

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

New publication from the Dr. Rath Research Institute

Accepted January 29, 2015
International Journal of Oncology

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Fanconi Anemia (FA): definition

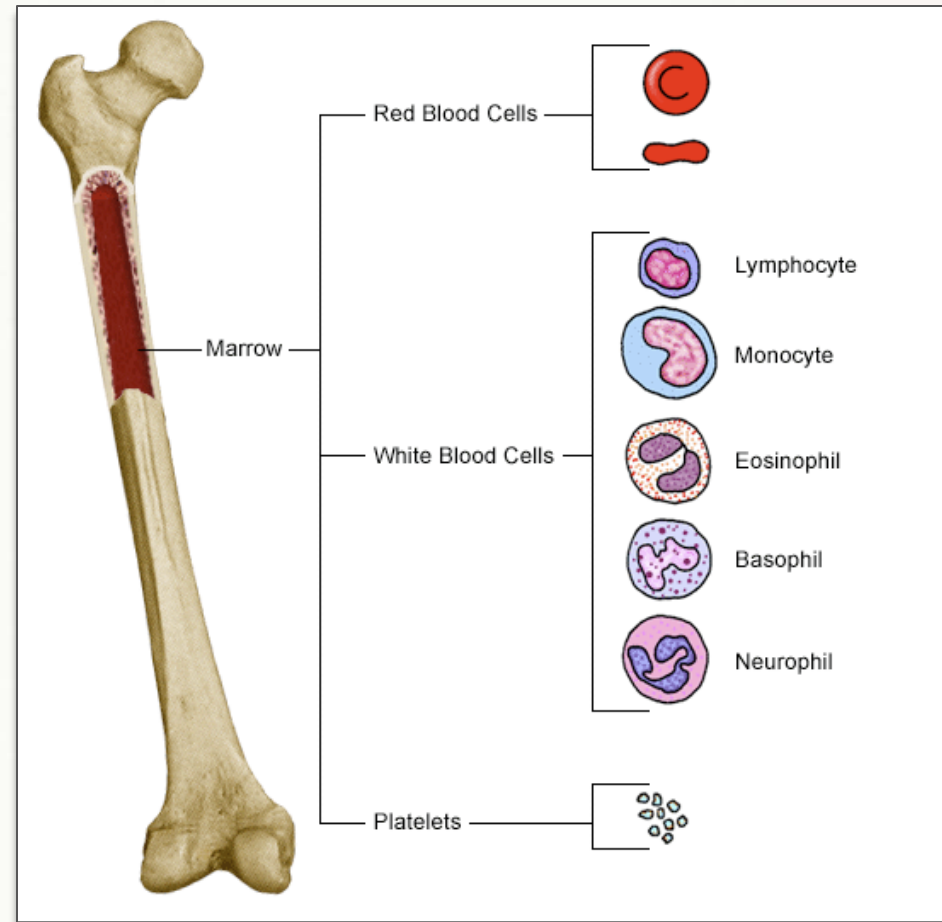
- Inherited blood disease
- Linked to 13 genes
- Can lead to
 - Bone marrow failure
 - Cancer, caused by a mutation of the FANC genes
 - High susceptibility to head & neck cancer
- Life expectancy: 20-30 years



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

	FA-associated HNSCC	Non-FA HNSCC
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 $\mu\text{g/ml}$

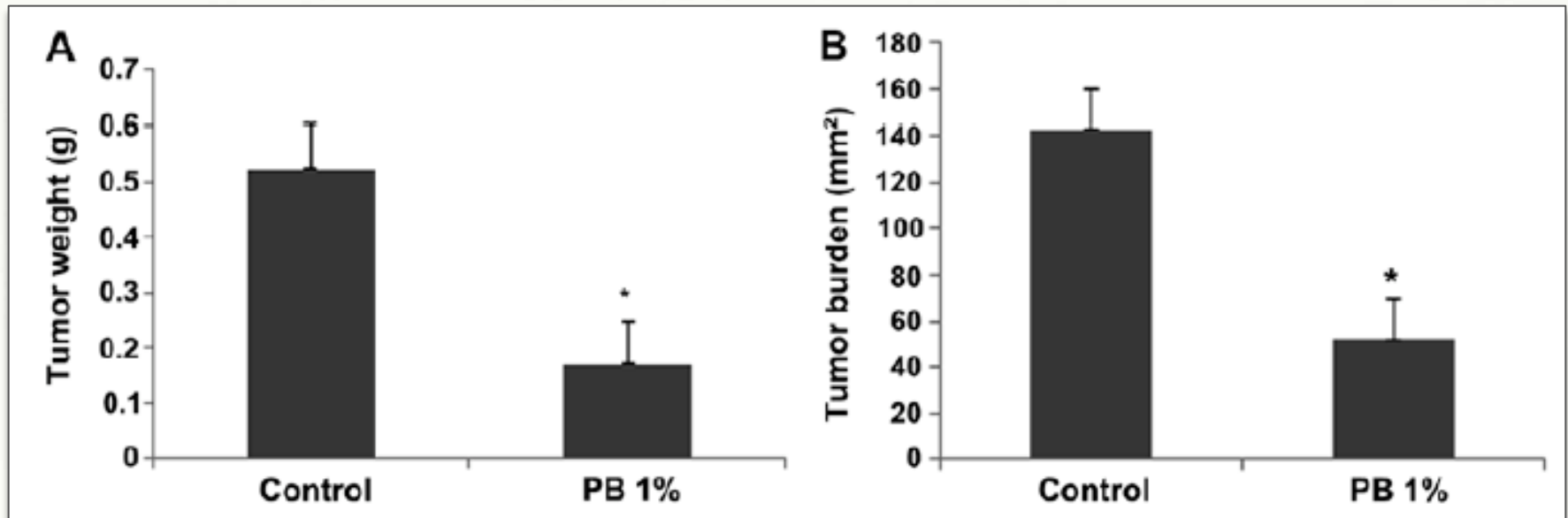
Results: In vivo studies (mice)

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



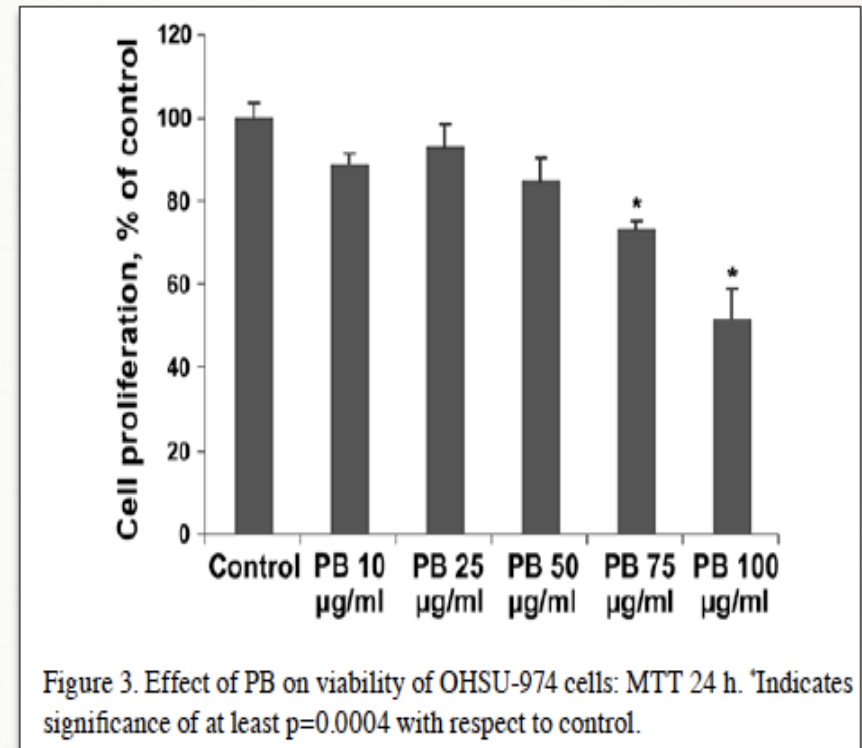
Suppression of tumor growth by PB

- 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 $\mu\text{g/ml}$ 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.

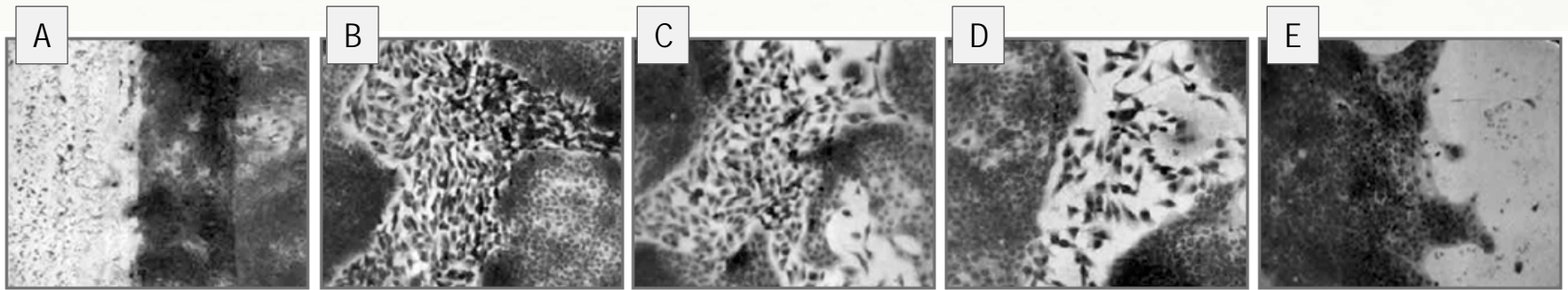


Figure 6. Effect of PB on migration: scratch test. (A) Control, 0h; (B) Control, 24h; (C) PB, 10µg/ml 24h; (D) PB, 25µg/ml 24h; (E) PB, 50µg/ml 24h;

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.