

# Anti-cancer efficacy of select phytonutrient mixture in Fanconi Anemia head and neck squamous cell carcinoma (HNSCC)

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# Fanconi Anemia (FA): definition

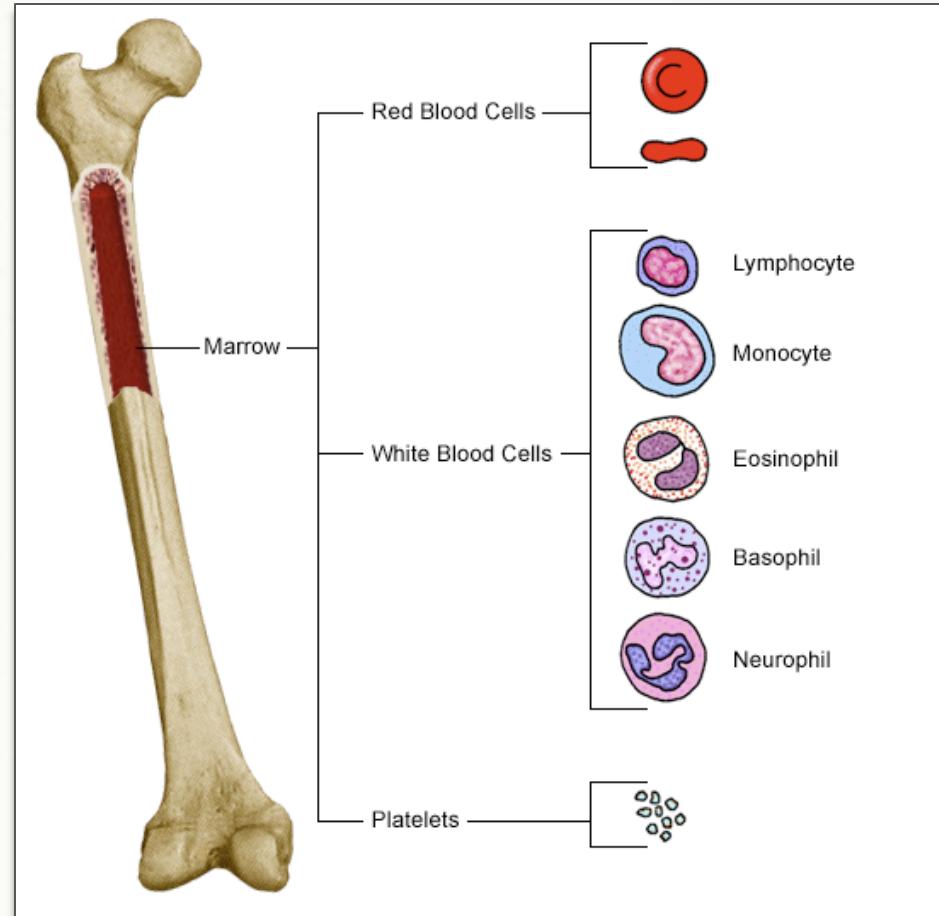
- Inherited blood disease
- Linked to 13 genes
- Can lead to
  - Bone marrow failure
  - Cancer, caused by a mutation of the FANC genes
  - High susceptibility to head & neck cancer
- Life expectancy: 20-30 years



# Healthy Bone Marrow

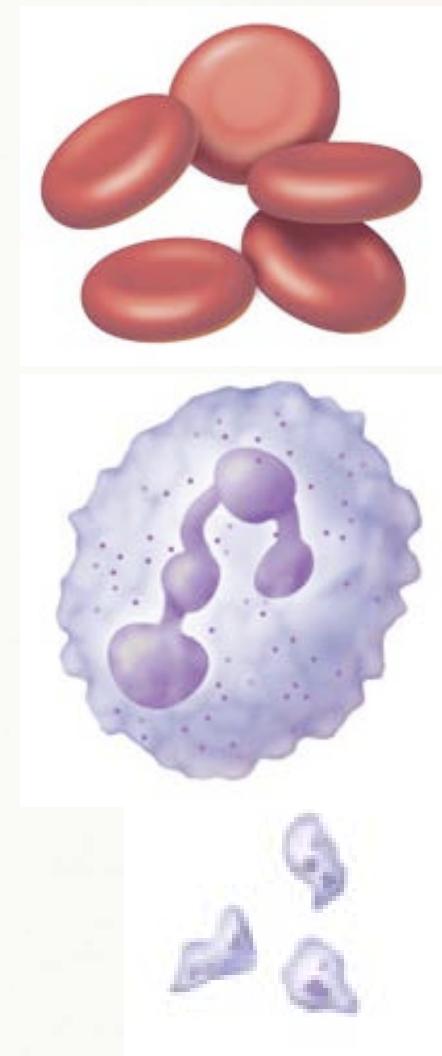
Contains stem cells that develop into:

- 1) Red blood cells:  
carry oxygen to all parts of the body & remove carbon dioxide
  
- 2) White blood cells:  
fight infections
  
- 3) Platelets:  
help the blood clot



# Health consequences of dysfunctions

- Red blood cells: body's tissues won't get enough oxygen to work well.
- White blood cells: the body will have problems fighting infections
- Platelets: the blood can't clot normally  
    > bleeding problems



# Symptoms FA

- Abnormal heart, lungs
- Bone problems (spine/hips/ ribs, short stature, missing radius bone)
- Abnormal arms / hands (missing or extra thumb, missing bones in the arm or hand)
- Skin discolorations (cafe au lait, hypo pigmented spots and hyperpigmented spots)
- Kidney problems (kidneys did not form correctly)
- Gastrointestinal problems (bowel issues)
- Small reproductive organs in males

# Skin discolorations

- Cafe-au-lait spots



# Skeletal anomalies: missing radius bone



# FA population & Head & Neck Cancer

***Table 1: Summary of the characteristics of HNSCC in the FA population***

	<b>FA-associated HNSCC</b>	<b>Non-FA HNSCC</b>
Cumulative incidence by age 40 years	14%*	0.038%
Age of presentation (median)	31 years	53 years
Tobacco and alcohol use	16%	>85%
Primary tumor site	Oral cavity: 65% Oropharynx: 10% Hypopharynx: 10% Larynx: 10% Unknown: 5%	Oral cavity: 27% Oropharynx: 24% Hypopharynx: 8% Larynx: 41%
Development of secondary primary tumors	63%	15%
2 year overall survival	49%	70%
Standard treatment	Surgery	Surgery, Radiation, Chemotherapy

# Treatment Head & Neck cancer in Fanconi Anemia patients: Conventional medicine

- ⌚ Surgery
- ⌚ Radiation therapy
- ⌚ Chemotherapy



# Current study - Objective

Investigate the Antineoplastic\* activity of a phytonutrient mixture on human Fanconi Anemia head and neck squamous cell carcinomas.

Nutrient mixture (PB): Quercetin, Curcumin, EGCG from green tea, cruciferex (cruciferous plants extract), resveratrol

\*Antineoplastic = *Acting to prevent, inhibit or halt the development of a neoplasm (tumor)*

# A: In Vivo Studies

- Male athymic mice (12):

*Athymic mouse = a laboratory animal without T-cells (type of white blood cells), useful in research because they do not reject tumor cells transplanted from mice/humans or other species.*

- Experimental design:

- Week 1: inoculated with cancer cells
- 2 groups: group 1 regular diet, group 2 regular diet + 1% nutrient mixture.
- Week 5: mice were sacrificed, their tumors processed for histology.

## B: In Vitro studies

- Human Cell Lines:
  - Human Head & neck squamous cell carcinomas (HNSCC) were grown in tissue culture plates
  - Cells were treated in triplicate with different concentrations of the nutrient mixture (PB): 0, 10, 25, 50, 75 and 100  $\mu\text{g}/\text{ml}$

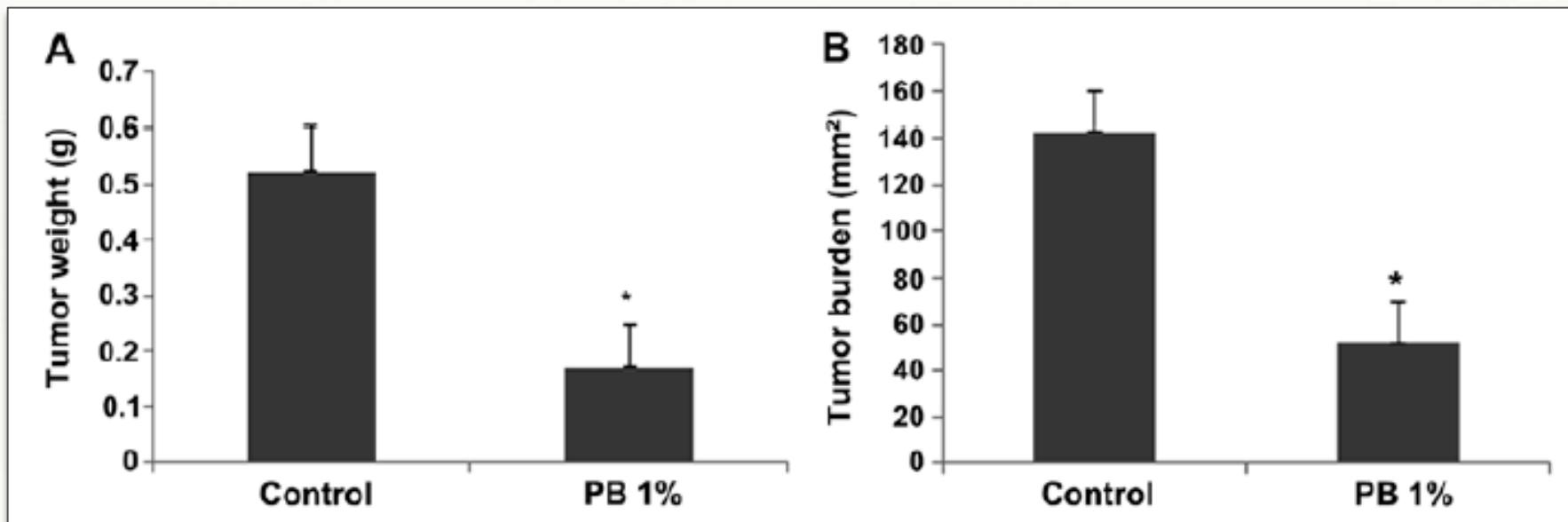
# Results: In vivo studies (mice)

- Dietary intake of the nutrient mixture can suppress tumor growth in mice in comparison with control group (standard diet)



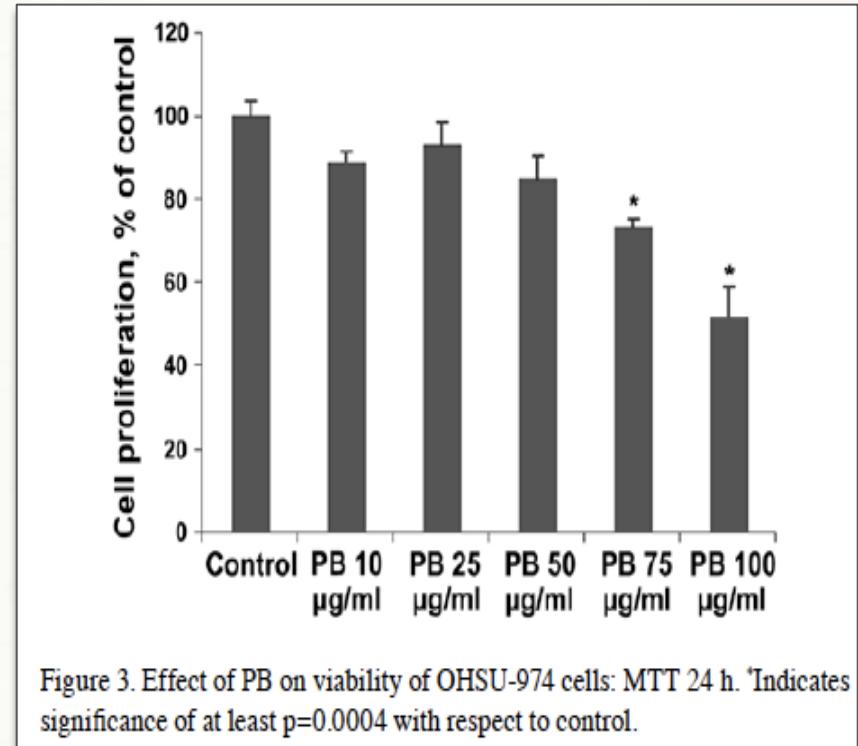
# Suppression of tumor growth by PB

- Mean tumor weight was inhibited by 67.6 % with dietary supplementation
- Tumor burden was inhibited by 63.3 %
- Tumors from supplemented mice: significantly smaller



# Decreased cancer cells growth: in vitro

- Inhibition of cell proliferation in a dose-dependent manner
- 48 % inhibition of cell growth in cells exposed to 100  $\mu\text{g}/\text{ml}$  nutrient mixture (= the highest dose used)



# Decreased cancer cells migration

- Reduced cell migration by PB in a dose-dependent manner
- Decreased secretion of extracellular matrix digesting enzymes, which are involved in cancer invasion & metastasis.

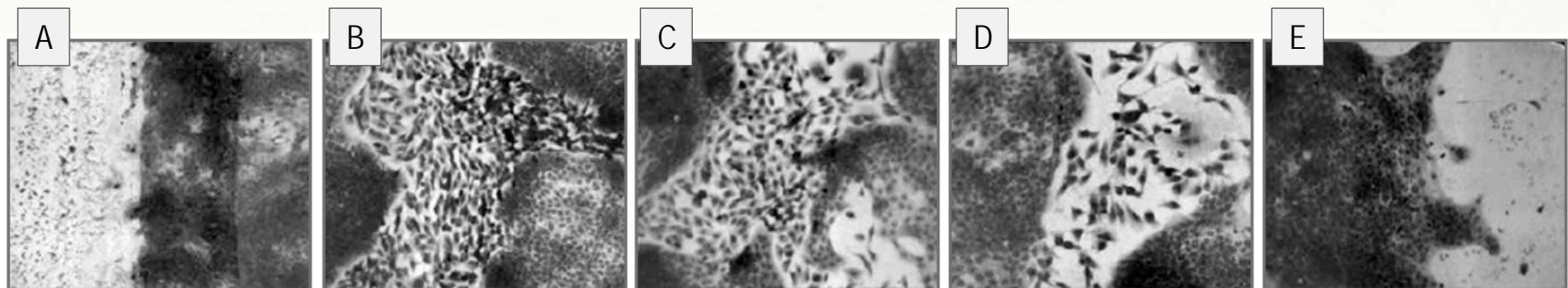


Figure 6. Effect of PB on migration: scratch test. (A) Control, 0h; (B) Control, 24h; (C) PB, 10 $\mu$ g/ml 24h; (D) PB, 25 $\mu$ g/ml 24h; (E) PB, 50 $\mu$ g/ml 24h;

# Conclusion

Current treatment methods for FA-associated cancers are ineffective and toxic

Dietary intake of the mixture of phytonutrients should be considered in developing safe and effective approaches to control FA-associated cancers.