Genetic Mutations Attributable to DNA Replication Errors in Women's Cancers:
A Random Problem Requiring a Precise Solution

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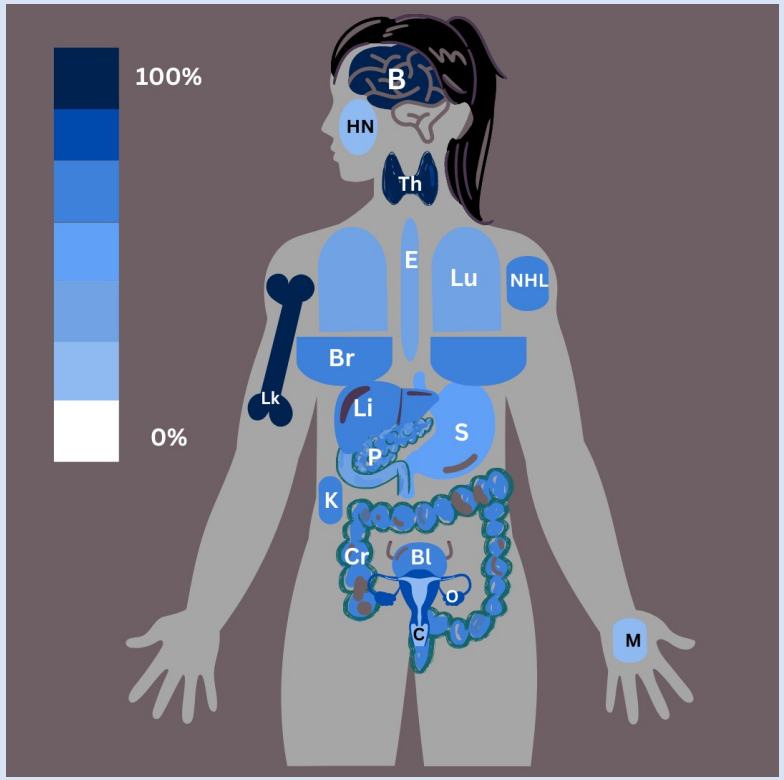
In addition to environment, lifestyle, and hereditary factors, **errors in DNA replication** (genetic material copied during cell division) can play an important role in cancer incidence. **About 2/3 of mutations in human cancers were caused by replication errors**[1], including mutations in cancers specific to the female sex.

This creates an interesting problem for cancer prevention. ***If these random errors are highly proportionate to genetic mutations responsible for certain cancers, how does preventive medicine come into play?***

Current prevention strategies include:

- education on important lifestyle changes such as smoking cessation
- understanding the risks of exposure to cancer-causing agents such as ultraviolet light

Precision medicine may play an important role in cancer prevention/early detection for rare yet deadly cancers, such as ovarian, for which most of their genetic mutations are caused by errors in DNA replication.



This figure[1] demonstrates the proportion of genetic mutations attributable to DNA replication errors in women; a considerable proportion of cancers unique to the female sex [Ovarian (O) and Uterine (U)] and more commonly in females [breast (Br)] due to this phenomenon.

[1]Figure adapted from Tomasetti, Li, and Vogelstein (*Science*, 2017).

Precision medicine is personal to one's own lifestyle, exposures, family history, and cells. Cancer prevention and treatment is no longer a one-size-fits-all process.

Multi-Cancer Detection tests may be able to detect the presence of various cancer types[2], allowing patients to be proactive in making informed oncology healthcare decisions.

- → These tests can detect signals in blood or other body fluids from a liquid biopsy that could suggest presence of cancer[2].
- → Hypothetical benefits include[2]:
  - → **potential for screening at organ sites that lack a current screening test**
  - → **a less invasive procedure**
  - → **earlier detection**
  - → **simultaneous screening for multiple cancers**

These tests have not been approved by the U.S. Food and Drug Administration but multiple Randomized Controlled Trials are being conducted[3] to understand their role in clinical practice.

Abbreviation	Organ/Site Name	Abbreviation	Organ/Site Name
B	Brain	E	Esophagus
HN	Head & Neck	Lu	Lung
Th	Thyroid	Br	Breast
NHL	Non-Hodgkin's Lymphoma	Li	Liver
M	Melanoma	K	Kidney
S	Spleen	P	Pancreas
Cr	Colorectal	U	Uterine
Bl	Bladder	O	Ovarian
C	Cervical	Lk	Leukemia

References

1. Tomasetti C, Li L, Vogelstein B. Stem cell divisions, somatic mutations, cancer etiology, and cancer prevention. Science [Internet]. 2017;355(6331):1330–4. Available from: https://www.science.org/doi/10.1126/science.aaf9011
2. Questions and answers - cancer screening with multi-cancer detection (MCD) tests [Internet]. Division of Cancer Prevention. 2022 [cited 2022 Dec 28]. Available from: https://prevention.cancer.gov/major-programs/mcd/questions-and-answers-cancer
3. Basharat S, Horton J. CADTH Horizon Scan Emerging Multi-Cancer Early Detection Technologies. Available from: https://www.cadth.ca/sites/default/files/hs-eh/EN0037-Multi-Cancer%20Early%20Detection%20Techs%20v.5.3-meta.pdf