# Dietary Evidence and Research in Plasma Cell Disorders Urvi A. Shah, MD

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Memorial Sloan Kettering Cancer Center

#### **Disclosures**

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Honoraria **MJH Life Sciences** Janssen ACCC MashUpMD RedMedEd Medical Advisory Board (uncompensated) Plant Powered Metro New York

### What food or supplements can I take?



Most likely question to be asked by patients

Least likely question to be answered by hematologists/oncologists

Dietary Research in Hematologic Malignancies is an unmet need

Malik M et al. Blood Cancer J 2022

### **Plasma Cell Disorders**

#### **Precursor disorders**

Monoclonal Gammopathy of Unknown Significance

- Abnormal (monoclonal) protein
- Abnormal plasma cells (<10%) in the bone marrow</li>
- No symptoms
- 1% per year progress to myeloma
- Not treated

Smoldering Multiple Myeloma

- Abnormal (monoclonal) protein
- Abnormal plasma cells (10-60%) in the bone marrow
- No symptoms
- 10% per year progress to myeloma
- Usually not treated

#### Cancer

#### **Multiple Myeloma**

- Abnormal (monoclonal) protein
- Abnormal plasma cells (>10%) in the bone marrow
- Symptoms such as:
- 1. Elevated blood calcium
- 2. Abnormal kidney function
- 3. Anemia
- 4. Bone lesions
  - **Treatment required**

Kim et al BMJ NPH 2021

# Patients are living longer than ever before



There is an opportunity to improve outcomes further with dietary and lifestyle interventions.

Timeline of drug discovery and year of multiple myeloma diagnosis (by decade)

Shah UA, Mailankody S. BMJ 2020

# 66-year-old male with multiple myeloma

#### **Past Medical History**

Coronary Artery Disease

Atrial fibrillation

Neuropathy

Hypertension

Hyperlipidemia

Stroke with weakness in wheelchair

Deep vein thrombosis

Sleep apnea

Morbid Obesity

Major depressive disorder

Frequent hospital admissions

Cognitive decline/dementia

Degenerative joint disease

Cellulitis

Abdominal hernia

- Kidney stone
- Hyperthyroidism
- Multifocal pneumonia
- Type 2 DM
- Congestive heart failure
- Preglaucoma
- left lower lymphedema from CABG.

#### **Past Surgical History**

- Right knee repair
- Right knee joint replacement surgery
   Umbilical hernia repair
- Tonsillectomy x 2
- Cardioversions x 10
- Multiple cardiac ablation.
- Coronary Artery Bypass Graft

Therefore, not a candidate for: Stem cell transplantation CAR T cell therapy Clinical trials Some intensive chemotherapy

Thus, decreased overall survival.

### **Dietary changes after a cancer diagnosis**

|                                       | 421 patients                 | s with plasma cell disorders<br>via HealthTree Foundation |          |
|---------------------------------------|------------------------------|---|----------|
| Since your diagno                     | sis, have you had questions  | s about diet and nutrition?                               | 82%      |
| Oncologist did not                    | address it                   |   | 57%      |
| If your oncologist                    | gave you recommendations     | , did you attempt to follow them?                         | 94%      |
| Patients' self repo                   | rted (pre versus post diagno | osis) –   |          |
| <ul> <li>Increase in fruit</li> </ul> | s, vegetables, whole grains  | s, plant proteins, seafood consumption (p.                | <0.0001) |

• Decrease in red meat and junk food consumption (p<0.0001)

Malik M et al. Blood Cancer J 2022

### **American Institute of Cancer Research Guidelines**



https://www.aicr.org/cancer-prevention/food-facts/

#### **Individualizing Nutrition Changes**

Disease Stage – Newly diagnosed, on maintenance, relapsed

Patient Choice – Receptive to hearing about this and empowered by it or overwhelmed to hear about it and would not help

Medical issues related to the cancer – Is there significant weight loss from the cancer and side effects to treatment like nausea and diarrhea that they aren't tolerating most foods.

Medical issues related to metabolic health – Obesity, diabetes, cardiovascular disease, high cholesterol

Gradual versus drastic changes to habits

# Healthy Lifestyle and Genetic Risk in Colorectal Cancer

UK Biobank Cohort

346,297 participants

2066 colorectal cancer cases

Healthy Lifestyle Score (sum of body fat, physical activity, sedentary time, diet, alcohol, smoking) Polygenic Risk Score (genetic risk score) Healthier lifestyle associated with reduced risk of

colorectal cancer

High genetic risk patients could benefit more from lifestyle modification than those in low genetic risk



### **Obesity and Cancer**

From 1999–2000 through 2017–2018, the prevalence of obesity increased from 30.5% to 42.4%.

About 1/3 of the population is overweight and only less than a third are normal weight.

(https://www.cdc.gov/obesity/)



# **Obesity and Risk of MGUS and MM**



However, patients that lose weight unintentionally due to a myeloma diagnosis are likely to do worse (HR 1.6)

### **Extreme BMI in newly diagnosed MM**

1.00 1.00 Progression-Free Survival 0.75 0.75 0.50 0.50 Overall 0.25 0.25 0.00 0.00 20 40 60 20 40 60 80 Time since diagnosis (months) Time since diagnosis (months) Number at risk (number censored) Number at risk (number censored) Normal 336 (0) 151 (94) 0 (177) 86 (112) 14 (166) Normal 336 (0) 191 (104) 146 (128) 38 (227) 3 (260) 6(2) Overweight 428 (0) 239 (72) 107 (112) 0 (191) Overweigh 0 (321) 128 (0) 303 (71) 225 (119) 55 (270) Obese (≥ 30 & < 35) 118 (26) 66 (46) 0 (96) (91 Obese (≥ 30 & < 35). 150 (27) 20 (124) 0 (144) 103 (52) Obese (≥ 35 73 (10) 0 (40) 33 (16) Obese (≥ 35 21 (65) 0 (84) 76 (18) 20 80 40 60 80 20 40 60 0 Time since diagnosis (months) Time since diagnosis (months)

1,120 multiple myeloma patients with diabetes in CoMMpass Registry

Severe obese vs. Normal: HR: 1.29; 95% CI: 0.99-1.67

Underweight vs. Normal: HR: 2.32; 95% CI: 1.09, 4.97 Severe obese vs. Normal: HR: 1.43; 95% CI: 0.98-2.08

# **Diabetes Mellitus and Risk of Myeloma**

10.5% of US population have diabetes mellitus; 34.5% of the adult US population have prediabetes



- DM ↑ risk of overall cancer, hematologic cancer and myeloma. Gong et al Diabetologia 2021; Dankner et al AJE 2016;
- DM ↑ risk of MGUS and myeloma within 6 months of diagnosis but not after. Maybe detection bias. Shah UA et al Haematologica 2021
- Metformin use for >4 years associated with a reduced risk of transformation of MGUS to MM. Chang et al. Lancet Haematol 2015

## **Dietary Patterns and Cancer**

France - French NutriNet-Santé cohort 42,544 adults Kane-Diallo, Int J Cancer 2018

- Higher plant-based dietary score associated with 15% lower risk of all cancers
- USA Adventist Health Study-2 69,120 people Tantamango-Bartley, Cancer Epidemiol Biomarkers Prev 2013
- Vegans had 16% less cancer than non vegetarians
- UK EPIC Oxford + Oxford Vegetarian Cohort 61,647 people Key, Am J Clin Nutr 2014
- Vegans had 19% less cancer than meat eaters.
- Vegetarians had 11% less cancer than meat eaters





Lee et al IJC 2020

EPIC Oxford + Oxford Vegetarian Cohort 61,647 people; 65 MM

 Vegans/vegetarians had 77% less multiple myeloma than meat eaters

Key, Am J Clin Nutr 2014

## **Fruits and Vegetable Intake and Cancer Risk**

- Prospective studies of fruit and vegetable intake and total cancer risk
- Fourteen studies
- Significant benefit for cruciferous vegetables & green-yellow vegetables.
- The USDA recommends 5-9 servings/day of fruits/vegetables.



https://www.cdc.gov/foodsafety/communication/steps-healthy-fruits-veggies.html

Aune et al. Int J Epidemiol 2017



International Journal of Epidemiology, 2017, 1029–1056 doi: 10.1093/ije/dyw319 Advance Access Publication Date: 22 February 2017 Original article



Miscellaneous

Fruit and vegetable intake and the risk of cardiovascular disease, total cancer and allcause mortality—a systematic review and doseresponse meta-analysis of prospective studies

Dagfinn Aune<sup>1,2,3</sup>\*, Edward Giovannucci<sup>4,5,6</sup>, Paolo Boffetta<sup>7</sup>, Lars T Fadnes<sup>8</sup>, NaNa Keum<sup>5,6</sup>, Teresa Norat<sup>2</sup>, Darren C Greenwood<sup>9</sup>, Elio Riboli<sup>2</sup>, Lars J Vatten<sup>1</sup> and Serena Tonstad<sup>10</sup>



# **Whole Grains and Cancer Risk**

- 640,065 participants and 34,346 cancer deaths Every 3 servings/day increase associated with
  - > 17% decrease in colorectal cancer risk
  - ➤ 15% decrease in total cancer mortality
- 1,575 participants and 174 colorectal cancer deaths Every 20 g/day increase associated with
  - > 18% decrease in cancer specific mortality

Aune et al, BMJ 2011 Aune et al, BMJ 2016 Song et al, JAMA Oncol 2017

Recommended daily intake









There is strong evidence that foods containing fiber decrease cancer risk... but **WHOLE GRAINS** offer much more than just **FIBER**:



- Source: AICR/WCRF. Diet, Nutrition, Physical Activity and Colorectal Cancer. 2017

1.0 0.8 0.8

stimated



For more information, visit www.aicr.org www. wholegrainscouncil.org





### **Carcinogenicity of Red and Processed Meat**

#### Carcinogenicity of consumption of red and processed meat

In October, 2015, 22 scientists from ten countries met at the International Agency for Research on Cancer (IARC) in Lyon, France, to evaluate the carcinogenicity of the consumption of red meat and processed meat. These assessments will be published in volume 114 of the IARC Monographs.<sup>1</sup> Red meat refers to unprocessed mammalian muscle meat-for example, beef, veal, pork, lamb, mutton, horse, or goat meat-including minced or frozen meat: it is usually consumed cooked. Processed meat refers to meat that has been transformed through salting, curing, fermentation, smoking, or other processes to enhance flavour or improve preservation. Most processed meats contain pork or beef, but might also contain other red meats, poultry, offal (eg, liver), or meat byproducts such as blood.

Red meat contains high biologicalvalue proteins and important micronutrients such as B vitamins, iron (both free iron and haem iron), and more than 200 g per person per day.<sup>4</sup> Less information is available on the consumption of processed meat.

The Working Group assessed more than 800 epidemiological studies that investigated the association of cancer with consumption of red meat or processed meat in many countries, from several continents, with diverse ethnicities and diets. For the evaluation. the greatest weight was given to prospective cohort studies done in the general population. High quality population-based case-control studies provided additional evidence. For both designs, the studies judged to be most informative were those that considered red meat and processed meat separately, had quantitative dietary data obtained from validated questionnaires, a large sample size, and controlled for the major potential confounders for the cancer sites concerned.

The largest body of epidemiological data concerned colorectal cancer. Data on the association of red meat

day of red meat and an 18% increase (95% Cl 1·10–1·28) per 50 g per day of processed meat.<sup>12</sup>

Data were also available for more than 15 other types of cancer. Positive associations were seen in cohort studies and population-based casecontrol studies between consumption of red meat and cancers of the pancreas and the prostate (mainly advanced prostate cancer), and between consumption of processed meat and cancer of the stomach. On the basis of the large amount of data and the consistent associations of colorectal cancer with consumption of processed meat across studies in different populations, which make chance, bias, and confounding unlikely as explanations, the majority of the Working Group concluded that there is sufficient evidence in human beings for the carcinogenicity of the consumption of processed meat. Chance, bias, and confounding could not be ruled out with the same



Upcoming meetings Feb 2–9, 2016, Volume 115: Some industrial chemicals; May 24–31, 2016, Volume 116: Coffee and some other hot beverages

#### IARC Monograph Working Group Members

B W Stewart (Australia)—meeting chair; S De Smet (Belgium); D Corpet, M Meurillon (France); G Caderni (Italy); S Rohrmann; P Verger (Switzerland); S Sasazuki, K Wakabayashi (Japan); M P Weijenberg (Netherlands);

#### MEAT AND CANCER HOW STRONG IS THE EVIDENCE?



# **Alkylating Signature in Colorectal Cancer**

- Whole-exome sequencing data from 900 colorectal cancer cases
- Alkylating mutational signature that was associated with red meat consumption



Gurjao et al. Cancer Discovery 2021

# **Mechanisms for Carcinogenicity of Meat**

- Alters gene signature (alkylator)
- Haem iron
- Lipid oxidation products
- Heterocyclic aromatic amines
- Polycyclic aromatic hydrocarbons
- N-Nitroso compounds
- Advanced glycation end products
- N-glycolylneuraminic acid
- No fiber, altered gut microbiome



### **Milk and Health**

#### The NEW ENGLAND JOURNAL of MEDICINE

#### **REVIEW ARTICLE**

Edward W. Campion, M.D., Editor

#### Milk and Health

Walter C. Willett, M.D., Dr.P.H., and David S. Ludwig, M.D., Ph.D.

From the Departments of Nutrition (W.C.W., D.S.L.) and Epidemiology (W.C.W.), Harvard T.H. Chan School of Public Health; Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School (W.C.W.); the Department of Pediatrics, Harvard Medical School (D.S.L.); and the New Balance Foundation Obesity Prevention Center, Boston Children's Hospital (D.S.L) — all in Boston.

N Engl J Med 2020;382:644-54.

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ILK PRODUCTS FROM COWS AND OTHER NONHUMAN MAMMALS ARE major components of traditional Western diets, especially in cold climates. The recommended intake of milk or equivalent portions of cheese, yogurt, or other dairy products in the United States is three 8-oz (237 ml) servings per day for adults and children 9 years of age or older, an amount that is substantially higher than the current average intake among adults of 1.6 servings per day.<sup>1</sup> The recommended intake amount has been justified to meet nutritional requirements for calcium and reduce the risk of bone fractures. However, the health benefit of a high intake of milk products has not been established, and concerns exist about the risks of possible adverse health outcomes. Therefore, the role of dairy consumption in human nutrition and disease prevention warrants careful assessment.

# Milk consumption correlates with cancer incidence, but this is not causation.



Ganmaa et al Med Hypoth 2005; Ganmaa et al IJC 2002; Willett et al NEJM 2020

### **Dairy and Hormonally Driven Cancers**



Jeyaraman et al. BMJ Open 2019

# Insulin like Growth Factor (IGF) 1 levels and Cancer Risk

The mean serum IGF-1 concentration was 13% lower in 92 vegan women compared with 99 meat-eaters and 101 vegetarians (P=0.0006)

#### Mean concentration of IGF-1 in EPIC cohort by dairy intake



#### Association between circulating IGF1 and cancer risk

| Variants       | Category                                   | Participants Ca/Co No. | No. of studies | OR (95% CI)      | Pa      |
|----------------|--|------------------------|----------------|------------------|---------|
| Overall effect |  | 14489/27061            | 63             | 1.15 (1.03–1.29) | 0.014   |
| Cancer site    | Prostate cancer                            | 5482/9415              | 21             | 1.24 (1.01–1.53) | 0.049   |
|                | Pre-menopausal breast cancer <sup>c</sup>  | 1525/2566              | 11             | 1.52 (1.23–1.88) | < 0.001 |
|                | Post-menopausal breast cancer <sup>c</sup> | 1142/1667              | 9              | 1.02 (0.78–1.34) | 0.885   |
|                | Colorectal cancer                          | 1909/3783              | 9              | 1.28 (1.02–1.61) | 0.031   |
|                | Endometrial cancer                         | 808/884                | 5              | 0.68 (0.43-1.06) | 0.376   |
|                | Lung cancer                                | 886/1841               | 5              | 0.96 (0.55-1.69) | 0.885   |
|                | Ovarian cancer                             | 627/1358               | 4              | 0.93 (0.51–1.67) | 0.799   |
|                | Pancreatic cancer                          | 374/1242               | 3              | 0.87 (0.57-1.33) | 0.507   |
|                | Other cancers                              | 1736/4305              | 5              | 0.92 (0.48-1.72) | 0.783   |
|                |  |                        | Chen et al l   | -<br>Eu I Hum Ge | n 2000  |

#### **Elevated IGF-1 levels increase cancer risk by 15%**



Weroha et al Endocr Metab Clin 2013

### **African American Diet vs Rural African Diet**

2-week diet switch in healthy middle aged

#### 20 African Americans 20 Rural Africans





Figure 1. Colonic Mucosal Immunohistochemistry of Proliferative and Inflammatory Biomarkers

### **Gut Microbiome in Humans**



### **Diet Rapidly and Reproducibly Alters the Gut Microbiome**

9 individuals. 5 days on each diet – plant-based and animal-based. Meals were provided.



Plant based diets increase healthy gut bacteria and stool butyrate concentration



David et al. Nature 2014

### Nitrogen Recycling Bacteria Accelerate MM Progression



Jian et al. Microbiome 2020

#### **Stool Butyrate Producers and Outcomes**



# How Many Different Plant Foods Do You Eat in a Week?

Stool samples from >10,000 individuals

>30 plant foods associated with

- ↑ Diversity
- ↓ Antibiotic resistance genes
- ↑ Conjugated linoleic acid abundance (polyunsaturated fatty acid with anti cancer and fat reducing properties)



McDonald et al mSystems 2018

### **Factors That Affect Immune Response**

#### **Non-Modifiable Factors**

Age Gender Race/Ethnicity Genetics Infections Vaccination Medical Conditions Cancer Rural/Urban Environment

#### **Modifiable Factors**

Nutrition/Dietary Patterns Obesity Diabetes Mellitus Microbiome Physical Activity Sleep Stress Smoking/Alcohol/Drugs Medications

# **Dietary Patterns Affect the Immune System**



### **Diet and COVID19 Severity**

Table 2Dietary intake of healthcare workers stratified by<br/>self-report of following plant-based diet among COVID-19<br/>cases  $(n=568)^*$ 

|                                       | Followed<br>plant-base<br>diet (n=41) | d plant-based<br>diet (n=527) | P value |  |  |  |  |
|---------------------------------------|---------------------------------------|-------------------------------|---------|--|--|--|--|
| Dietary intake, times/week (mean, SD) |                                       |                               |         |  |  |  |  |
| Total fruits                          | 9.8 (6.4)                             | 8.5 (6.5)                     | 0.23    |  |  |  |  |
| Total vegetables                      | 14.5 (8.7)                            | 10.4 (7.1)                    | <0.001  |  |  |  |  |
| Potatoes                              | 2.1 (1.9)                             | 2.1 (1.8)                     | 0.90    |  |  |  |  |
| Legumes                               | 3.7 (2.9)                             | 1.9 (1.6)                     | <0.001  |  |  |  |  |
| Nuts                                  | 3.5 (2.6)                             | 2.3 (2.9)                     | 0.01    |  |  |  |  |
| Refined grains                        | 7.5 (5.5)                             | 8.6 (5.2)                     | 0.17    |  |  |  |  |
| Dark or whole grain breads            | 2.5 (2.2)                             | 2.2 (2.5)                     | 0.55    |  |  |  |  |
| Sweets and desserts                   | 5.8 (5.8)                             | 6.8 (6.9)                     | 0.35    |  |  |  |  |
| Eggs                                  | 2.0 (1.8)                             | 2.3 (1.9)                     | 0.30    |  |  |  |  |
| Dairy                                 | 12.9 (9.1)                            | 13.3 (7.9)                    | 0.73    |  |  |  |  |
| Poultry                               | 1.2 (1.5)                             | 2.3 (1.6)                     | <0.001  |  |  |  |  |
| Red and processed meats               | 1.3 (2.3)                             | 3.8 (2.8)                     | <0.001  |  |  |  |  |
| Fish and seafood                      | 2.5 (2.7)                             | 3.1 (2.6)                     | 0.12    |  |  |  |  |
| Soups                                 | 1.4 (1.7)                             | 1.4 (1.4)                     | 0.78    |  |  |  |  |
| Croquettes, dumplings, pizza          | 0.8 (0.8)                             | 1.0 (1.0)                     | 0.14    |  |  |  |  |
| Sugar-sweetened beverages             | 1.1 (2.1)                             | 2.5 (3.4)                     | 0.01    |  |  |  |  |
| Fruit juices                          | 0.4 (0.9)                             | 1.0 (1.9)                     | 0.06    |  |  |  |  |
| Vegetable oil                         | 3.6 (3.3)                             | 3.8 (3.2)                     | 0.67    |  |  |  |  |
| Butter                                | 1.4 (2.0)                             | 1.9 (2.3)                     | 0.15    |  |  |  |  |
| Alcohol                               | 2.2 (3.0)                             | 3.7 (4.3)                     | 0.03    |  |  |  |  |
| Coffee                                | 6.5 (5.1)                             | 7.7 (6.8)                     | 0.27    |  |  |  |  |
| Теа                                   | 1.9 (2.5)                             | 2.1 (3.6)                     | 0.68    |  |  |  |  |

In 2884 front-line healthcare workers from six countries (France, Germany, Italy, Spain, UK, USA) Individuals on plant-based diets higher in vegetables, legumes and nuts, and lower in poultry and red and processed meats, had 73% lower odds of moderateto-severe COVID-19



Kim et al BMJ NPH 2021

# **Diet and COVID19 Severity**

592,571 participants - smartphone-based COVID-19 Symptom Study (UK and USA)

31,815 COVID-19 cases were documented

hPDI: healthful Plant-Based Diet Index.

Healthy plant-based diet was associated with lower risk and severity of COVID-19.



Merino et al. BMJ Gut 2021

### **Evidence Behind Plant-based and Ketogenic Diets**

Figure. Association of Plant-Based Diets With Multiple Additional Pathways That Suppress Cancer Growth Compared With Ketogenic Diets



Currently, there are 46 KD trials (20 active, 10 completed, 6 terminated [poor accrual/compliance]; 5 with unknown status) and only 8 WFPBD trials (6 active, 2 completed, and 0 terminated)

Shah UA et al. JAMA Oncol 2022

# **Dietary Interventions in Cancer**

#### Prevention

**Dietary therapies as backbone** 

Reducing the risk of development of a primary or secondary cancer.

Prevent other medical problems and cancers.



#### Treatment

Synergy with

- Checkpoint inhibitors
- Bispecific antibodies
- CAR T cells
- Monoclonal antibodies
- Vaccines
- Immunomodulatory drugs
- Chemotherapies

Fewer comorbidities means fewer side effects and ability to give full dose treatment.

#### Survivorship

In combination with maintenance therapy or as single agent

Decreasing the likelihood of a relapse once in remission.

Reduce the risk of other medical problems and cancers.

Given early detection, as hematologists and oncologists, we have an Opportunity for Secondary Prevention



### **Tilting the Scale for Myeloma Development**

In the US population, 70% have an elevated BMI and 45% are prediabetic/diabetic Additionally, ≥3% of the population ≥50 years has MGUS/SMM MGUS/SMM with an elevated BMI are twice as likely to progress to MM



# **NUTRIVENTION Trial**



# **Demographics and Compliance**

| Median Age, years        | 62 (40-79) |
|--------------------------|------------|
| Sex                      |            |
| Male                     | 43%        |
| Female                   | 57%        |
| Race                     |            |
| Non-Hispanic White       | 57%        |
| Black/Other/Hispanic     | 43%        |
| Diagnosis                |            |
| MGUS                     | 52%        |
| SMM                      | 48%        |
| BMI Category             |            |
| Overweight (BMI 25-29.9) | 26%        |
| Obese 1 (BMI 30-34.9)    | 35%        |
| Obese 2 (BMI 35-39.9)    | 22%        |
| Obese 3 (BMI 40+)        | 17%        |
| Diabetes/Prediabetes     |            |
| Yes                      | 26%        |
| No                       | 74%        |

- 3 patients dropped out during 12-week intervention and were replaced.
- 2 patients were lost to follow up after 12 weeks and were not replaced.
- 18 patients are on track to complete the study so far.
- Meets its feasibility endpoint (adherence >70% at 12 weeks)
- Patients were eating to satiety with no calorie restriction
- Median calorie reduction from baseline to 12 weeks: 511 calories.





Shah UA et al ASH 2022

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# **Metabolic and Microbiome Results**

| Biomarker                                | Median change % 12 weeks |
|--|--------------------------|
| BMI (feasibility)                        | -7.4% ↓                  |
| Elevated HgbA1c (>5.7%)                  | -10% 🗸                   |
| Elevated LDL cholesterol (>100 mg/dL)    | -18% 🗸                   |
| Insulin                                  | -8% 🗸                    |
| IGF-1 (ng/mL)                            | -12% 🗸                   |
| Relative abundance of butyrate producers | 90% 个                    |
| Stool butyrate                           | 25% 个                    |

- Meets its weight loss feasibility endpoint (BMI reduction >5% at 12 weeks)
- Higher adiponectin leptin ratio implies less insulin resistance.
- Low adiponectin, high leptin, high insulin and high IGF-1 are associated with myeloma progression.



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# **NUTRIVENTION-3 Trial is Enrolling**

Q: Impact of dietary vs supplementary vs placebo interventions on the microbiome especially butyrate production in MGUS and SMM patients



• To also open at Emory in 2023 (site PI: Nisha Joseph, MD)

Shah UA et al. ASH 2022

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# **Dietary Synergism with Conventional Therapies**

#### Treatment

#### Synergy with

- Checkpoint inhibitors
- **Bispecific antibodies**
- CAR T cells
- Monoclonal antibodies
- Vaccines
- Immunomodulatory drugs
- Chemotherapies

Fewer comorbidities means fewer side effects and ability to give full dose treatment.



Additive or synergistic activity of diet with standard of care?

#### Improved

- MRD Negativity?
- PFS?
- OS?
- Quality of Life?

### **IDEAL Trial in Acute Lymphoblastic Leukemia**

- 40 patients
- Prospective, nonrandomized
- NCT02708108
- 20% caloric deficit 10% reduced calorie intake and 10% increased exercise
- 28 days during cycle 1
- Primary endpoint: % change in fat mass during induction



### **Dietary Fiber and Probiotics in Melanoma**

- 128 patients
- Melanoma on immune checkpoint blockers
- High dietary fiber without probiotics
- Improved PFS



Spencer et al. Science 2021

## **Dietary Interventions to Improve Survival**

#### Survivorship

In combination with maintenance therapy or as single agent

Decreasing the likelihood of a relapse once in remission.

Reduce the risk of other medical problems and cancers.



# **Diet, Microbiome and Sustained MRD Negativity**



Shah UA et al. Clin Can Res 2022

# **Diet & Microbiome Correlate with Sustained MRD Negativity**



Shah UA et al. Clin Can Res 2022

### Hypothesis and Mechanisms for this Correlation



Enrolling at MSK (NYC) - NCT04497961 Primary Endpoint: Quality of Life

### **The Fiber Gap**

Recommended Daily Intake: 30 grams from food sources (only plants)

#### **THE FIBER GAP**

67% consumers believe they meet their fiber needs (International Food Information Council)

#### In reality, only 5% do so! (2009-2010 NHANES survey data)



Desai et al Cell 2016

### **Some Practical Dietary Tips to Consider Incorporating**

#### **Carbohydrates** $-\uparrow$ whole, unrefined

- ↑Whole grains (>3 servings/day)
- Unprocessed/refined carbs/foods
- ↓↓Sugary foods/drinks
- ↑Fiber (>30 grams/day)
- ↑ Fruits/Vegetables (>5-6 servings/day)
- ↑Diversity of plant foods (>30 types/week)
   Protein Plant >> Animal sources
- ↑Beans/Tofu/Tempeh
- ↓Red/processed meats

#### Fats – ↑ Unsaturated fats

- ↑Nuts/Seeds, fish, olive oil, avocados
- ↓Fried foods
- ↓Dairy/Cheese
- Regular omega 3 fatty acids
- Vitamin D (>30 ng/mL)
- Calorie counting and calorie restriction are difficult to sustain long term
- Meal planning and preparation in advance
- Regular mealtimes not waiting until one is starving
- Ensure adequate hydration
- Learning to read ingredient lists and nutrition labels
- Gradual changes are more sustainable
- Making healthy swaps
- Make it a lifestyle and not a diet

## **Diet and Kidney Disease (National Kidney Foundation)**



#### **PROCESSED MEATS** Ρυτ Δ strain on YOUR KIDNEYS AND YOUR LIFE. THAT'S NO



So give your kidneys a boost with Meatless Monday and replace deli meats with veggie protein instead.



National Kidney Foundation\* MeatlessMonday.com

#### PLANT-BASED DIET AND KIDNEY HEALTH

Eating more plant-based foods such as vegetables and grains in place of animal-based foods such as red meat may help prevent and slow the progression of chronic kidney disease, Type 2 diabetes, high blood pressure, and heart disease.



#### **The Benefits of Plant-Based Diets on Kidney** Health

Studies show that eating whole grains, nuts, fruits and vegetables is one of the most important ways to keep kidneys healthy.

- The Right Foods Help Keep You Healthy and Fight Chronic Disease
- Plant Based Diets Help Prevent Kidney Disease for People with Type 2 Diabetes
- 10 Common Habits That May Harm Your Kidneys
- Plant-Based vs. Animal-Based Diets: The Jury is in!

#### A Guide to Plant-Based Diets

Starting a plant-based diet does not mean that you need to become a vegetarian and cut all sources of animal protein from your diet.

- What is a Plant-Based Diet, and Is It Good for Your Kidnevs?
- The Beginner's Guide to Starting a Plant-**Based** Diet
- Plant-Based Diet or Vegetarian Diet What is the Difference?
- How to Stock a Plant-Based Pantry
- · Myths and Misconceptions About Plant-Based Diets

#### The Role of Plant-Based **Diets for Patients With Kidney Disease**

With guidance from a registered dietitian nutritionist (RDN), a carefully planned plantbased diet may be helpful in the setting of kidney disease, depending on a patient's specific needs.

- How Much Plant-Based Protein Can You Eat Based on Your Stage of Kidney Disease?
- Breaking Down Dietary Protein: What is it?
- Maintaining a Vegetarian Diet with Kidney Disease

https://www.kidney.org/atoz/content/plant-based

#### Understanding calorie density instead of calorie counting



#### Plant based diets can be many of many varieties

#### VEGAN

Zero animal products.

Ethical and environmental reasons.

No meat, fish, eggs, dairy.

Doesn't have to be healthy.

#### **VEGETARIAN**

Some animal products.

Ethical or religious reasons.

No meat or fish. Eggs and dairy allowed.

Doesn't have to be healthy.

#### WHOLE FOODS PLANT BASED

Minimal animal products.

Health reasons.

Focus on whole foods & mainly plants, avoids processed foods.

Healthy.



Whole Food Plant-based Vegan Whole Food Plant-based Vegetarian Whole Food Plant-based Pescatarian Whole Food Plant-based Mediterranean Whole Food Plant-based Paleo Whole Food Plant-based Low Carb Whole Food Plant-based Keto

### Conclusions



### **Nutrition and Wellness Chapter with HealthTree Foundation**



#### In collaboration with HealthTree Foundation

#### **NUTRIVENTION-2 Trial to Open This Year**



#### HealthTree Telehealth Randomized Study

Castro F et al. ASH 2022

#### Surveys through the HealthTree Foundation

### **Please Consider Participating in Dietary Survey Research**

#### **Racial Differences in Dietary Patterns**

#### **Study Question:**

In patients with plasma cell disorders, are there significant differences in diet between racial groups?

#### **Study Population:**

Individuals with plasma cell disorders

#### Method:

30-minute Block Food Frequency Questionnaire



#### **Supplement Use and Perceptions**

#### **Study Question:**

Since being diagnosed, what changes have plasma cell disorder patients made to their supplement use habits of Vitamin D, Omega 3 Fatty acids, Turmeric/Curcumin and probiotics?

#### **Study Population:**

Individuals with plasma cell disorders

#### Method:

15-minute survey



# Interested in Participating in a NUTRIVENTION Trial?



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CLETY OF THE RICH





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Patients with plasma cell disorders