferation, apoptosis, metastasis, and angiogenesis (11). Another possible mechanism by which omega-3 fatty acids may inhibit the proliferation of tumor cells may be by involvement in apoptosis (programmed cell death), which likely involves lipid peroxides and free oxygen radicals (27). Metabolites of lipid peroxidation are associated with increased oxidative stress, which in turn has been implicated as a significant mediator of apoptosis (29). Experimental evidence suggests that when incorporated into the cell membrane, omega-3 fatty acids enhance lipid peroxidation which can lead to increased apoptosis in transformed or malignant mammary epithelial cells (27). In addition, in exploring the effect of DHA, an omega-3 fatty acid, on membrane function, Pascale et al. (19) found lipid-modified tumor cells to be more sensitive to cytolysis by alloreactive CTL.

E. CURRENT WORK:

Over the past several years, we have done work on the dietary use of whole canola seed to increase an anticancer agent (conjugated linoleic acid) in milk of dairy cows. Also, we have been investigating the influence of nutrition (e.g., energy intake, methyl nutrients) in mammary cancer using in vivo (chemically-induced mammary carcinogenesis in rats) and in vitro (human breast cancer cell lines) models.

F. FACILITIES AND EQUIPMENT:

The Animal Nutrition and Physiology Center includes a separate area to maintain rats and is available for use by Dr. Park. This research building contains large, small, and laboratory animal preparation, surgery, and recovery rooms; and laboratory space for processing of samples, with microscopes, centrifuges, freezers, etc. The Department of Animal and Range Sciences is located in Hultz Hall. The principal investigator's (C.S. Park) laboratory occupies approximately 1,200 square feet, with 580 square feet of bench top space. His laboratory currently consists of 2 doctoral and 2 master's graduate students. Most equipment needed for the studies proposed herein is located in the department. The departments of Biochemistry, Veterinary and Microbiological Sciences, and Zoology (located either within or close to Hultz Hall) are very

cooperative in sharing their facilities with us when needed. Unless otherwise designated, major equipment is located in Dr. Park's laboratory; this equipment includes cell culture equipment (laminar flow hood, incubators, environmental orbital shaker, microscope, etc), electrophoresis units (PAGE/agarose, transfer apparatus), centrifuges (high speed and microcentrifuges), freezers (deep and ultralow), and a hybridization oven, Polaroid camera/transilluminator, and thermal cycler. Available in nearby laboratories are gamma counters, chromatographs (HPLC and gas), liquid scintillation counter, UV/Vis spectrophotometer, microplate reader, autoclave, Immulite 1000, Dako autostainer, Agilent 2100 bioanalyzer, ABI Prism 7000 sequence detection system (real time thermal cycler), Hemavet 950, gel drier, Speed-Vac, sequence gel apparatus, table-top ultracentrifuge, Kjeldahl apparatus, and additional microscopes and cameras.

G. PROJECT TIMETABLE:

This research will require one year to complete. The animal trial and immune cell culture studies will be carried out during the first 9 months. Data analyses and final report will be completed during the final 3 months.

H. LITERATURE CITED:

1. Agriculture and Agri-Food Canada. 2004. The United States canola industry: situation and outlook. Bi-weekly Bulletin 17(4):1-4.
2. American Cancer Society. 2006. Breast cancer facts & figures 2005-2006. American Cancer Society, Atlanta, GA. Available at: http://www.cancer.org/downloads/STT/CAFF2005BrF.pdf.
3. Benyon, L. S., E. J. Eisen, and E. E. Jones. 1997. Effects of canola oil-based high fat diets on growth, fat deposition and serum triglyceride and cholesterol levels in lines of mice selected for high and low fat percentage. Braz. J. Genet. 20:203-213.
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14. Martin-Moreno, J. M., W. C. Willett, L. Gorgojo, J. R. Banegas, F. Rodriguez-Artalejo, J. C. Fernandez-Rodriguez, P. Maisonneuve, and P. Boyle. 1994. Dietary fat, olive oil intake and breast cancer risk. Int. J. Cancer 58:774-780.
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16. Menendez, J. A., L. Vellon, R. Colomer, and R. Lupu. 2005. Oleic acid, the main monounsaturated fatty acid of olive oil, suppresses Her-2/*neu* (*erb*B-2) expression and synergistically enhances the growth inhibitory effects of trastuzumab (Herceptin^{TM}) in breast cancer cells with Her-2/*neu* oncogene amplification. Ann. Oncol. 16:359-371.
17. Moon, Y. S., W. L. Keller, and C. S. Park. 1998. Dietary lipotrope-mediated mammary carcinogenesis in female rats. Nutr. Res. 18:1605-1614.
18. Norman, H. A., V. L. Go, and R. R. Butrum. 2004. Review of the International Research Conference on Food, Nutrition, and Cancer, 2004. J. Nutr. 134(Suppl. 12):3391S-3393S.
19. Pascale, A. W., W. D. Ehringer, W. Stillwell, L. K. Sturdevant, and L. J. Jenski. 1993. Omega-3 fatty acid modification of membrane structure and function. II. Alteration by docosahexaenoic acid of tumor cell sensitivity to immune cytolysis. Nutr. Cancer 19:147-157.
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24. Simopoulos, A. P., A. Leaf, and N. Salem, Jr. 1999. Workshop on the Essentiality of and Recommended Dietary Intakes for Omega-6 and Omega-3 fatty acids. J. Am. Coll. Nutr. 18:487-489.
25. Simopoulos, A. P. 2004. Omega-6/omega-3 essential fatty acid ratio and chronic diseases. Food Rev. Int. 20:77-90.
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I. PERSONNEL SUPPORT

Name: ***Chung S. Park,*** Professor and Principal Investigator

A. Professional Preparation

Seoul National University	Animal Science	BS	1964
University of Georgia, Athens	Animal Nutrition	MS	1972
Virginia Polytechnic & State Univ., Blacksburg	Nutritional Physiology	PhD	1975
Virginia Polytechnic & State Univ., Blacksburg	Lactation	Postdoctorate	1975/77
Purdue University, W. Lafayette, IN	Mammary Biology	Postdoctorate	1977/78

B. Appointments

1988-present Professor, Dept. of Animal and Range Sciences, North Dakota State Univ., Fargo

1994-1994 Interim Chair, Dept. of Animal and Range Sciences, North Dakota State Univ., Fargo

1985-1986 Visiting Professor, Dept. of Cell Biology, Lawrence Berkeley National Laboratory, Univ. of California, Berkeley (Dr. Mina Bissell)

1986-1986 Visiting Professor, Dept. of Medicine/Oncology, Stanford Univ. Medical School, Stanford (Dr. Frank Stockdale)

1982-1988 Associate Professor, Dept. of Animal and Range Sciences, North Dakota State Univ., Fargo

1978-1982 Assistant Professor, Dept. of Animal Science, North Dakota State Univ., Fargo

C. Selected Publications (From a total of 60 refereed journal articles/book articles: 7 invited; 106 abstracts)

1. Kim, H.H., and C.S. Park. 2002. Lipotropes regulate bcl-2 gene expression in the human breast cancer cell line, MCF-7. In Vitro Cell. Dev. Biol. Anim. 38:205-207.

2. Moon, Y.S., and C.S. Park. 2002. Effects of controlled compensatory growth on mammary gland development and lactation in rats. Asian-Australas. J. Anim. Sci. 15:1364-1370.

3. Park, C.S. 2002. Heifer rearing for optimum lifetime production. In Recent Developments in Ruminant Nutrition 4. (P.C. Garnsworthy and J. Wiseman, eds.), Nottingham University Press, Nottingham, England. Pp 581-596.

4. Schroeder, J.W., W.L. Keller, and C.S. Park. 2002. Glucose restriction and refeeding regimen alters proliferation and differentiation of HC11 mammary cells. In Vitro Cell. Dev. Biol. Anim. 38:135-136.

5. Joo, N.E., and C.S. Park. 2003. Inhibition of excitotoxicity in cultured rat cortical neurons by a mixture of conjugated linoleic acid isomers. Pharmacol. Res. 47:305-310.

6. Kim, H.H., and C.S. Park. 2003. Methionine cytotoxicity in the human breast cancer cell line MCF-7. In Vitro Cell. Dev. Biol. Anim. 39:117-119.

7. Kim, H.H., and C.S. Park. 2004. A compensatory nutrition regimen during gestation stimulates mammary development and lactation potential in rats. J. Nutr. 134:756-761.

8. Park, C.S., and G.L. Lindberg. 2004. The mammary gland and lactation. In Dukes' Physiology of Domestic Animals (W.O. Reece, ed.), 12th ed., Cornell University Press, Ithaca, NY. Pp 720-741.

9. Chichlowski, M.W., J.W. Schroeder, C.S. Park, W.L. Keller, and D.E. Schimek. 2005. Altering the fatty acids in milk fat by including canola seed in dairy cattle diets. J. Dairy Sci. 88:3084-3094.

10. Lewis, F.M., D.R. Bae, M.S. Laubach, W.L. Keller, D.E. Schimek, and C.S. Park. 2005. Effect of ground canola seed on milk production and composition, and blood metabolites of lactating Holstein cows. J. Dairy Sci. 88(Suppl. 1):97 (Abstr.).

11. Park, C.S. 2005. Role of compensatory mammary growth in epigenetic control of gene expression. FASEB J. 19:1586-1591.

12. Carlson, D.B., M.S. Laubach, W.L. Keller, and C.S. Park. 2006. Effect of prepartum compensatory nutrition regimen on metabolism and performance of dairy cows. Livest. Sci. 101:251-261.

UNITED STATES DEPARTMENT OF AGRICULTURE
COOPERATIVE STATE RESEARCH, EDUCATION, AND EXTENSION SERVICE

OMB Approved 0524-0039

BUDGET

ORGANIZATION AND ADDRESS North Dakota State University, Fargo, ND 58105				USDA AWARD NO.			
PROJECT DIRECTOR(S) Chung S. Park				DURATION PROPOSED MONTHS: 12 **Funds Requested by Proposer**	DURATION PROPOSED MONTHS: _____ **Funds Approved by CSREES** (If different)	Non-Federal Proposed Cost-Sharing/ Matching Funds (If required)	Non-federal Cost-Sharing/Matching Funds Approved by CSREES (If Different)
A. Salaries and Wages	**CSREES-FUNDED WORK MONTHS**						
1. No. Of Senior Personnel	Calendar	Academic	Summer				
a. ____ (Co)-PD(s)							
b. ____ Senior Associates							
2. No. of Other Personnel (Non-Faculty) a. _____ Research Associates/Postdoctorates							
b. ____ Other Professionals							
c. ____ Paraprofessionals							
d. _1_ Graduate Students				17,000			
e. _1_ Prebaccalaureate Students				3,000			
f. ____ Secretarial-Clerical							
g. ____ Technical, Shop and Other							
Total Salaries and Wages →				20,000			
B. Fringe Benefits (If charged as Direct Costs)				400			
C. Total Salaries, Wages, and Fringe Benefits (A plus B) →				20,400			
D. Nonexpendable Equipment (Attach supporting data. List items and dollar amounts for each item.)							
E. Materials and Supplies				9,000			
F. Travel				1,500			
G. Publication Costs/Page Charges				1,000			
H. Computer (ADPE) Costs							
I. Student Assistance/Support (Scholarships/fellowships, stipends/tuition, cost of education, etc. Attach list of items and dollar amounts for each item.)							
J. All Other Direct Costs (In budget narrative, list items and dollar amounts, and provide supporting data for each item.)							
K. Total Direct Costs (C through J) →				31,900			
L. F&A/Indirect Costs (If applicable, specify rate(s) and base(s) for on/off campus activity. Where both are involved, identify itemized costs included in on/off campus bases.)							
M. Total Direct and F&A/Indirect Costs (K plus L) →				31,900			
N. Other →							
O. Total Amount of This Request →				31,900			
P. Carryover -- (If Applicable) Federal Funds: $ **Non-Federal funds: $** **Total $**							
Q. Cost-Sharing/Matching (Breakdown of total amounts shown on line O) **Cash (both Applicant and Third Party)** → **- Non Cash Contributions (both Applicant and Third Party)**							
AME AND TITLE (Type or print)				**SIGNATURE** (required for revised budget only)			**DATE**
Project Director Chung S. Park							
Authorized Organizational Representative							
Signature (for optional use)							

Form CSREES-2004 (12/2000)

Budget Narrative

Salaries and Wages

Chung Park, Principal Investigator (10% effort), will be responsible for overall administration and direction of the project; however, his time will not be charged to this grant.

Support is requested for a Ph.D. graduate student stipend (Lawrence Mabasa) for one year ($17,000). This student will devote 100% of his time to the proposed studies and will be responsible for most aspects of the proposed study which is assigned as his Ph.D. thesis research. One undergraduate student (10 hours/week) will be hired to assist with animal care and some laboratory analyses.

As requested by North Dakota State University, fringe benefits will be paid as part of direct costs (2% for students).

Materials and Supplies

The materials and supplies cost represents a reasonable estimate of what is needed to carry out the experiment ($9,000).

Animal and Diet Costs ($1,500): The costs of purchasing approximately 30 female Spraque Dawley rats and diet.

Chemicals and Supplies ($7,500): Nitrosomethylurea; cell culture media and components such as fetal bovine serum, antibiotics, and mitogens; proliferation assay kits; miscellaneous chemicals; and general laboratory supplies.

Travel

Funds are requested for support of the research team members to disseminate information at meetings of canola growers and appropriate commodity groups in the region and to cover partial costs to attend one national scientific meeting ($1,500).

Publication Costs

Funds are requested to defray page charges and other costs of publication ($1,000/year).