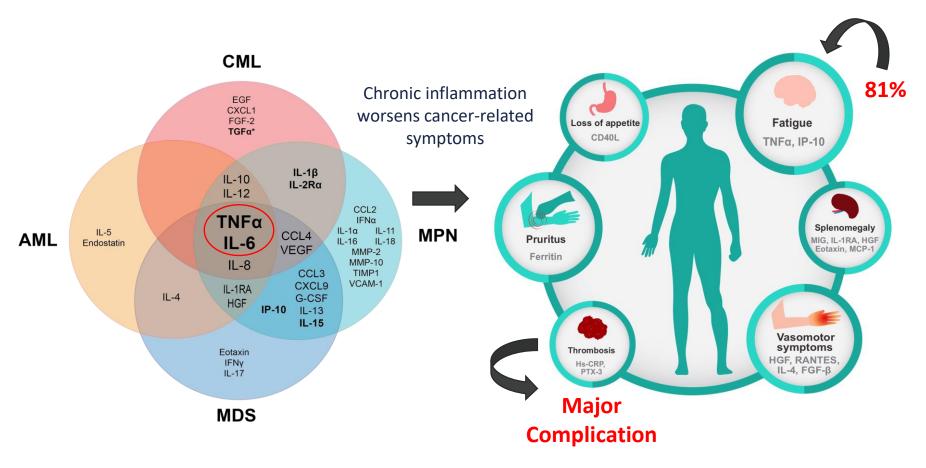
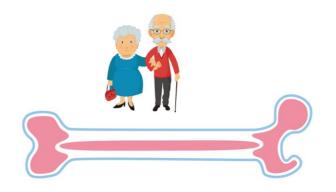


# Inflammatory cytokines correlate with symptom burden and a worse prognosis



## **Challenges of treatment in MPN**

- Impact of physical symptoms is under-recognized
- Most therapies focus on blood counts
- Treated with "watch and wait" management
- All patients undergo antiplatelet therapy (thrombosis)
- FDA approved drugs for MF: JAK inhibitors



**Definite cure:** bone marrow transplant

Significant Risks of Transplant

- Symptom burden has a major impact on the quality of life of MPN patients
  - Need to focus on identifying therapies for managing symptoms
- In addition to preventing disease progression



## **Anti-inflammatory diet: Mediterranean Diet**

 The Mediterranean diet has proven to be beneficial in metabolic diseases, which are characterized by chronic subclinical inflammation.



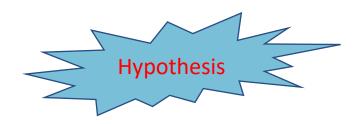
## Primary Prevention of Cardiovascular Disease with a Mediterranean Diet

Ramón Estruch, M.D., Ph.D., Emilio Ros, M.D., Ph.D., Jordi Salas-Salvadó, M.D., Ph.D.,
Maria-Isabel Covas, D.Pharm., Ph.D., Dolores Corella, D.Pharm., Ph.D., Fernando Arós, M.D., Ph.D.,
Enrique Gómez-Gracia, M.D., Ph.D., Valentina Ruiz-Gutiérrez, Ph.D., Miquel Fiol, M.D., Ph.D.,
José Lapetra, M.D., Ph.D., Rosa Maria Lamuela-Raventos, D.Pharm., Ph.D., Lluís Serra-Majem, M.D., Ph.D.,
Xavier Pintó, M.D., Ph.D., Josep Basora, M.D., Ph.D., Miguel Angel Muñoz, M.D., Ph.D., José V. Sorlí, M.D., Ph.D.,
José Alfredo Martínez, D.Pharm, M.D., Ph.D., and Miguel Angel Martínez-González, M.D., Ph.D.,
for the PREDIMED Study Investigators\*

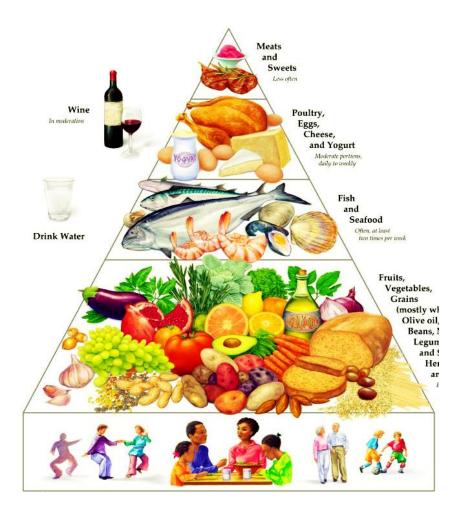
 Among persons at high cardiovascular risk, a Mediterranean diet supplemented with EVOO or nuts reduced the incidence of major cardiovascular events, as well as hsCRP and IL-6 levels (P= 0.005).

## **Properties of the Mediterranean Diet**

- Fiber
- Resveratrol
- Mono-unsaturated fatty acids



Following a Mediterranean dietary pattern might reduce inflammatory cytokines in MPN patients thus relieving their symptom burden and may also blunt disease trajectory



Avocados are naturally FULL of nutrition, so there's no need for special labels. They're full of flavor; think of all the meals you can healthify with avocado!

#### HEALTH TIP!

Avocados are one of the only fruits that contain heart healthy monounsaturated fat (the good-for-you fat) that helps boost good (HDL) cholesterol and lowers bad (LDL) cholesterol.



Healthy Diet Basics



Anti-aging tool for your skin!



## Recipe:

#### Directions:

1. In a bowl combine the kale, olive oil, juice of 1/4 lemon and 1/8 teaspoon salt

2. Massage with your hands for about 1 minute, until the kale

3. Slice the avocado in half, reserving 1/2 of one avocado for thin slice. Scoop the rest into a small bowl and mash gently with a fork. Season with 1/8 tbs kosher salt, black pepper and juice from 1/4 of a lemon.

4. Toast the slices of whole wheat bread

5. Spread the avocado mash across the toasted bread, top with slices and sprinkle with cumin, salt and pepper (more lemon juice if desired)

6. Top each with the massaged kale, radish and chia, finish with pinch salt and black pepper to taste

#### Avocado Toast with Lemon and Kale

#### You will need:

- 1 cup shredded kale (no stems)
- 1/2 lemon
- 1 teaspoon olive oil
- 4 slices multigrain bread, 4 oz total
   kosher salt and black pepper
   4 ounces avocado (1 small haas)
- 1/8 teaspoon cumin
- 4 thin slices radish
- 1 tea spoon chia seeds

All images and text @Gina Homolka for Skinnytaste



### Healthy Diet for MPN Patients

The food pyramid is a great guide to good nutrition. So if you're not sure your eating the fruits and vegetables that you need, take a glance at the bright stripes of the food pyramid - they'll help keep you on track to make sure you're achieving your nutrition goals.

#### Fats, oils, Sparingly sweets 2-3-Meat, poultry, fish, dry beans, servings eggs, nuts yogurt, daily Fruits 2-4 servings 3-5 servings Breads, cereal, rice, pasta 6-11 servings

Following the Food

**Pyramid** 

Grain group: choose at least 3 that are whole grain

dried beans and peas, and fish Oils: choose mono- and polyunsaturated oils Discretionary calories: an allotment of 100 to 300 calories can be used on foods with fats or sugars, like dessert

 Vegetable group: include green and orange
 Fruit group: choose a variety of fruits of different colors Milk group: yogurt, milk and cheese (low-fat or fat-free

Meat and beans group: lean meats, chicken, eggs, nuts,

**Fact** 

#### Week 1

Healthy Diet Basics



#### **FOOD PYRAMID:** Portion Size

- · One-ounce equivalent or serving of grains: one-half cup cooked pasta, rice, or cereal; one bread slice; or one cup dry cereal
- One serving of vegetables: one-half cup vegetable juice, one-half cup cut vegetables or one cup of raw leafy vegetables (such as spinach or salad)
- One serving of fruit: one-half cup fruit juice, one piece of medium-sized fruit (like an orange apple, or banana), one-half cup cut fruit, or onequarter cup dried fruit
- One cup equivalent of milk: one cup yogurt or milk, 1 1/2 ounces low-fat or fat-free natural cheese, or 2 ounces processed or packed cheese
- One ounce equivalent of meat or beans: onequarter cup cooked beans; one tablespoon peanut butter or other nut butter; one egg; one ounce cooked meat, chicken, or fish
- One serving of oil: one teaspoon any vegetable oil, one tablespoon low-fat mayo, or two tablespoons light salad dressing





### Tips for saving leftover avocado

- To store unused 1/2 of avocado, wrap tightly with plastic wrap and place in
- Leave the pit in and get the wrap as close to the surface of the fruit as
- If browning occurs, gently scrape the exposed flesh with a butter knife.





Symptom	1 to 10 (0 if absent) ranking 1 is most favorable and 10 least favorable
Di Cal /	

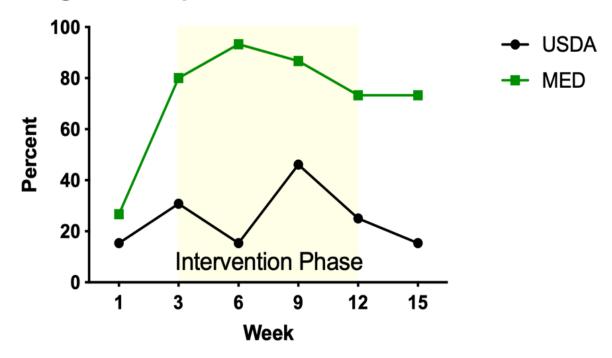
Please rate your fatigue (weariness,

Questions	Criteria for 1 point
1. Do you use olive oil as main culinary fat?	Yes
2. How much olive oil do you consume in a given day (including oil used for frying, salads, out-of-house meals, etc.)?	≥4 tbsp
3. How many vegetable servings do you consume per day? (1 serving : 200 g [consider side dishes as half a serving])	≥2 (≥1 portion raw or a a salad)
4. How many fruit units (including natural fruit juices) do you consume per day?	≥3
5. How many servings of red meat, hamburger, or meat products (ham, sausage, etc.) do you consume per day? (1 serving: 100–150 g)	<1
6. How many servings of butter, margarine, or cream do you consume per day? (1 serving: 12 g)	<1
7. How many sweet or carbonated beverages do you drink per day?	<1
8. How much wine do you drink per week?	≥7 glasses
9. How many servings of legumes do you consume per week? (1 serving : 150 g)	≥3
10. How many servings of fish or shellfish do you consume per week? (1 serving 100–150 g of fish or 4–5 units or 200 g of shellfish)	≥3
11. How many times per week do you consume commercial sweets or pastries (not homemade), such as cakes, cookies, biscuits, or custard?	<3
12. How many servings of nuts (including peanuts) do you consume per week? (1 serving 30 g)	≥3
13. Do you preferentially consume chicken, turkey, or rabbit meat instead of veal, pork, hamburger, or sausage?	Yes
14. How many times per week do you consume vegetables, pasta, rice, or other dishes seasoned with sofrito (sauce made with tomato and onion, leek, or garlic and simmered with olive oil)?	≥2
doi:10.1371/journal.pone.0043134.t001    months   (Aosent) 0 1 2 3 4 3 6 7 8 9 10 (Worst Imagmatile)	



# Adherence among MPN patients to a Mediterranean dietary pattern

Percentage of Partcipants with Med Adherence Score ≥ 8

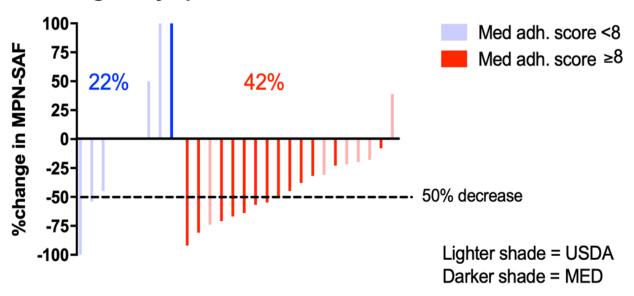


Mediterranean adherence score increased over time in both cohorts



# Reduction in symptom burden by adhering to a Mediterranean Diet

### Change in symptoms week 9 vs baseline



Comparing to COMFORT-I study: ruxolitinib decrease MPN-SAF by  $\geq$  50% in 46.1% and placebo decreased MPN-SAF by  $\geq$  50% in 5.3%



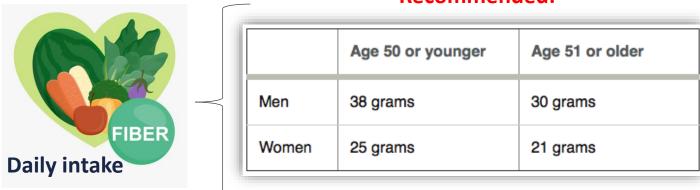
## **Specific Mediterranean Diet components**

- ASA24® (24-hour food recall) nutrition profile
- Reports:
  - Daily calories
  - Daily food group targets
  - Nutrients
  - Saturated fat
  - Added sugars
  - Alcohol
  - Sodium

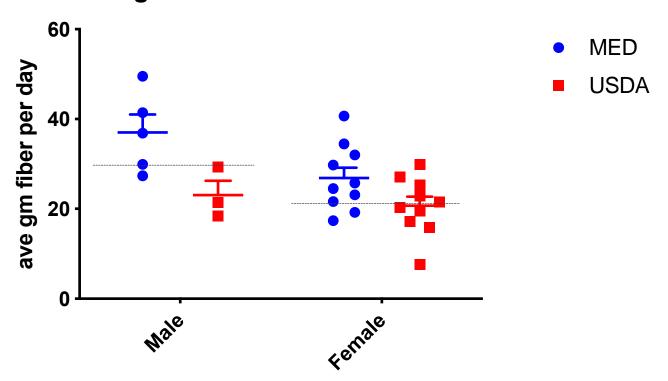
Nutrients	Target	Actual Eaten	Status
Calcium (mg)	1200	372	Under
Carbohydrate (g)	130	191	ОК
Cholesterol (mg)	No Daily Target	0	ОК
Choline (mg)	425	156	Under
Copper (mg)	0.9	1.9	ОК
Folate (µg DFE)	400	518	ОК
Iron (mg)	8	10	ОК
Linoleic Acid (g)	11	15	ОК
Magnesium (mg)	320	358	ОК
Niacin (mg)	14	13	Under
Phosphorus (mg)	700	707	ОК
Potassium (mg)	4700	3267	Under
Protein (g)	46	26	Under
Riboflavin (mg)	1.1	1	Under
Saturated Fat (% kcal)	No Daily Target	6	ОК
Selenium (µg)	55	31	Under
Sodium (mg)	No Daily Target	1827	ОК
Thiamin (mg)	1.1	1	Under
Total Fat (% kcal)	20	41	OVER
Total Fiber (g)	21	37	ОК
Vitamin A (µg RAE)	700	722	ОК
Vitamin B12 (µg)	2.4	0	Under
Vitamin B6 (mg)	1.5	1.9	ОК
Vitamin C (mg)	75	167	ОК
Vitamin D (μg)	15	0	Under
Vitamin E (mg AT)	15	12	Under
Vitamin K (μg)	90	309	ОК
Zinc (mg)	8	6	Under





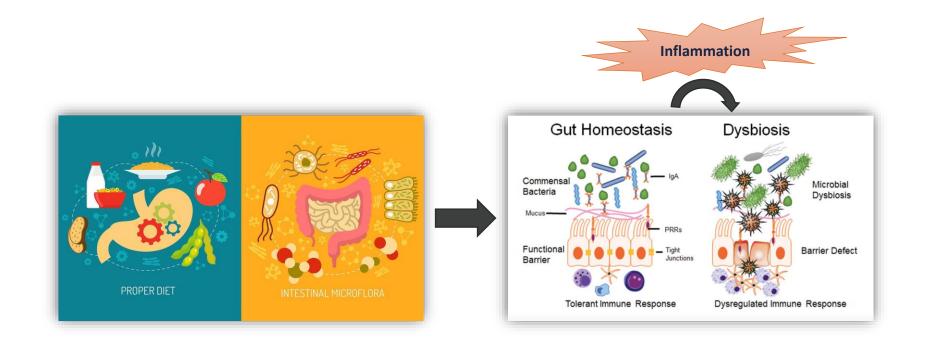


## Fiber intake during weeks 3-12 med/usda next to each other





# Microbiome: fairly unexplored field in MPN



Interested in how the Mediterranean diet might influence the microbiome of MPN patients



## **Methods**

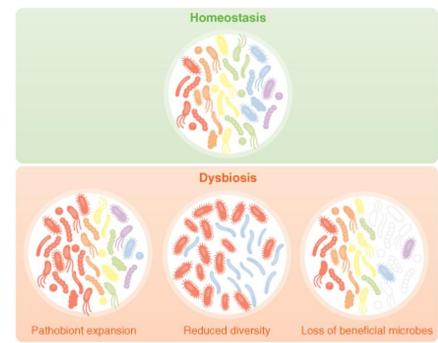
#### **Established collaboration with Whiteson Lab**





RNA/DNA shield fecal collection tubes

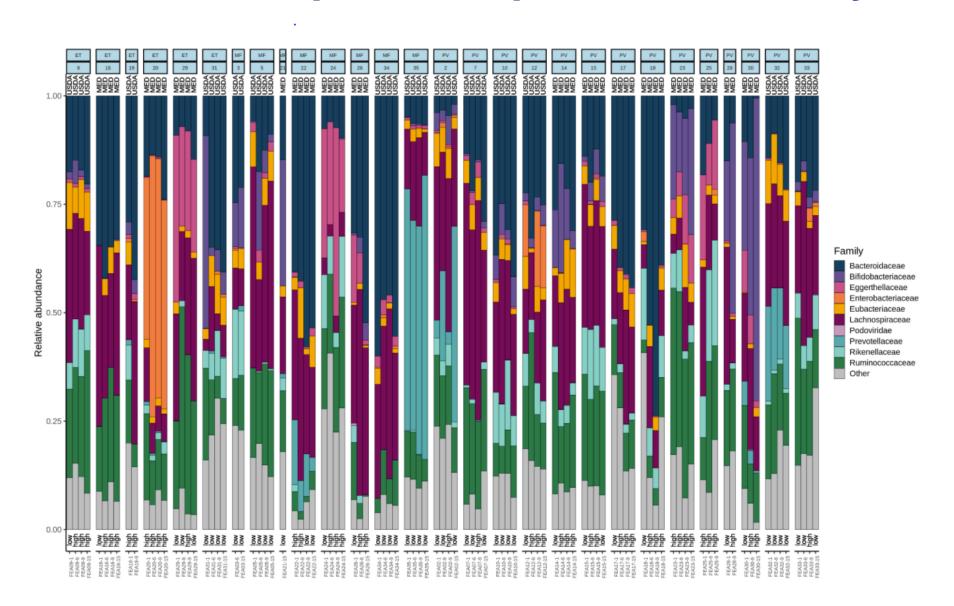




Changing the intestinal microbiota through an anti-inflammatory diet (Med diet) might increase the overall bacterial diversity in the MPN gut microbiome



# Microbiome profile of patients on study



## **Work in Progress**

- Measurement of inflammatory biomarkers
- Microbiome analysis
- Testing the role of different diets in animal MPN models

## **Acknowledgments**



- Laura Mendez Luque
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