

## Peer Review

# Review of: "Hereditary Decreased Cancer Risk: Reality or Mirage? A Review"

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The author is correct in stating that most genetic studies aim to identify cancer susceptibility rather than cancer resistance. Specific alleles of genes that can cause cancer may be considered “protective” if they are alleles other than those causing a specific cancer. They are not really protective; they simply do not code for susceptibility to somatic mutations that cause a particular cancer. The truly protective genes are those that prevent the expression of somatic mutations leading to malignancy (such as DNA repair genes) or underlie strong immune reactions to malignant cells, destroying them.

Although no specific studies of cancer-free population samples were conducted to detect genes conferring cancer resistance, we have a natural experiment showing that such genes do exist: most people do not develop cancer during their lifetimes. This is a result of the long-term evolution of the human genome. Cancers were always present in human populations, as evidenced by studies of ancient skeletal remains, but their incidence has now increased. This increase is partly due to increased longevity and to carcinogenic factors, but it is also related to genetic changes. Cancers whose genetic causes are known are caused by specific alleles whose population frequencies are relatively low. These genes entered the human gene pool as a result of mutation-selection balance tilted towards deleterious mutations. This occurred when modern medicine and public health reduced natural selection pressures against deleterious alleles (e.g., You W, Henneberg M. 2017 Cancer incidence increasing globally: The role of relaxed natural selection, *Evolutionary Applications*, EVA-2017-022-OA.R2). The same “tilt” did not increase frequencies of truly protective genes; to the contrary, the probable mutation effect probably reduced their frequencies.

The study aimed at identifying truly cancer-protective genes is much needed, given that many malignancies cannot be effectively treated with surgical, pharmacological, or immunotherapeutic techniques.

## **Declarations**

**Potential competing interests:** No potential competing interests to declare.