Canine Fur: An Underutilized Specimen to Advance Companion Animals as Sentinels for Monitoring Environmental Exposure and Disease Susceptibility in Humans

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Introduction

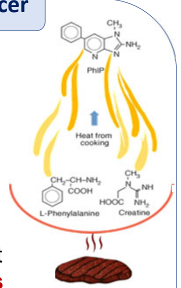
Hair is a non-invasive biospecimen that serves as a matrix to biomonitor exposures to a wide range of chemicals, including illicit drugs, narcotics, pesticides, tobacco toxicants, endocrine disruptors, androgen anabolic steroids, and other endogenous chemicals.[1] The follicles of human hair and animal fur can capture the bioavailable dose of many chemicals from the air, diet, and water, and some of their metabolites formed *in vivo*. Many biomarkers accrued in the hair are long-lived and represent long-term exposures. Thus, hair and fur have some advantages over urine and blood, where many chemicals are short-lived, and sensors which are often limited to detecting environmental exposures in the air. During our work on heterocyclic aromatic amines, a class of cancer-causing agents formed in well-done cooked meats and poultry, we unexpectedly discovered the occurrence of 2-amino-1-methyl-6-phenylmi-dazo[4,5-*b*]pyridine (PhIP) in canine fur.[2-4] PhIP is a possible human colorectal, pancreatic, and prostate carcinogen.[5] We have also examined the relationship between PhIP hair levels and prognostic pathology markers of prostate cancer patients.


CNN Health
Well-done red meat linked to aggressive prostate cancer
By Amanda Gardner, Health.com

- What **chemical/s** contained in red meat is/are responsible for **DNA damage** of the prostate?
- Looking for **biomarkers** to understand the chemical agents that contribute to DNA damage of the prostate
- Develop strategies for **cancer prevention**

Meat consumption and human cancer

- **Red meat** is classified as '**probably carcinogenic to humans**' inducing colorectal, pancreatic and prostate cancers (Group 2A)
- **PhIP** is a carcinogenic HAA formed in high-temperature cooked meats
- PhIP is the only mutagen formed in cooked meat that induces **prostate tumors in rodent models**
- PhIP's carcinogenic effects are driven by its capacity to form DNA adducts that **induce mutations**



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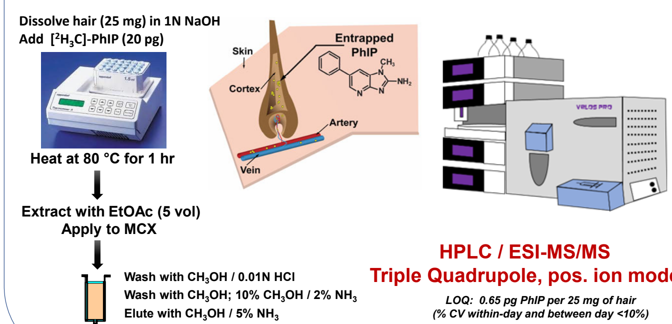
Analytical approach

Rapid Microscale Extraction and Biomonitoring of HAAs in Human Hair and Canine Fur



Identification of PhIP in canine fur

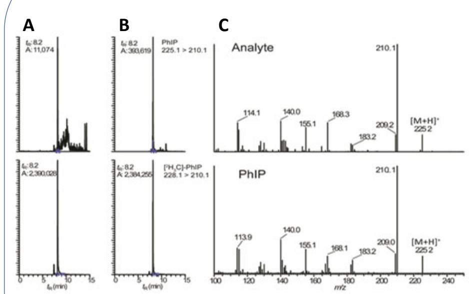


Fig. 4. LC-MS[2] of PhIP in (A) white fur and (B) black fur of Dog #11, and (C) the product ion spectra of the PhIP in the black fur and synthetic PhIP.

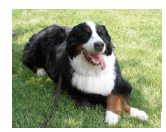
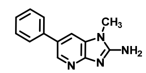


Fig. 2. Dog 11. Our canine volunteer Moses Turesky



PhIP

Measurement of PhIP in canine fur and human hair

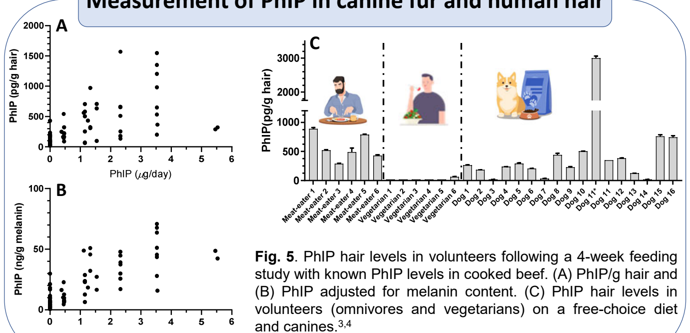
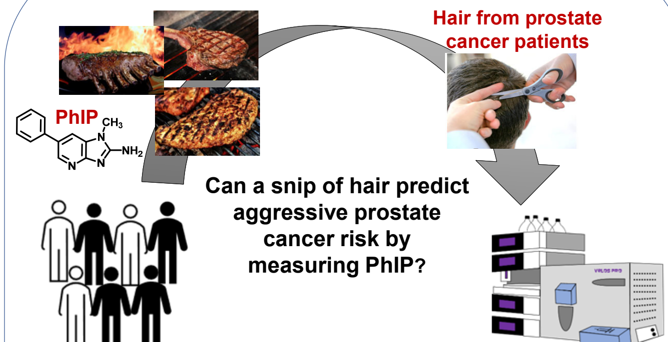


Fig. 5. PhIP hair levels in volunteers following a 4-week feeding study with known PhIP levels in cooked beef. (A) PhIP/g hair and (B) PhIP adjusted for melanin content. (C) PhIP hair levels in volunteers (omnivores and vegetarians) on a free-choice diet and canines.[3,4]

PhIP and prostate cancer risk



Demographics and PhIP Hair Levels Associated with Prostate Pathology Biomarkers for Patients Treated at UMN

Variable	Patients, *n*	Mean, SD	Pathology	PhIP (pg/g hair)[a] *n*[b]	PhIP (pg/g hair)[a] Geometric Mean (IQR)[c]	PhIP (pg/g hair)[a] p	PhIP (ng/g melanin)[a] *n*[b]	PhIP (ng/g melanin)[a] Geometric Mean (IQR)[c]	PhIP (ng/g melanin)[a] p
Age years)	325	65.9 ± 8.5	**PSA ng/mL (binary)**						
BMI (kg/m^2)	322	28.4 ± 4.7	PSA < 4	44	26.6 (36.5)	0.030	44	3.3 (3.7)	0.136
			PSA ≥ 4	133	38.6 (60.9)		133	4.1 (5.7)	
Ethnicity			**Gleason score (binary)**						
White/Non-Hispanic Latino	286	65.8 ± 8.4	Benign and 6	71	27.0 (38.4)	0.021	71	3.1 (3.6)	0.025
African-American	26	64.3 ± 7.9	7 and above	131	37.7 (59.5)		131	4.1 (5.9)	
Others	13	73.3 ± 10.5							
			Surgical procedure						
			Prostatectomy	141	38.4 (58.2)	0.021	141	4.2 (6.3)	0.044
Surgical procedure			Cystoprostatectomy (bladder cancer)	38	25.1 (35.0)		38	3.0 (3.4)	
Prostatectomy	193		Benign prostate hyperplasia	6	29.7 (36.8)		24	2.9 (2.6)	
Cystoprostatectomy	61								
TURP	22		**Cancer status**						
HoLEP	40		- Benign	52	26.2 (33.5)	0.028	52	3.1 (3.6)	0.087
			- Malignant	150	36.5 (59.9)		150	4.0 (5.7)	

[a] Associations between PhIP hair levels using the average values of PhIP obtained from the scalp and abdomen reported at or above the LOQ value (25 pg/g hair) or ½ the LOQ was assigned to subjects below the LOQ.
[b] n = number of subjects assayed for PhIP hair biomarker.
[c] Geometric mean for categorical covariates with interquartile range.

Conclusions

- High-density canine fur can be used as part of the battery of specimens employed for sentinel monitoring human exposures and investigating our pets' health and vitality.
- Targeted and untargeted analyses of the hair/fur exposome can potentially identify a wide-range of environmental toxicants.
- Elevated PhIP hair levels are associated with high-risk PSA and Gleason prostate pathology scores, supporting the well-done cooked red meat paradigm in prostate cancer risk.

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Masonic Cancer Center
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