

“Nutrition and kidney cancer”

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Disclosure

- Research funding: Syndax, Merck, Genentech, BMS

Disclosure



"Pili nuts are a rich buttery tasting nut grown in the volcanic soil of the Philippine peninsula. High in protein, calcium and potassium, pili nuts are a healthy snack with a delicious flavor. They also make a wonderful addition to desserts and baked goods. Try these dry roasted and unsalted pili nuts for yourself and discover what makes them so unique and incredible"

PILI NUTS



Objectives

- To discuss how nutrition and diet may have an impact on patients with kidney cancer
- To discuss the potential immunomodulatory effect of dietary protein restriction

Nutrition

“Nutrition is nourishment or energy that is obtained from food consumed or the process of consuming the proper amount of nourishment and energy. An example of nutrition is eating a healthy diet”

Why focus on diet and cancer?



Cancer is impacted by diet and lifestyle



➤ Diet is intimately linked with development of prostate cancer¹⁻⁹.

➤ **Vegetable and legume consumption**

- Lower CaP incidence^{4,5,6}
- Lower chance of CaP progression & mortality post diagnosis^{4,5,6,7}
- Reduced circulating Insulin-like Growth Factor 1 (IGF-1)²
 - IGF-1 is a potent mutagen linked to the development and progression of CaP



<https://www.happycow.net/blog/the-home-project/>

➤ **Animal proteins**

- Higher incidence, progression and mortality related to CaP^{1,3,4,8,9}
- Aggressive / Advanced stage CaP^{2,8,9}
- Increased circulating IGF-1^{1,2}

(Yang, Chavarro, et al 2015, *Cancer Prevention Research*)



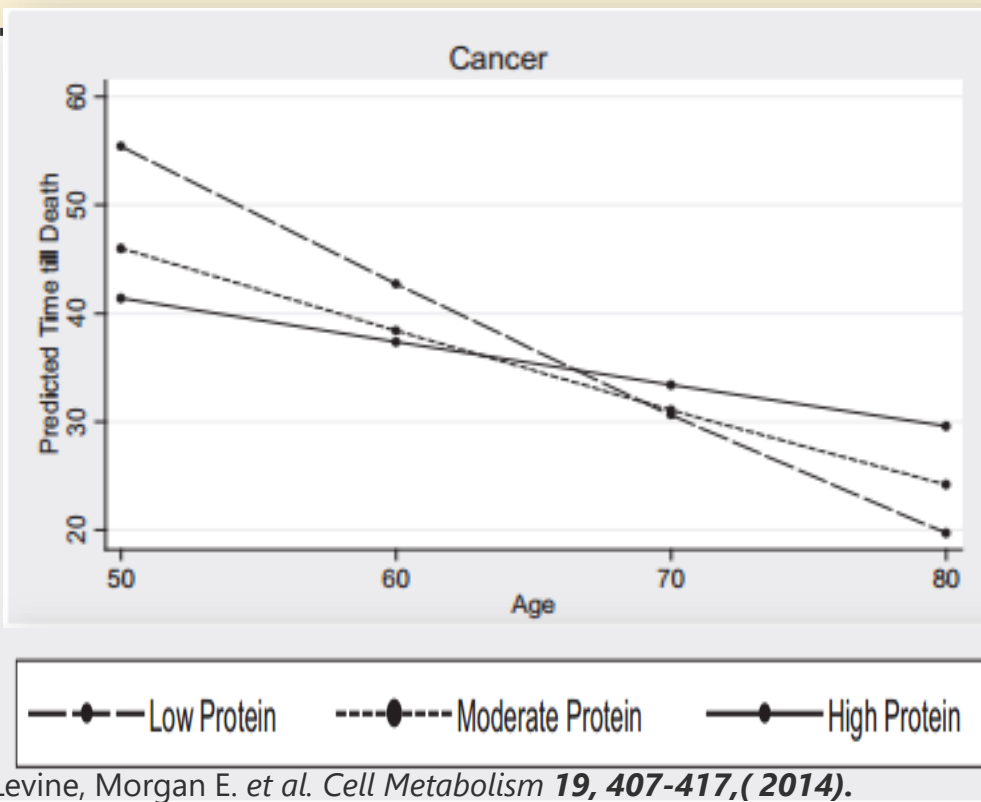
<http://www.feednavigator.com/Markets/Meat-protein-Can-supply-match-growing-demand>

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2. Fontana, et al, *Aging Cell*, 4, 2451-2461 (2008)
3. Hachshaw-McGeagh, et al., *Trials*, 17:123 (2016)

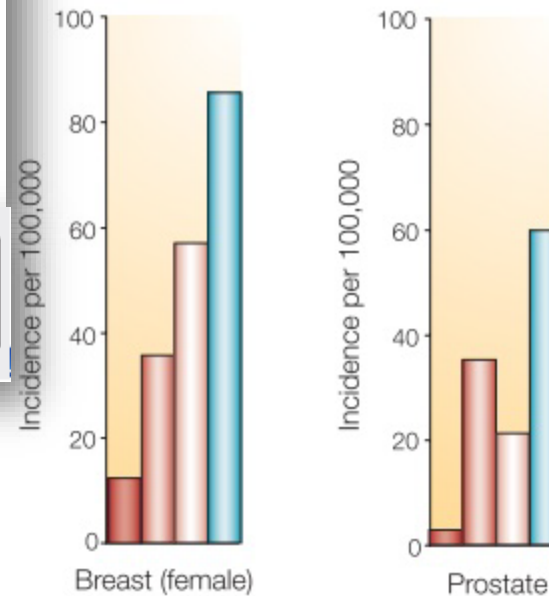
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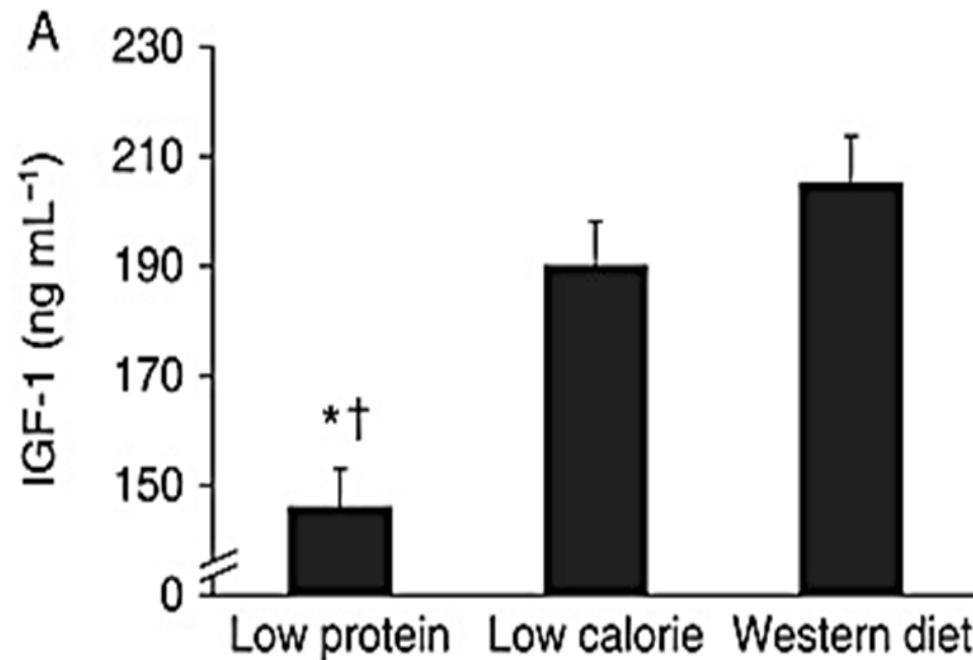
Dietary protein content and cancer



- Moderate to high protein consumption results in increased cancer incidence and mortality
- Shift from Eastern to Western diet results in increased cancer incidence



Western diet compared to low protein diet consumption results in high circulating insulin growth factor (IGF-1)



Fontana, L. *et al. Aging Cell* **4**, 2451-2461 (2008).

Association of Low-Fat Dietary Pattern With Breast Cancer Overall Survival

A Secondary Analysis of the Women's Health Initiative Randomized Clinical Trial

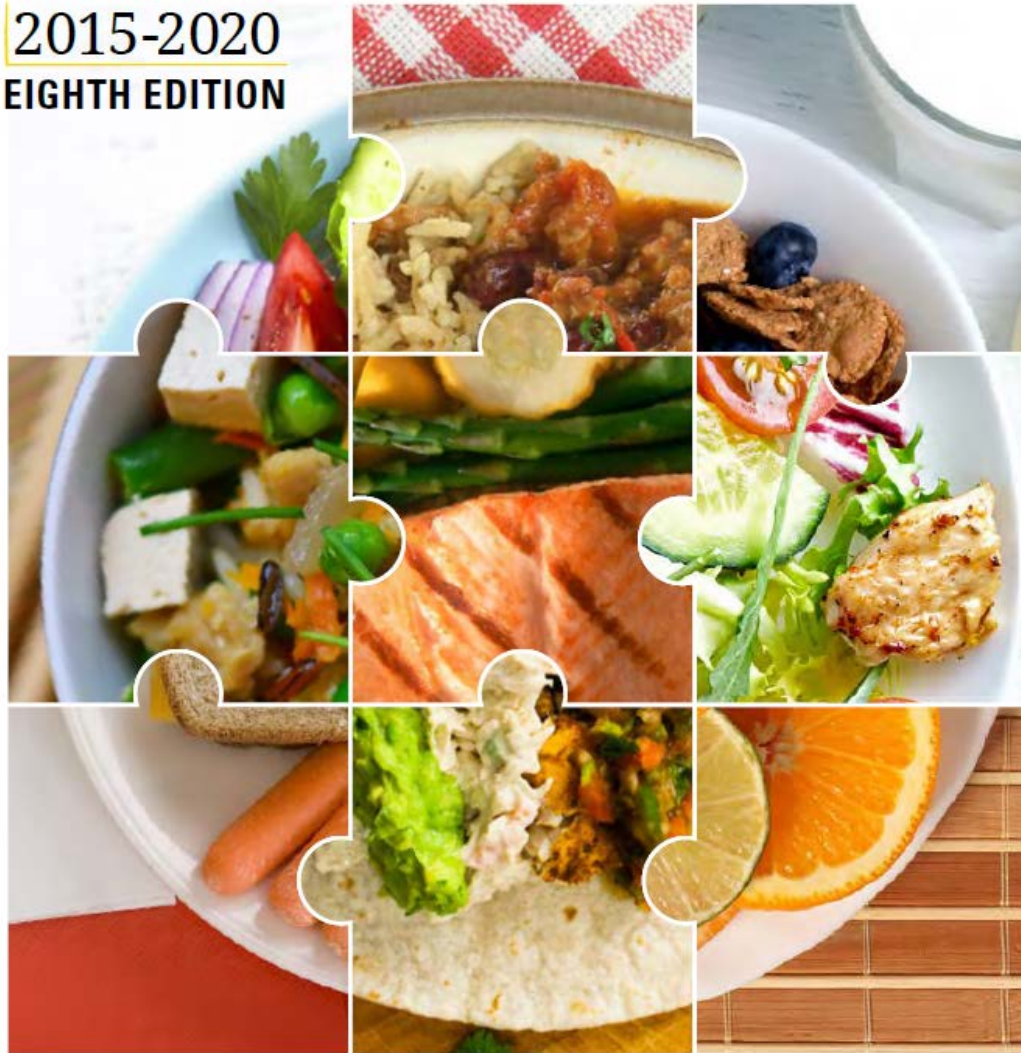
Rowan T. Chlebowski, MD, PhD; Aaron K. Aragaki, MS; Garnet L. Anderson, PhD; Michael S. Simon, MD, MPH; JoAnn E. Manson, MD, DrPH; Marian L. Neuhouser, PhD; Kathy Pan, MD; Marcia L. Stefanick, PhD; Thomas E. Rohan, MBBS, PhD; Dorothy Lane, PhD; Lihong Qi, PhD; Linda Snetselaar, PhD; Ross L. Prentice, PhD

RESULTS Of 1764 women diagnosed with breast cancer during the dietary intervention period, mean (SD) age at screening was 62.7 (6.7) years and age at diagnosis was 67.6 (6.9) years. With 516 total deaths, breast cancer overall survival was significantly greater for women in the dietary intervention group than in the usual-diet comparison group (10-year survival of 82% and 78%, respectively; hazard ratio [HR], 0.78; 95% CI, 0.65-0.94; $P = .01$). In the dietary group there were fewer deaths from breast cancer (68 vs 120; HR, 0.86; 95% CI, 0.64-1.17), other cancers (36 vs 65; HR, 0.76; 95% CI, 0.50-1.17), and cardiovascular disease (27 vs 64; HR, 0.62; 95% CI, 0.39-0.99).

CONCLUSIONS AND RELEVANCE In women who received a diagnosis of breast cancer during the dietary intervention period, those in the dietary group had increased overall survival. The increase is due, in part, to better survival from several causes of death.



DIETARY GUIDELINES FOR AMERICANS 2015-2020 EIGHTH EDITION



DietaryGuidelines.gov

https://health.gov/dietaryguidelines/2015/resources/2015-2020_Dietary_Guidelines



MELVIN AND BREN SIMON
CANCER CENTER
INDIANA UNIVERSITY

Key Messages

❑ Start with shifts, or small changes:

- ✓ All foods and beverages count toward a healthier meal pattern
- ✓ Shift toward more nutrient-dense choices within and across food groups
- ✓ Small changes add up
- ✓ Accommodate personal tastes and cultural preferences to make the shift easier to maintain

Courtesy of Rachel Bordogna, RDN

https://health.gov/dietaryguidelines/2015/resources/2015-2020_Dietary_Guidelines

American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention

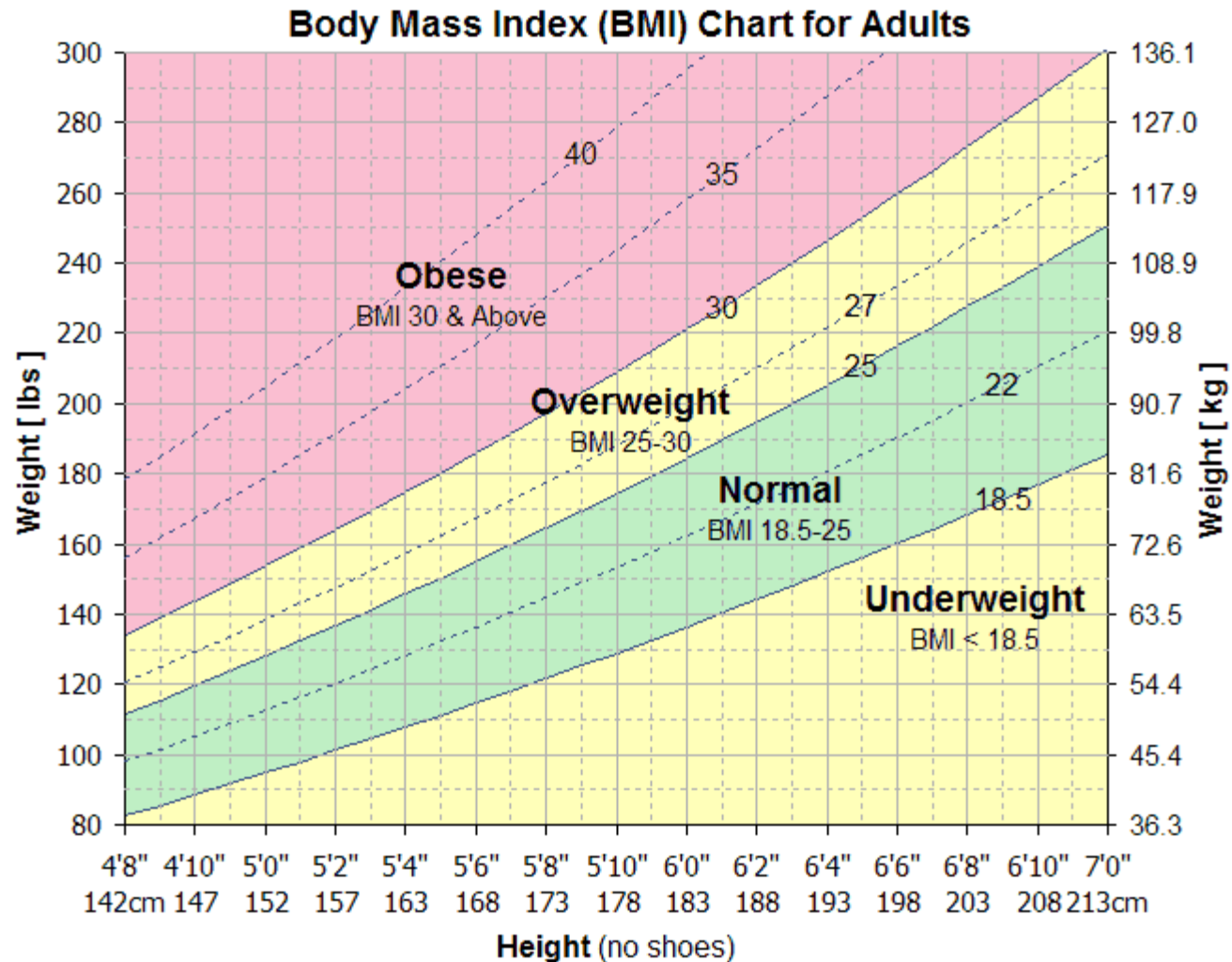
Reducing the Risk of Cancer With Healthy Food Choices and Physical Activity

Lawrence H. Kushi, ScD¹; Colleen Doyle, MS, RD²; Marji McCullough, ScD, RD³; Cheryl L. Rock, PhD, RD⁴; Wendy Demark-Wahnefried, PhD, RD⁵; Elisa V. Bandera, MD, PhD⁶; Susan Gapstur, PhD, MPH⁷; Alpa V. Patel, PhD⁸; Kimberly Andrews⁹; Ted Gansler, MD, MBA, MPH¹⁰ and The American Cancer Society 2010 Nutrition and Physical Activity Guidelines Advisory Committee

TABLE 1. American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention

ACS RECOMMENDATIONS FOR INDIVIDUAL CHOICES	
Achieve and maintain a healthy weight throughout life.	
<ul style="list-style-type: none"> • Be as lean as possible throughout life without being underweight. • Avoid excess weight gain at all ages. For those who are currently overweight or obese, losing even a small amount of weight has health benefits and is a good place to start. • Engage in regular physical activity and limit consumption of high-calorie foods and beverages as key strategies for maintaining a healthy weight. 	
Adopt a physically active lifestyle.	
<ul style="list-style-type: none"> • Adults should engage in at least 150 minutes of moderate intensity or 75 minutes of vigorous intensity activity each week, or an equivalent combination, preferably spread throughout the week. • Children and adolescents should engage in at least 1 hour of moderate or vigorous intensity activity each day, with vigorous intensity activity occurring at least 3 days each week. • Limit sedentary behavior such as sitting, lying down, watching television, or other forms of screen-based entertainment. • Doing some physical activity above usual activities, no matter what one's level of activity, can have many health benefits. 	
Consume a healthy diet, with an emphasis on plant foods.	
<ul style="list-style-type: none"> • Choose foods and beverages in amounts that help achieve and maintain a healthy weight. • Limit consumption of processed meat and red meat. • Eat at least 2.5 cups of vegetables and fruits each day. • Choose whole grains instead of refined grain products. 	
If you drink alcoholic beverages, limit consumption.	
<ul style="list-style-type: none"> • Drink no more than 1 drink per day for women or 2 per day for men. 	

“Know you own BMI”



The objectives of a cancer dietitian

- Identify goals of healthy eating for cancer survivorship
- Identify risks for malnutrition
- Gain tools to gradually change eating habits

Cancer diet

- Depends on Goals
- Treatment
- Current Side Effects
- Appetite

Goals of nutrition during treatment

- Weight maintenance
- Adequate hydration
- Avoid nutrition related treatment breaks
- Maintain skin integrity

Malnutrition

- 50-80% of patients may develop malnutrition or cachexia during treatment
- Malnutrition is associated with increased morbidity, mortality & decreased response to therapy
- Nutrition support may help prevent or diminish the progression of malnutrition

Characteristics of malnutrition

- Decreased energy intake over 5 days
- Weight loss (1-2% over 1 week)
- Subcutaneous fat and muscle loss
- Fluid accumulation
- Decreased functional capacity

Inflammation

- What is it?
 - a” disorganized” immune response
- Why is it harmful?
 - It tends to suppress the good immune response against germs and tumors cells by inducing “immunotolerance”



Anti-inflammatory eating

- Reduces risk for cancer
- Reduces risk for diabetes
- Reduces risk for heart disease
- Improves mood
- Reduces joint pain
- Improves blood pressure

Foods cause inflammation

- Processed foods
- Excess meat - especially red meat
- Saturated fat



Anti-inflammatory eating

- Avoid processed foods
- Eat more plant based foods



Courtesy of Beth Kirsch, RDN

Why plant based eating?

- High in vitamins, minerals, fiber
- High in Phytochemicals
 - Give plants color and flavor
 - Cancer and inflammation fighters



Plant based eating

- Eat more Vegetables & Fruit
 - 1 ½ cups of fruits & 2-3 cups of vegetables daily
- Fill half your plate with Vegetables & Fruit



Plant based eating

- Change the way you think about meat
 - Use as a garnish
 - Limit red meat (including pork) to less than 18 oz. per week
 - Use beans as a protein source



Courtesy of Beth Kirsch, RDN

Plant Based Eating

- Increase intake of beans, seeds, nuts
 - Good source of minerals
 - Good source of fiber
 - Good source of healthy fats
 - Use in place of some or all of meat in an entrée for protein



Plant based eating

- Eat sea food twice a week
 - Fatty fish like salmon provides omega -3 fatty acids
 - Low in saturated fat



Plant based eating

- Use healthy fats in cooking & eating
 - Extra virgin olive oil, nuts seeds, avocados



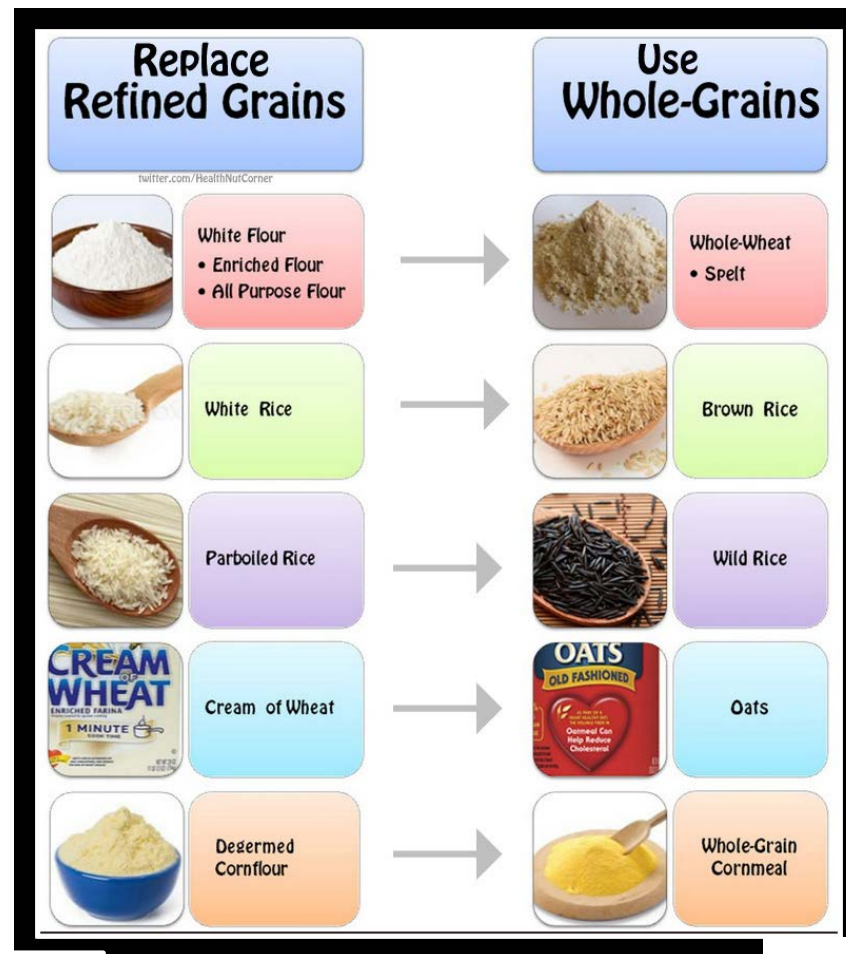
Plant based eating

- Switch to Whole Grains
 - Contain more fiber
 - More vitamins/minerals
 - Less processed
 - Look for the words “whole wheat” on the label
 - Complex Carbohydrates
 - High in phytochemicals
 - Examples: old fashioned oats, quinoa, whole wheat bread



EAT 48g OR MORE OF
WHOLE GRAINS DAILY

Plant based eating

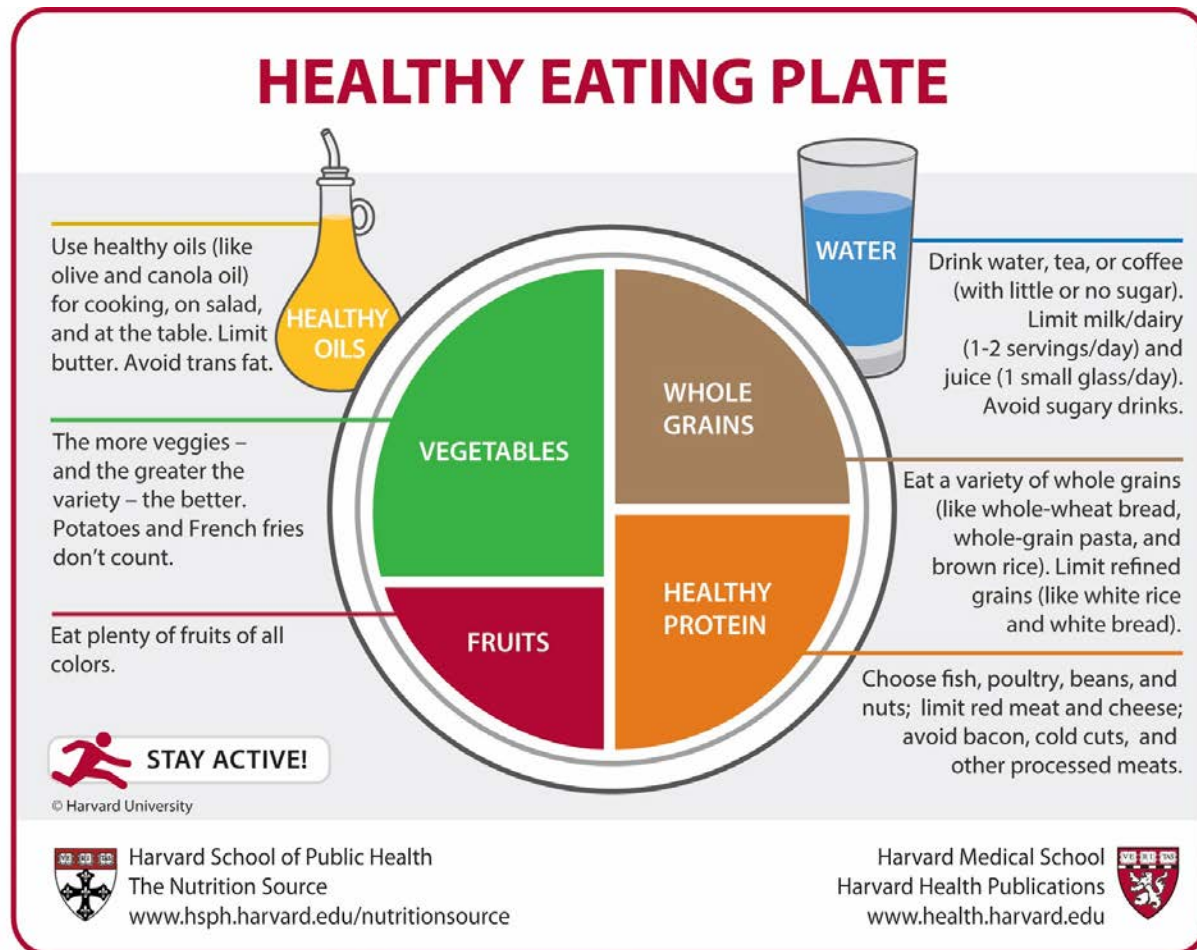


Plant based eating

- Avoid simple/processed sugars

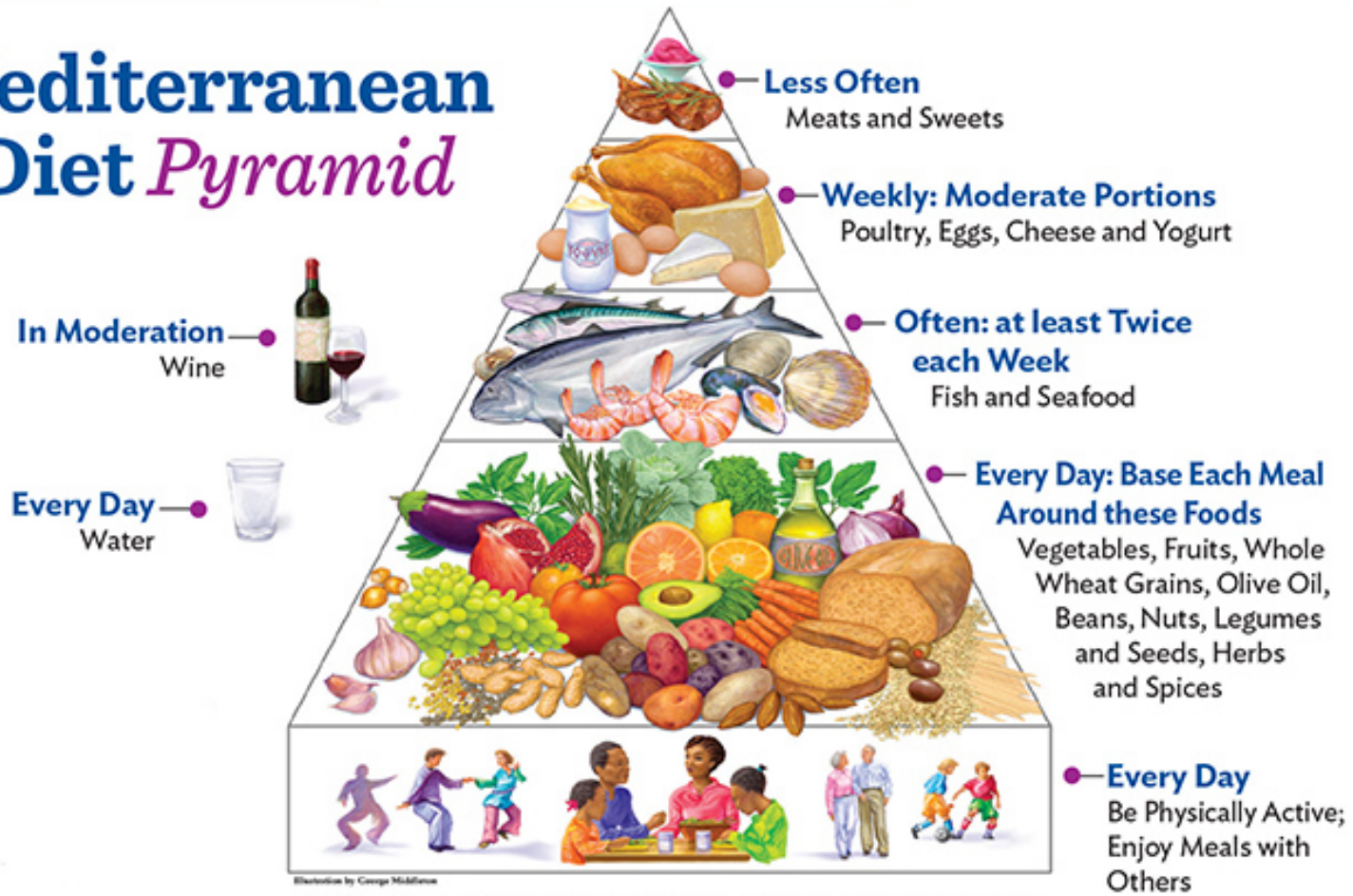


Harvard Plate



Mediterranean Pyramid

Mediterranean Diet *Pyramid*



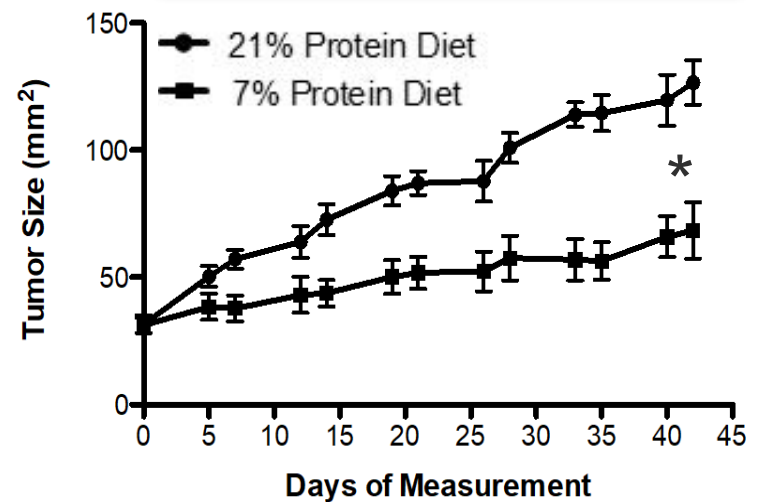
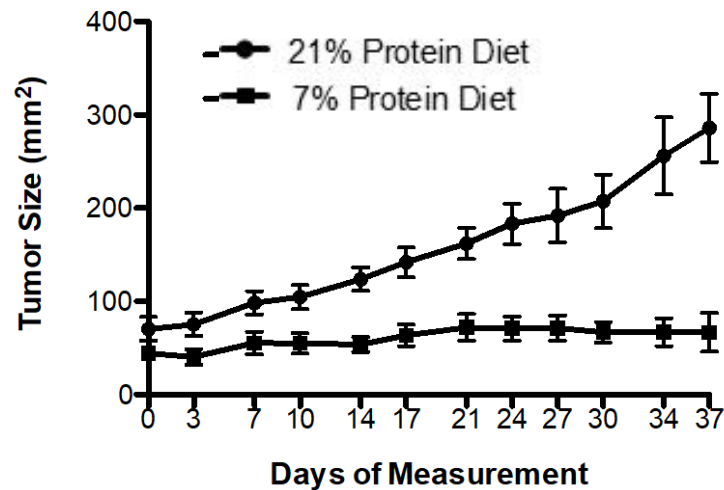
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My take home message

- To reduce inflammation, especially during immunotherapy, I would recommend the following:
 - Avoid dairy product, red meat
 - Increase plant-based proteins and fibers
 - Increase cruciferous vegetables (broccoli, cauliflower, and cabbage)
 - Eat more fish
- The only supplements I would consider are Vitamin D and Vitamin C
- I would integrate dietary changes with regular physical activity

Dietary protein restriction inhibits tumor growth in human xenograft models of prostate and breast cancer

Luigi Fontana^{1,2,3,*}, Remi M. Adelaiye^{4,5,*}, Antonella L. Rastelli¹, Kiersten Marie Miles⁴, Eric Ciamporcero^{4,6}, Valter D. Longo⁷, Holly Nguyen⁸, Robert Vessella⁸, and Roberto Pili^{4,5}



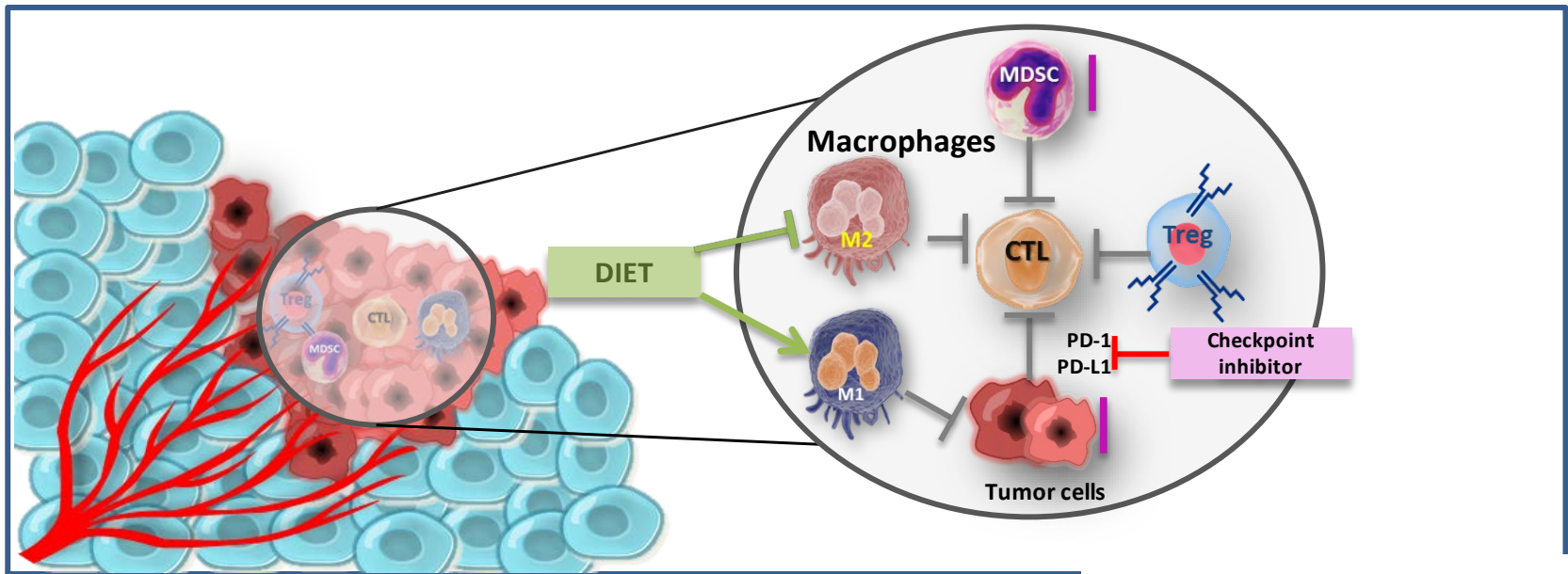
Low protein diet increases the antitumor effect of immunotherapy

Cancer Therapy: Preclinical

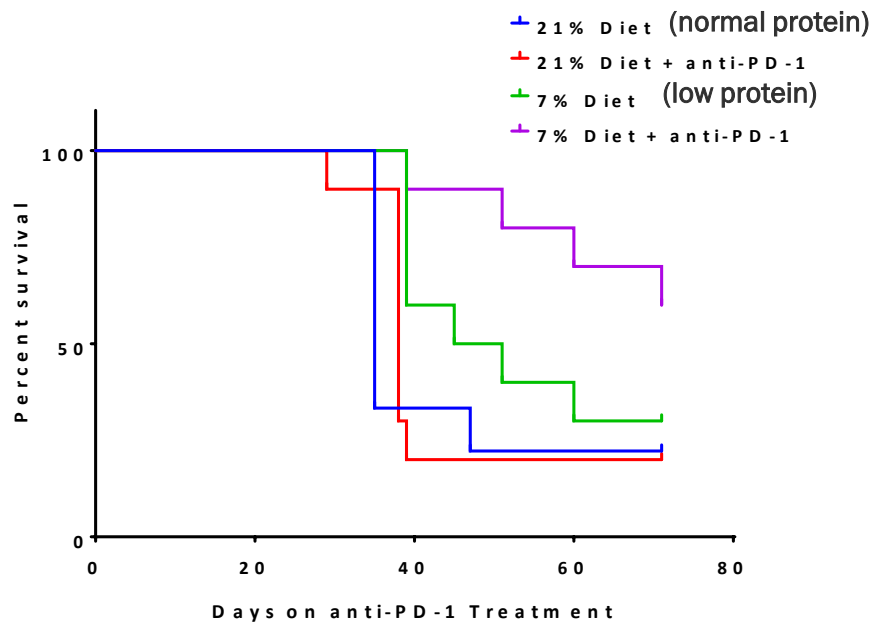
Clinical
Cancer
Research

Dietary Protein Restriction Reprograms Tumor-Associated Macrophages and Enhances Immunotherapy

Ashley Orillion^{1,2}, Nur P. Damayanti¹, Li Shen³, Remi Adelaiye-Ogala^{1,4}, Hayley Affronti², May Elbanna¹, Sreenivasulu Chintala¹, Michael Ciesielski³, Luigi Fontana⁵, Chinghai Kao⁶, Bennett D. Elzey^{6,7}, Timothy L. Ratliff⁸, David E. Nelson⁹, Dominic Smiraglia², Scott I. Abrams¹⁰, and Roberto Pili¹



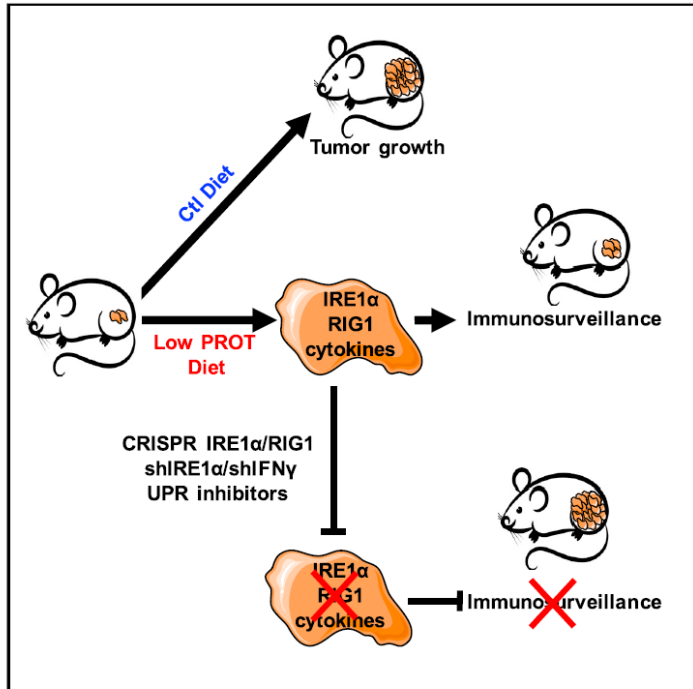
Low protein diet increases the antitumor effect of immunotherapy in a renal cell carcinoma model



Group	Median Survival	p value to control	p value to combo
21% Diet	35		
21% Diet + anti-PD-1	38	0.2616	**0.0035
7% Diet	48	*0.0459	0.0751
7% Diet + anti-PD-1	>71	**0.0070	

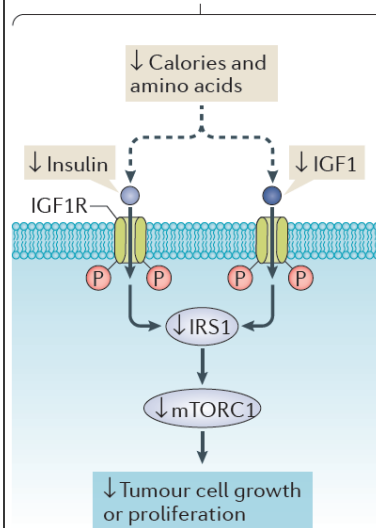
Low-Protein Diet Induces IRE1 α -Dependent Anticancer Immunosurveillance

Camila Rubio-Patiño,^{1,9} Jozef P. Bossowski,^{1,9} Gian Marco De Donatis,¹ Laura Mondragón,¹ Elodie Villa,¹ Lazaro E. Aira,¹ Johanna Chiche,¹ Rana Mhaidly,¹ Cynthia Lebeaupin,¹ Sandrine Marchetti,¹ Konstantinos Voutetakis,^{2,3} Aristotelis Chatzioannou,^{2,4} Florence A. Castelli,⁵ Patricia Lamourette,⁵ Emeline Chu-Van,⁵ François Fenaille,⁵ Tony Avril,^{6,7} Thierry Passeron,¹ John B. Patterson,⁸ Els Verhoeven,¹ Béatrice Bailly-Maitre,¹ Eric Chevet,^{6,7} and Jean-Ehrland Ricci^{1,10,*}

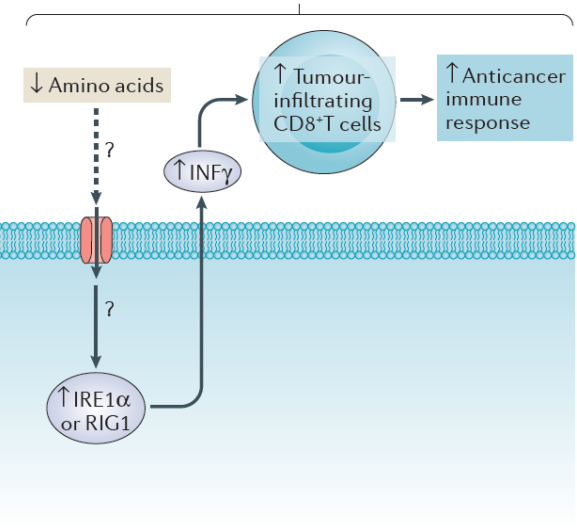


Low-protein diet in cancer: ready for prime time?

Substantial dietary protein restriction



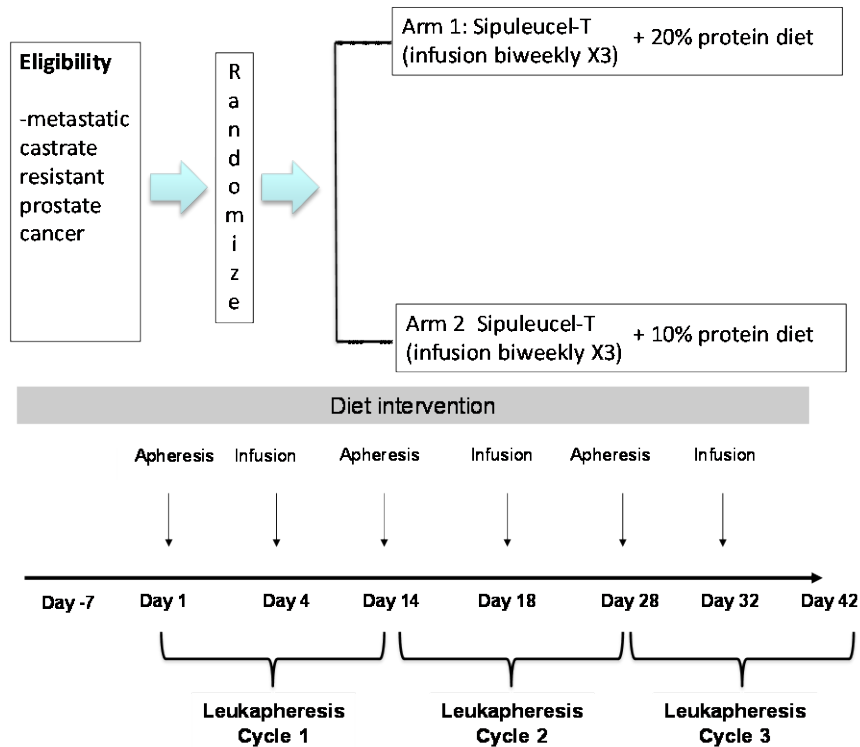
Moderate dietary protein restriction



Nature Reviews | [Endocrinology](#)

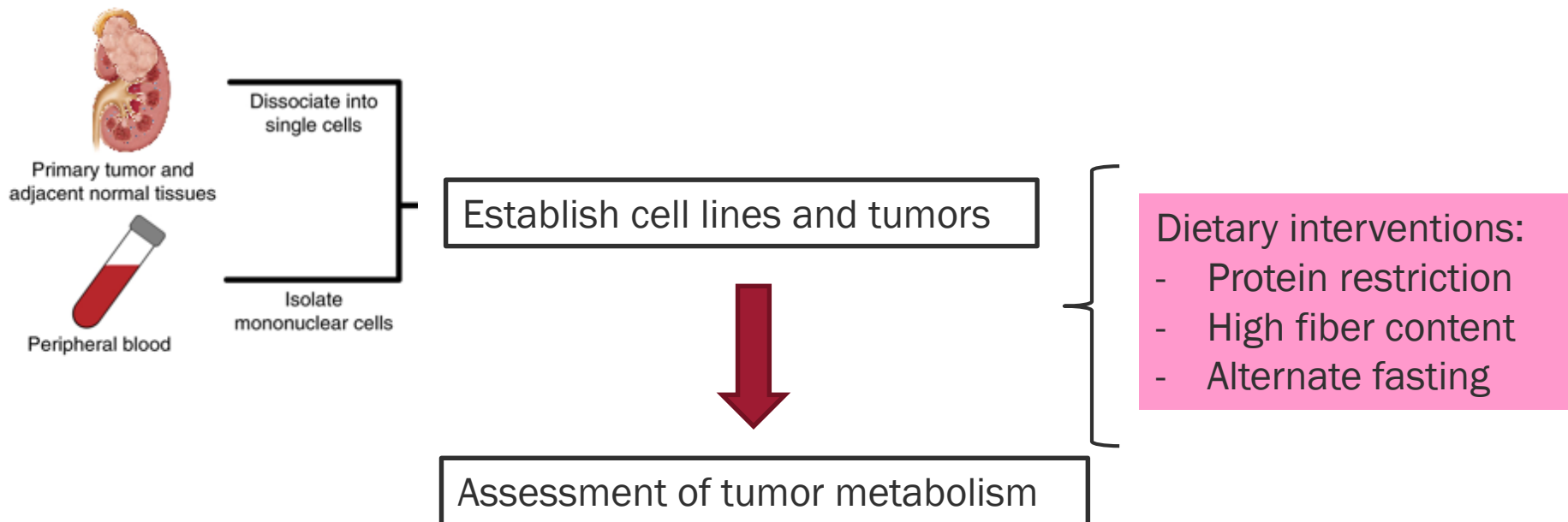
Pili R and Fontana L (2018)

Immunomodulation by protein diet restriction

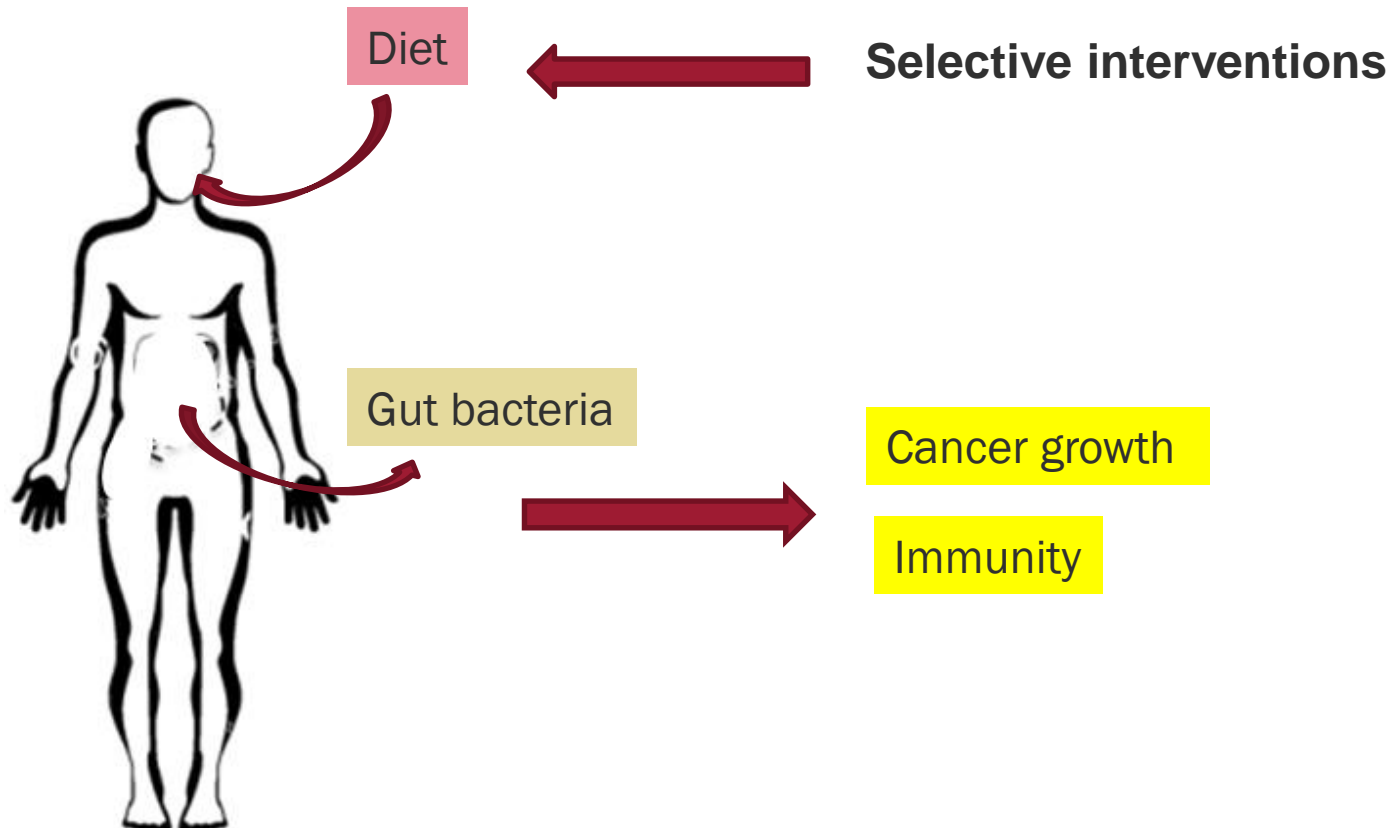


**Pilot randomized study
normal vs low protein
diet with sipuleucel-T**

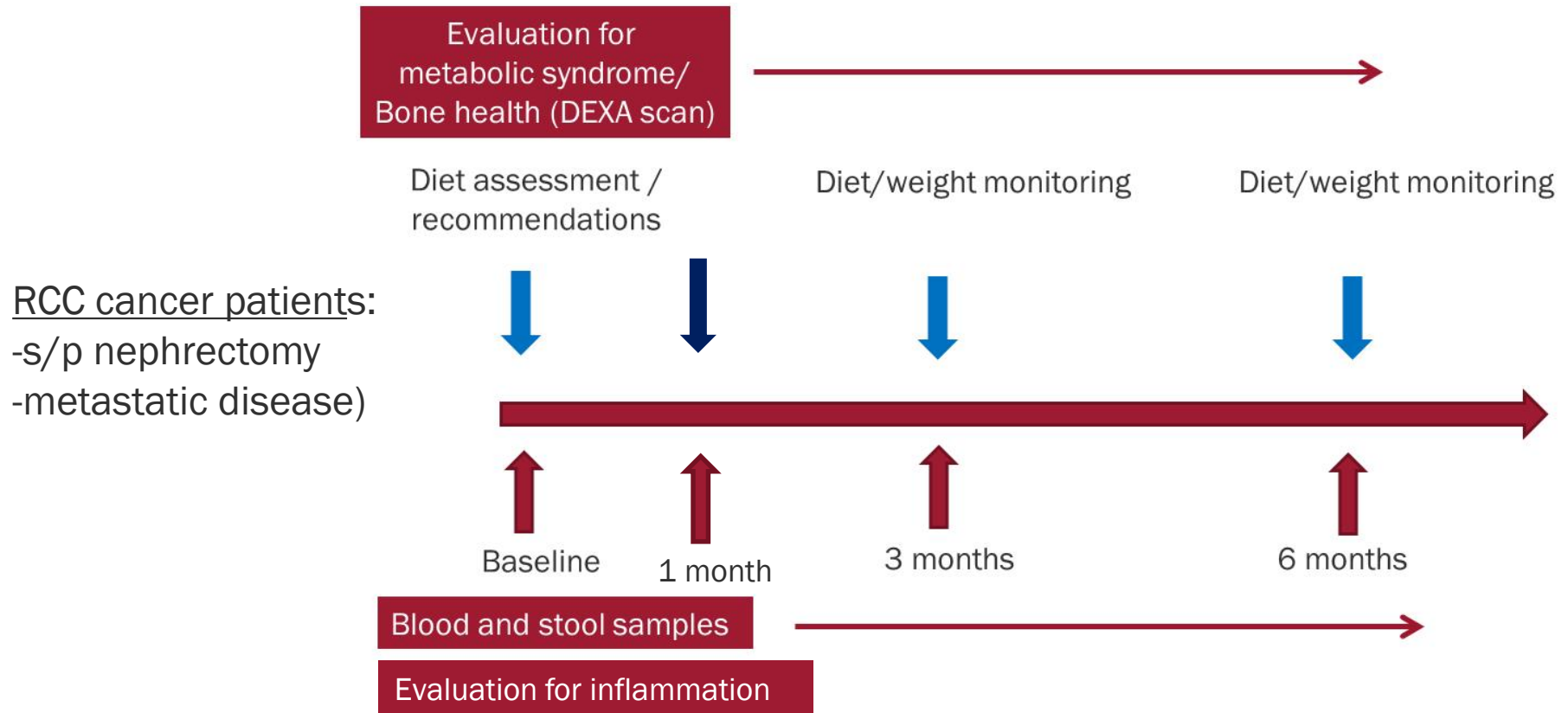
Future personalized dietary interventions for kidney cancer patients



Diet and gut microbiota: A new frontier in medicine and oncology



SNAC Clinic (Science, Nutrition And Cancer Clinic) at Indiana University



Integrating the dietitian as a personal trainer



Patients need different counseling depending on the stage of their disease:

- Early stage disease patient may benefit for weight loss if BMI is high
- Late stage disease patient may need weight maintenance

A comprehensive approach for kidney cancer patients



Summary

- There is an unmet need to integrate nutritional support for kidney cancer patients
- Our overall goals are:
 - Integrate immune-based therapies and dietary interventions for kidney cancer
 - Improve patient quality of life and implement survivorship initiatives for patients with recurrent or advanced kidney cancer
 - **Establish a JNKCF chapter in Indianapolis**

Thanks for Listening!



Special thanks to:

-Beth Kirsch, RDN, Clinical Dietitian Specialist (IU Health Simon Cancer Center)

-Rachel Bordogna RDN, Clinical Dietitian Specialist (Purdue University)