



# RESEARCH UPDATES

For the latest in worldwide integrated cancer care

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**InspireHealth**  
INTEGRATED CANCER CARE

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*Research Updates* is produced once a month by InspireHealth to inform those interested of newly published articles in integrative cancer care. Authoritative articles are selected based on their evidence and their relevance to this area of medicine.

Thank you to The Canadian Breast Cancer Foundation BC/Yukon Chapter for their generous support.



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## Breast

Kallianpur, AR, S. -A Lee, Y. -T Gao, et al. **Dietary Animal-Derived Iron and Fat Intake and Breast Cancer Risk in the Shanghai Breast Cancer Study.** *Breast Cancer Res Treat.* 2008 Jan; 107(1): 123-132. Background: Dietary fats and other constituents have been studied extensively in relation to breast cancer risk. Iron, an essential micronutrient with pro-oxidant properties, has received little attention, and specific fats may augment its toxicity. We investigated the effects of iron and fats from various food sources on the risk of breast cancer. Methods: Participants in a population-based case-control study, 3,452 breast cancer cases, and 3,474 age-frequency-matched controls, completed in-person interviews, including a detailed food-frequency questionnaire. Plant- and animal-derived iron and fat intakes were derived from dietary intake data and food composition tables. Unconditional logistic regression models were used to study the independent and interactive effects of different forms of iron and fats on breast cancer risk. Results: Animal-derived (largely heme) iron intake was positively associated with breast cancer risk ( $P_{trend} < 0.01$ ; OR = 1.49 in the highest vs. lowest quartile, 95% confidence interval [CI] 1.25-1.78) after adjustment for known risk factors, antioxidant vitamin and isoflavone intake, and vitamin supplement use. The effect of animal-derived iron was similar in pre- and postmenopausal women. Intake of animal-derived fats was also associated with increased risk (adjusted OR = 1.34, 95% CI 1.14-1.58), particularly after menopause. A significant interaction between iron and fat from animal sources was observed ( $P < 0.01$ ). Conclusions: A high intake of animal-derived (heme) iron may be associated with an increased risk of primary breast cancer in Chinese women, and saturated and mono-unsaturated fats that are also derived from animal sources may augment this effect. Combined reductions in animal-derived iron and fat consumption have the potential to reduce breast cancer risk.

Lissowska, J, M. M. Gaudet, L. A. Brinton, et al. **Intake of Fruits, and Vegetables in Relation to Breast Cancer Risk by Hormone Receptor Status.** *Breast Cancer Res Treat.* 2008 Jan; 107(1): 113-117. The inconsistent associations between fruit and

vegetable intake and breast cancer risk may be due to heterogeneity of associations by estrogen (ER) and progesterone receptor (PR) status of the tumors. We evaluated this hypothesis in a large (2,386 cases and 2,503 controls) population-based case-control study in Poland, conducted between 2000 and 2003. We observed significant associations between reduced overall risk of breast cancer and increasing levels of total fruit intake (odds ratio (OR) for highest versus lowest quartile = 0.76, 95%CI = 0.63-0.91; p-trend = 0.01), but not for total vegetable intake (1.13 (0.93-1.37), p-trend = 0.25), after controlling for age, energy intake and known risk factors for breast cancer. The inverse association with total fruit intake was stronger for risk of ER+ (0.69 (0.54-0.88), p-trend = 0.01) than ER- tumors (0.89 (0.67-1.19), p-trend = 0.57) (p-heterogeneity = 0.02). In conclusion, this study suggests that fruit intake might have differential associations for breast tumor subtypes defined by ER status.

Zimmermann, T, N. Heinrichs and D. H. Baucom. **"does One Size Fit all?" Moderators in Psychosocial Interventions for Breast Cancer Patients: A Meta-Analysis.** *Annals of Behavioral Medicine.* 2007 34(3): 225-239. Background: A variety of psychosocial interventions have been developed to promote better adjustment to breast cancer (BC) and their efficacy has been demonstrated repeatedly. However, the effect sizes (ES) vary considerably across studies. Purpose: This article intends to shed light on potential moderators of intervention efficacy for BC patients, such as the intervention type (e.g., education, supportive), the composition of the sample (only BC patients or BC mixed with other cancer types), and the practitioner of the intervention (psychologist, nonpsychologist). Methods: Fifty-six randomized-controlled studies investigating the effectiveness of psychosocial interventions with adult BC patients were meta-analytically reviewed. Results: The overall ES of  $d = 0.26$  was similar to previous meta-analyses and moderated by several variables. The ES varied notably based on the composition of the sample, the profession offering the intervention, and the type of intervention. Studies with samples consisting of only BC patients and studies with nonpsychologist-led interventions showed lower ES. Psychoeducation yielded the strongest ES. These moderators maintained their significance

even when controlling for the nature of the control group, the format of the intervention, the timing of the intervention, or the stage of disease. Conclusions: These results suggest that among current interventions, psychoeducation is a treatment of choice for BC patients, preferably prior to surgery and led by individuals with a medical expertise. Other psychosocial interventions appear most effective when administered individually and led by a psychologist. In addition, there is a need for improved psychosocial interventions to enhance the present ES for women with BC.

## Prostate

Kositsawat, J, R. C. Flanigan, M. Meydani, Y. -K Choi and V. L. Freeman. . **The Ratio of Oleic-to-Stearic Acid in the Prostate Predicts Biochemical Failure After Radical Prostatectomy for Localized Prostate Cancer.** *J Urol.* 2007 Dec; 1786: 2391-2396. Purpose: To identify lifestyle related factors that may influence the prognosis of clinically localized prostate cancer we evaluated the relative impact of obesity and prostatic fatty acid concentrations at diagnosis on the risk of biochemical failure following radical prostatectomy. Materials and Methods: Height and weight were measured in 195 men scheduled for radical prostatectomy for clinically localized prostate cancer. Fatty acids were measured in nonmalignant prostate tissue collected at surgery. Biochemical failure was defined as detectable serum prostate specific antigen (0.1 ng/ml or greater). Cox proportional hazards models and logistic regression, respectively, were used to analyze the association of obesity (body mass index 30 kg/m<sup>2</sup> or greater) and prostatic fatty acid concentrations with time to biochemical failure and the relative odds of biochemical failure at different time points after accounting for prostate specific antigen at diagnosis, surgical margin status, pathological stage, Gleason sum, patient age, race/ethnicity and other factors. Results: During an average followup of 56 months the oleic-to-stearic acid ratio predicted the risk of biochemical failure (multivariate HR 1.50, 95% CI 1.17-1.91, p = 0.001 per 1 standard deviation increase). Obesity did not correlate with biochemical failure during the entire study period. However, obesity tended to be associated with biochemical failure within the first 2 years (multivariate OR 2.55, 95% CI 0.84-7.77, p = 0.10). Conclusions: The oleic-to-stearic acid ratio in the prostate predicts the risk of biochemical failure following radical prostatectomy for clinically localized prostate cancer. This observation and the tendency of obesity to be associated with biochemical failure during the first 2 years in our cohort suggest that lifestyle related factors influence the prognosis of clinically early stage prostate cancer.

Janssen, T. **Counselling of the Prostate Cancer Patient as a Whole Person.** *European Urology, Supplements.* 2008 Feb; 71: 29-34. Objectives: This paper aims to explain the importance of implementing the psycho-neuro-endocrino-immunologic approach in the treatment of patients with prostate cancer. Methods: Relevant articles and literature data were selected and presented during the New Horizons in Urology 2007 meeting in Monte Carlo, Monaco. Results: Viewing the brain and behaviour from an evolutionary perspective, the theory of the triune brain describes the three levels of human experience, including the body, the mind, and the 'soul'. Furthermore, the scientific acknowledgement of the constant interplay between the physical and emotional systems fed the concept of psycho-neuro-endocrino-immunology. In contrast to conventional medicine, complementary and alternative therapies (most of them originating in traditional medicine) value and use the power of positive psychology on health and disease. Conclusions: Based on this integrated vision of the human being, the conventional vertical patient approach could be transformed into counselling patients as "body-mind whole persons" from a more holistic viewpoint. Therefore, integrative medicine may be the next challenge for tomorrow's clinical practice, aiming to really heal by respecting a patient in all his dimensions and creating positive emotions.

 Thank you to the **BC Foundation for Prostate Disease** for their generous support.  
[www.BCPROSTATECANCER.org](http://www.BCPROSTATECANCER.org)

## Lung

Jin, YR, M. S. Lee, J. H. Lee, et al. **Intake of Vitamin A-Rich Foods and Lung Cancer Risk in Taiwan: With Special Reference to Garland Chrysanthemum and Sweet Potato Leaf Consumption.** *Asia Pac J Clin Nutr.* 2007 163: 477-488. A case-control study was conducted to investigate the association between the consumption of local common foods that are rich in vitamin A and the risk of lung cancer in Taiwan. A total of 301 incident lung cancer cases, 602 hospital controls, and 602 neighborhood controls were recruited. The consumption of 13 food items and vitamin supplements was estimated by use of a food frequency questionnaire. The conditional logistic regression models were used to estimate the adjusted odds ratios (AOR) and 95% confidence intervals (CI) for lung cancer risk with each control group as reference by adjustment of covariates. A reduced risk for lung cancer was found to be associated with increased intakes of vitamin A, alpha-carotene, and beta-carotene from 13 food items. More servings of vegetables (AOR for the highest versus the lowest quartile = 0.67-0.70, 95% CI = 0.42-1.08, (plinear trend) = 0.04), garland chrysanthemum (AOR for the highest versus the lowest tertile = 0.58-0.74, 95% CI = 0.37-1.14, (plinear trend) <= 0.04) and sweet potato leaves (AOR for the highest versus the lowest tertile = 0.43-0.65, 95% CI = 0.28-0.96, (plinear trend) <= 0.03) were associated with the reduced risk for lung cancer. In conclusion, higher consumption of vitamin A-rich vegetables, especially garland chrysanthemum and sweet potato leaves might provide potential protection from lung cancer.

Misirlioglu, CH, T. Demirkasimoglu, B. Kucukplakci, E. Sanri and K. Altundag. **Pentoxifylline and Alpha-Tocopherol in Prevention of Radiation-Induced Lung Toxicity in Patients with Lung Cancer.** *Medical Oncology.* 2007 243: 308-311. Combined use of pentoxifylline and vitamin E is reported to reduce radiation-induced toxicity in normal tissues at molecular level. We plan to evaluate the role of combined use of pentoxifylline (PTX) and alpha-tocopherol (vitamin E; Vit E) for minimizing radiation-induced lung toxicity. A total of 91 lung cancer patients were randomized. Among them, 44 received PTX (400 mg three times a day orally and Vit E 300 mg twice a day orally during the entire period of radiotherapy. PTX and Vit E were further administered at doses of 400 mg once a day and 300 mg once a day, respectively for 3 months after radiotherapy. A total of 47 patients were assigned as a control group. Radiation related acute and late toxicities are evaluated by radiation RTOG/EORTC toxicity scale. Median age was 59 (range, 41-75). Median follow-up was 13 months (range, 3-28 months). Radiation-induced lung toxicity was more frequent in control group for all phases than in pentoxifylline and alpha-tocopherol group (acute phase, P = 0.042, subacute phase P = 0.0001, late phase P = 0.256). PTX and Vit E combination might be considered especially in patients with lung cancer who receive concurrent chemo-radiotherapy, or have a poor respiratory function tests.

## Endometrial

Bandera, EV, L. H. Kushi, D. F. Moore, D. M. Gifkins and M. L. McCullough. **Consumption of Animal Foods and Endometrial Cancer Risk: A Systematic Literature Review and Meta-Analysis.** *Cancer Causes & Control.* 2007 Nov; 189: 967-988. This article summarizes and quantifies the current evidence relating dietary intake of animal products and endometrial cancer. Literature searches were conducted to identify peer-reviewed

manuscripts published up to December 2006. Twenty-two manuscripts from three cohort studies and 16 case-control studies were identified. One of these cohort studies evaluated only fried meat and another only milk consumption; they were not included in our meta-analyses. The third cohort study identified did not present exposure levels and could not be included in dose-response meta-analysis. This cohort study did not show an association with meat or red meat consumption. Random-effects dose-response summary estimates for case-control studies evaluating these foods were 1.26 (95% CI: 1.03-1.54) per 100 g/day of total meat, 1.51 (95% CI: 1.19-1.93) per 100 g/day of red meat, 1.03 (95% CI: 0.32-3.28) per 100 g/day of poultry, 1.04 (95% CI: 0.55-1.98) per 100 g/day of fish, and 0.97 (95% CI: 0.93-1.01) per serving of dairy. Our meta-analysis, based on case-control data, suggests that meat consumption, particularly red meat, increases endometrial cancer risk. The current literature does not support an association with dairy products, while the evidence is inconsistent for poultry, fish, and eggs. More studies, particularly prospective studies, are needed. [References: 51]

## Biofeedback

Tsai, P, P. Chen, Y. Lai, M. Lee and C. Lin. . **Effects of Electromyography Biofeedback--Assisted Relaxation on Pain in Patients with Advanced Cancer in a Palliative Care Unit.** *Cancer Nurs.* 2007 09; 305: 347-353. Most patients with advanced cancer experience pain. However, many cancer patients do not find satisfaction with conventional treatment of pain relief. This study examined the effect of electromyography (EMG) biofeedback-assisted relaxation on cancer-related pain in advanced cancer patients. We hypothesized that changes in EMG activity in frontal muscles underlie the efficacy of EMG biofeedback-assisted relaxation. This was a randomized control study. The experimental group (n = 12) received 6 EMG biofeedback-assisted relaxation sessions over a 4-week period, whereas the control group (n = 12) received conventional care. The primary efficacy measure was the level of pain, measured by the Brief Pain Inventory. Findings from this study show that relaxation training supplemented with visual and auditory EMG biofeedback signals is effective in reducing cancer-related pain in advanced cancer patients, possibly through a mechanism of attenuation of physiological arousal. Electromyography biofeedback-assisted relaxation training may be used along with medications for effective pain management in patients with advanced cancer.

## Exercise

Schneider, CM, C. C. Hsieh, L. K. Sprod, S. D. Carter and R. Hayward. **Cancer Treatment-Induced Alterations in Muscular Fitness and Quality of Life: The Role of Exercise Training.** *Annals of Oncology.* 2007 Dec; 1812: 1957-1962. Background: Cancer survivors experience muscular weakness and reduced mobility, thereby compromising quality of life. This investigation utilized moderate prescriptive exercise to improve upper- and lower-body muscular fitness, flexibility, depression and quality of life in cancer patients. Patients and methods: One hundred and thirty-five breast and prostate cancer survivors received cancer and medical history screening and a medical examination, as well as assessments of muscular strength (handgrip dynamometer) and endurance (bench press, lateral pull-down, leg press, shoulder press and curl-up crunch test), flexibility (Modified Sit and Reach), depression (Beck Depression Inventory) and quality of life (Quality of Life Index). Following the exercise assessments, cancer survivors trained in resistance exercise for 6 months during treatment or following treatment based on their results from the assessments and health status. Results: Cancer survivors following treatment showed significant (P = 0.006) improvements in upper-body muscular endurance (+46.8%), lower-

body muscular endurance (+67.1%), core muscular endurance (+32.5%) and flexibility (+6.2%), with concomitant improvements (P = 0.013) in depression (-25.6%) and total quality of life (+7.2%). Cancer survivors during treatment showed significant (P = 0.012) improvements in upper-body muscular endurance (+79.1%) and lower-body muscular endurance (+49.7%) while maintaining core endurance and flexibility in conjunction with improvements (P = 0.022) in depression (-43.0%) and quality of life (+11.5%). Conclusions: Moderate-intensity individualized prescriptive exercise is a safe and efficacious means to augment muscular function and improve the quality of life of cancer survivors. copyright 2007 European Society for Medical Oncology.

## Nutrition

Tsang, Y-, K. -H Chi, C. -J Hu, C. -L Tseng, F. -W Tseng and Y. -S Wang. . **Chemotherapy-Induced Immunosuppression is Restored by a Fermented Soybean Extract: A Proof of Concept Clinical Trial.** *Nutr Res.* 2007 Nov; 2711: 679-684. Depressed activity of natural killer (NK) cells is often associated with a higher incidence of infection and tumor recurrence. Despite evidence that NK cell activity is depressed after chemotherapy, there have been no clinical trials reporting the amelioration of this side effect. ChemoYoung, a fermented soybean extract, has been shown to activate NK cells in vivo. We conducted a randomized clinical trial to examine the effect of ChemoYoung on the restoration of NK cell activity during chemotherapy. Thirty-two patients were recruited for a self-controlled, randomized, crossover chemotherapy program with 2 consecutive, identical dose intensity chemotherapy cycles, with or without the oral intake of ChemoYoung during each cycle of chemotherapy. Patients were administered ChemoYoung (MicroBio Biotech Comp, Taipei, Taiwan) for 21 days during chemotherapy. The NK cell activity, T4/T8 ratio, NK cell number, and serum interleukin (IL) 2 level on day 21 of each cycle were compared. The mean white blood cell nadir, T4/T8 (%), NK number (%), and IL-2 serum level (ng/mL) of the combined group vs the chemotherapy-alone group were 3096/muL vs 2404/muL, 35.3/15.2 vs 29.2/13.7, 19% vs 17%, and 3.2 vs 2.0, respectively (all P > .1). However, the NK activity was 13.4 +/- 10.3 for the combined treatment group and 4.5 +/- 3.2 for the chemotherapy-alone group (P = .001). Natural killer cell activities were significantly reduced in patients who received chemotherapy without the adjuvant use of ChemoYoung. A trend to a better quality of life was also noted as assessed using the instrument of the European Organization for Research and Treatment of Cancer core questionnaire.

Edefonti, V, A. Decarli, C. La Vecchia, et al. **Nutrient Dietary Patterns and the Risk of Breast and Ovarian Cancers.** *International Journal of Cancer.* 2008 01 Feb; 1223: 609-613. The issue of diet and breast and ovarian cancers has been considered in terms of foods and nutrients, but rarely in terms of dietary patterns. We examined the associations between dietary patterns and breast and ovarian cancers in 2 Italian multicentric case-control studies. Cases were 2,569 breast cancers and 1,031 ovarian cancers hospitalized in 4 Italian areas between 1991 and 1999. Controls were 3,413 women from the same hospital network. Dietary habits were investigated through a validated food-frequency questionnaire. Dietary patterns were identified on a selected set of nutrients through principal component factor analysis. Odds ratios (OR) and 95% confidence intervals (CI) for both cancers were estimated using unconditional multiple logistic regression models on quartiles of factor scores and continuous factor scores. We identified 4 major dietary patterns named Animal products, Vitamins and fiber, Unsaturated fats and Starch-rich. The animal products pattern and the unsaturated fats pattern were inversely associated with breast cancer (OR = 0.74, 95% CI: 0.61-0.91 and OR = 0.83, 95% CI: 0.68-1.00, respectively, for the highest consumption quartile), whereas the starch-rich pattern was directly associated with it (OR = 1.34, 95% CI: 1.10-1.65). The

vitamins and fiber pattern was inversely associated with ovarian cancer (OR = 0.77, 95% CI: 0.61-0.98), whereas the starch-rich pattern was directly associated with it (OR = 1.85, 95% CI: 1.37-2.48). In conclusion, the starch-rich pattern is potentially an unfavorable indicator of risk for both breast and ovarian cancers, while the animal products and the vitamins and fiber patterns may be associated with a reduced risk of breast and ovarian cancers, respectively.

Gomes, FDS. **Carotenoids: A Possible Protection Against Cancer Development.** *Rev Nutr.* 2007 Sep; 205: 537-548. This study is a literature review that discusses the likelihood of dietary carotenoids offering protection against cancer. Carotenoids have been demonstrating a protective action against carcinogenesis both in vitro and in vivo, in animals and humans. Among them, beta-cryptoxanthin, fucoxanthin, astaxanthin, capsanthin, crocetin and phytoene have been little explored and literature is still very lacking and little conclusive. Experimental studies with humans have shown beta-carotene to have no effect or reverse effect; however, they have never included interventional and interactive variables that should have been controlled. Scientific evidence based on epidemiological studies and recent experimental assays and the elucidation of phytochemical activity mechanisms associated with greater protection against cancer, a diet rich in carotenoids from fruits and vegetables may protect against carcinogenesis.

## Supplements

Colomer, R, J. M. Moreno-Nogueira, P. P. Garcia-Luna, et al. **N-3 Fatty Acids, Cancer and Cachexia: A Systematic Review of the Literature.** *Br J Nutr.* 2007 May; 975: 823-831. Use of n-3 fatty acids (FA) has been reported to be beneficial for cancer patients. We performed a systematic review of the literature in order to issue recommendations on the clinical use of n-3 FA in the cancer setting. A systematic search was performed in MEDLINE, EMBASE, Cochrane and Healthstar databases. We selected clinical trials or prospective observational studies including patients with cancer and life expectancy >2 months, in which enteral supplements with n-3 FA were administered. Parameters evaluated individually were clinical (nutritional status, tolerance, survival and hospital stays), biochemical (inflammatory mediators), and functional (functional status, appetite and quality of life (QoL)). Seventeen studies met the inclusion criteria; eight were of high quality. The panel of experts established the following evidence: (1) oral supplements with n-3 FA benefit patients with advanced cancer and weight loss, and are indicated in tumours of the upper digestive tract and pancreas; (2) the advantages observed were: increased weight and appetite, improved QoL, and reduced post-surgical morbidity; (3) there is no defined pattern for combining different n-3 FA, and it is recommended to administer > 1.5 g/day; and (4) better tolerance is obtained administering low-fat formulas for a period of at least 8 weeks. All the evidences were grade B but for 'length of treatment' and 'advantage of survival' it was grade C. Our findings suggest that administration of n-3 FA (EPA and DHA) in doses of at least 1.5 g/day for a prolonged period of time to patients with advanced cancer is associated with an improvement in clinical, biological and QoL parameters. [References: 29]

## CAM of the Month

Hordern, A and A. Street. **Issues of Intimacy and Sexuality in the Face of Cancer: The Patient Perspective.** *Cancer Nurs.* 2007 Nov-Dec; 306: E11-8. Experiencing a diagnosis of cancer has the potential to dramatically alter the way in which a person experiences intimate and sexual aspects of their lives. This article draws on data from a larger study into issues of intimacy and sexuality from the perspectives of patients and health professionals in cancer and palliative care. A 3-

stage reflexive inquiry involved semistructured participant interviews (n = 82), textual analysis of national and international clinical practice guidelines (n = 33), and participant feedback at 15 patient and health professional educational forums. This article will present the analysis of 50 patient interviews, which showed 5 clusters of responses to a cancer diagnosis: "focus on survival," "trust in health professional," "desire for choices," "search for normality," and "need for negotiated communication." Most patients were searching for a reflexive, patient-centered and negotiated style of communication from the health professional of their choice, at a time and in a manner that suited their individual needs. Many patients were disappointed by the lack of information, support, and practical strategies provided by health professionals to assist them to live with the sexual and intimate changes they had experienced in the face of a life-limiting disease. Implications for nursing practice are discussed.

Penson, RT, F. Gu, S. Harris, et al. **Hope.** *Oncologist.* 2007 Sep; 129: 1105-1113. Shortly before his death in 1995, Kenneth B. Schwartz, a cancer patient at Massachusetts General Hospital (MGH), founded The Kenneth B. Schwartz Center at MGH. The Schwartz Center is a nonprofit organization dedicated to supporting and advancing compassionate health care delivery that provides hope to the patient, support to caregivers, and encourages the healing process. The Center sponsors the Schwartz Center Rounds, a monthly multidisciplinary forum where caregivers reflect on important psychosocial issues faced by patients, their families, and their caregivers, and gain insight and support from fellow staff members. A patient with recurrent ovarian cancer, now in a 12-year remission after recurrence, and her surgeon, discussed their experiences and feelings around the hopes and fears of cancer and its treatment. Hope sustains many through dark times, and is at the core of the wonderful resilience of many who wrestle with cancer. Concerns about false hope, unrealistic expectations, assumptions, engaging in realistic hopefulness, and the joys and stresses embodied in hope and how they frame the caregiver-patient relationship are discussed. The literature and limited evidence base are reviewed. [References: 44]

InspireHealth provides an integrated whole person approach to health for individuals living with cancer. Our medical doctors guide patients to explore and learn about a variety of wellness approaches to health and healing in addition to conventional cancer treatment. This integrated medical model, which engages people in their own care, improves quality of life and reduces the likelihood of cancer recurrence. The editorial board includes: Dr. Hal Gunn, CEO and Co-founder, Dr. Janice Wright, Dr. Teresa Clarke and Dr. Ron Puhky.

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