

HELI Σ AFE[®]

Cancer Driver Interception

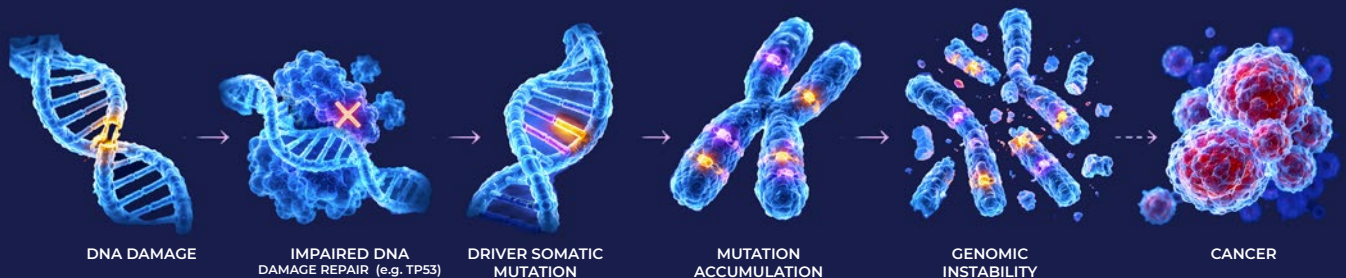
Longitudinal molecular surveillance of somatic mutations

HELIXAFE - CANCER DRIVER INTERCEPTION

is not a screening, risk assessment, early detection, or diagnostic test. It is a cancer prevention programme designed to monitor the molecular changes that may precede clinically detectable disease. With **HELIXAFE**, the paradigm of cancer prevention shifts from early detection to Cancer Driver Interception: from identifying cancer once it has already formed to monitoring the biological processes that can precede its development.

Through a simple 10–20 mL blood sample, **HELIXAFE** analyses cell-free DNA (cfDNA) using Next-Generation Sequencing (NGS) to measure acquired somatic mutations and track genomic instability over time. Rather than searching for cancer, **HELIXAFE** follows its molecular trajectory before disease becomes clinically evident.

CARCINOGENESIS



WHAT PROTECTS US FROM CANCER

Every day, our DNA suffers thousands of lesions, driven by external risk factors such as pollution, smoking and alcohol, and by endogenous processes such as oxidative stress and replication errors.

Tumour suppressor genes detect and neutralise this damage, preserving genomic integrity and preventing cancer from developing.

Monitoring how efficiently these genes perform their role allows us to intercept carcinogenesis before cancer appears.

THE PRECURSOR CONDITION TO CANCER

WHEN TUMOR SUPPRESSOR GENES BECOME INACTIVE

Tumour suppressor genes detect and repair the damage our DNA suffers every day. When these genes become inactive, the cell loses its defences. DNA damage goes undetected, unrepaired and unchecked. This unrepaired damage becomes permanent in the form of somatic mutations, which can accumulate over 10 to 20 years. This condition, known as genomic instability, is the pathophysiological phase that precedes cancer.

GENOMIC INSTABILITY THE SILENT PATHOPHYSIOLOGICAL PHASE THAT PRECEDES CANCER.

When tumour suppressor genes stop functioning, DNA damage is no longer properly repaired. This unrepaired damage becomes fixed as somatic mutations, which accumulate progressively over time. Their accumulation marks genomic instability - the precursor condition that can drive cancer development years before disease becomes clinically visible.

CURRENT GENETIC TEST LIMITATION

GERMINAL INHERITED MUTATION

- Tests such as *BRCA1* and *BRCA2* identify **inherited germline mutations**.
- They reveal **lifelong predisposition and risk**.
- These mutations are inherited and **cannot be modified**.
- They **do not show** whether that risk is actively turning into disease.

MULTI-CANCER EARLY DETECTION

- Often presented as prevention, they detect cancer **only after it has formed**.
- Diagnosis may be anticipated, but the disease is **already biologically present**.
- They **do not prevent** cancer.

WHAT cfDNA REVEALS THAT DNA CANNOT

SOMATIC ACQUIRED MUTATION

Circulating cell-free DNA (cfDNA) reveals acquired mutations, providing a real-time view of genomic changes.



Conventional DNA testing

Analyzes germline DNA and reveals hereditary mutations as indicators of predisposition.



Longitudinal cfDNA monitoring

Reveals acquired (somatic) mutations that arise over time and reflect changes in genomic stability.



A progressive accumulation of somatic mutations is the marker of genomic instability.



Genomic instability is the silent condition that drives cancer.



This is the process that conventional testing does not intercept.

HELIXAFE

cfDNA MOLECULAR MONITORING



THE MRI DELAY IN CANCER PREVENTION

POTENTIAL MOLECULAR LEAD TIME

10-15 YEARS

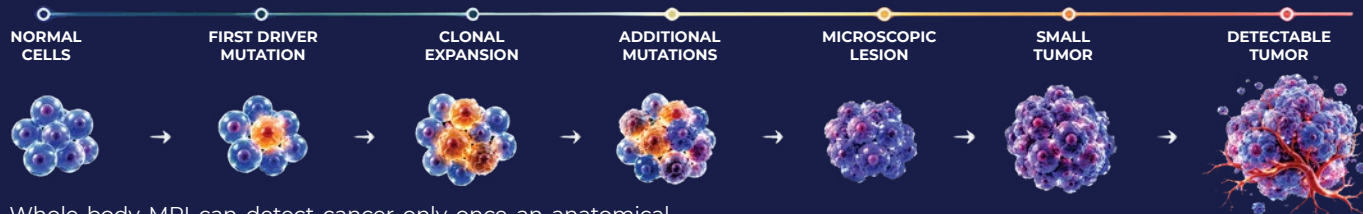
WHOLE-BODY CT/MRI

IMAGE-VISIBLE LESIONS



MOLECULAR CHANGES

VISIBLE GROWTH



Whole-body MRI can detect cancer only once an anatomical lesion is large enough to be seen. By then, the molecular evolution of the disease may have been underway for years. Rather than scanning the body for lesions, **HELIXAFE** scans the genome for early molecular warning signs. From a simple blood sample, it analyses cfDNA across a broad panel

of tumour suppressor genes and proto-oncogenes, verifying that the former remain intact and the latter have not acquired activating mutations. In this way, **HELIXAFE** intercepts the molecular condition that drives cancer, which often takes a decade or more to become a visible lesion.

WHO IS HELIXAFE FOR?

RECOGNISED RISK FACTORS

People with lifestyle, environmental or familial risk factors.



Current or past smoking



Alcohol consumption



Excess weight



Family history of cancer



Environmental exposure (pollution, toxins)



Occupational exposure

CONDITIONS UNDER SURVEILLANCE

People with pre-cancerous conditions or findings that require follow up.



Barrett's oesophagus



Removed colorectal polyps



Pancreatic cysts



Chronic hepatic conditions



Lung nodules



Fatty liver disease



INHERITED PREDISPOSITION

People carrying *BRCA1* and *BRCA2* variants or with Lynch syndrome, Li-Fraumeni syndrome or another hereditary condition.

Germline testing defines inherited predisposition.

HELIXAFE monitors how this risk may be expressed at the molecular level.



PREVIOUS CANCER

People who have had cancer and are in follow up.

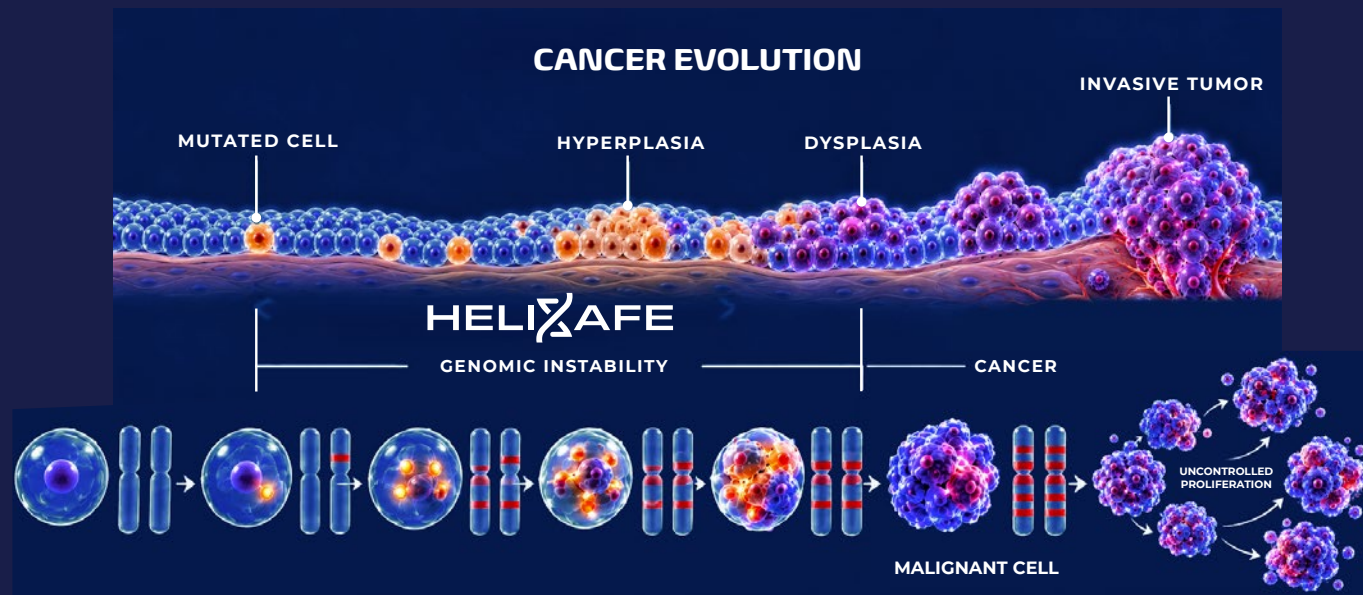
In selected survivors, serial cfDNA testing may complement imaging, tumour markers and clinical follow up, providing early signals of molecular changes.



PREVENTIVE PROGRAMMES AND TIMING

Adults enrolled in structured preventive-health programmes.

Molecular surveillance can be part of a personalised prevention plan, to assess and monitor risk over time.



THE UNMET NEED IN CANCER PREVENTION

What cancer prevention still lacks is the ability to monitor and manage the condition that drives cancer before the disease forms, just as we measure cholesterol and blood pressure to prevent heart disease. This approach has transformed cardiology: over the past 30 years, deaths from heart attack have fallen by 56.1%, while cancer cases have risen by 35.7%. Today, cancer prevention relies on early detection, which reduces deaths but not the disease itself: over the same period, cancer mortality has fallen by 23.6%, while the number of patients has kept rising.

SUMMARY OF CHANGE (1995-2025)

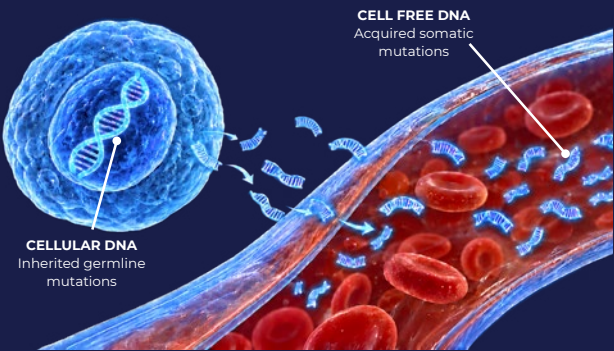
CANCER INCIDENCE
Increased
+35.7%



CANCER MORTALITY
Decreased
-23.6%



DEATHS FROM HEART ATTACK
Decreased
-56.1%



WHY TRUE CANCER PREVENTION IS NOW POSSIBLE

In the past, detecting somatic mutations, the essential first step in assessing genomic instability, required a biopsy of every tissue under investigation. Today, advances in cell-free DNA (cfDNA) sequencing allow information collection from a single blood draw, when once multiple biopsies were required. cfDNA consists of DNA fragments released into the bloodstream by cells throughout the body. This makes testing accessible to healthy individuals, and therefore usable for prevention.

THE GOAL OF TRUE CANCER PREVENTION

To achieve true cancer prevention, rather than early diagnosis - which does not prevent cancer - we must intercept the pathophysiological condition that precedes the disease. Such conditions are easier to modify and treat successfully than established diseases, potentially avoiding invasive treatments that are not always effective. This condition is Genomic Instability, which results from the progressive accumulation of somatic mutations when DNA damage goes unrepaired because tumour suppressor genes remain inactive over time.

MOLECULAR ANALYSIS BEFORE SCREENING

Exposure to genotoxic factors, such as tobacco smoke, alcohol, radiation, pollutants, chronic infection and inflammation, can trigger the molecular mechanisms that set carcinogenesis in motion. To intercept and address these driver conditions, we must investigate the molecular consequences of such exposures. Established screening methods, including mammography, colonoscopy, cervical screening, low-dose CT and PSA testing, generally assess tissue changes that are already present. **HELIXAFE** is an early warning: it analyses the molecular mechanisms at the origin of cancer before a tumour forms, potentially years before it becomes detectable by conventional screening.

RISK-STRATIFIED cfDNA MONITORING PROGRAMMES

HELI $\times$ PAN

is a pan-cancer prevention programme designed for adults seeking broad molecular surveillance, not limited to a single organ. It is particularly relevant for people with multiple risk factors, such as smoking, alcohol consumption, excess weight, occupational exposures or a family history of different cancer types. **HELI $\times$ PAN** offers periodic cfDNA monitoring of somatic alterations associated with carcinogenesis, through a panel of 52 genes covering more than 900 point mutations, 99 gene fusions and 12 copy number alterations.



HELI $\times$ GUT

is a cancer prevention programme designed for people at increased risk of colorectal cancer. It is particularly relevant for those with a family history of colorectal cancer, previously removed polyps or inflammatory bowel disease, and for people with lifestyle-related risk factors, such as excess weight, smoking, alcohol consumption or a diet rich in red and processed meat. For those at increased risk, **HELI $\times$ GUT** offers periodic cfDNA monitoring of somatic alterations associated with colorectal carcinogenesis, across a panel of 14 genes and 246 mutational hotspots.



HELI $\times$ GYN

is a cancer prevention programme designed for women at increased risk of breast and ovarian cancer. It is also relevant for women undergoing hormonal treatments, such as hormonal contraception, hormone replacement therapy or ovarian stimulation for IVF, and for those with a family history of breast or ovarian cancer. For these women, **HELI $\times$ GYN** offers periodic cfDNA monitoring of somatic alterations associated with breast and ovarian carcinogenesis, across a panel of 10 genes and 157 mutational hotspots.



HELI $\times$ LUNG

is a cancer prevention programme designed for people at increased risk of lung cancer. It is particularly relevant for current and former smokers, and for those with other risk factors, such as exposure to air pollution, radon or occupational carcinogens, a family history of lung cancer or chronic lung diseases such as COPD. For those at increased risk, **HELI $\times$ LUNG** offers periodic cfDNA monitoring of somatic alterations associated with lung carcinogenesis, across a panel of 11 genes and 169 mutational hotspots.



THE IMPORTANCE OF LONGITUDINAL MONITORING

HELI $\times$ AFE is designed to detect genomic instability, the condition that drives cancer. Genomic instability does not appear all at once: it builds gradually, as unrepaired DNA damage accumulates over time. This is why no single analysis can reveal it. A first test establishes the baseline. Only monitoring over time can show whether somatic mutations are stable, emerging or accumulating. It is this trajectory, not any isolated result, that signals genomic instability. And because genomic instability can arise at any stage of life, the test should be repeated regularly, just as we routinely check cholesterol and blood pressure. One test captures a moment; monitoring it's results.

TREATING THE CANCER DRIVER: THE ROLE OF CHEMOPREVENTION

Chemoprevention uses drugs, biological agents and natural compounds to stop, slow or reverse carcinogenesis by acting on its driver conditions: genomic instability, chronic inflammation and DNA damage. It is already established medicine. The US FDA has approved tamoxifen and raloxifene for breast cancer risk reduction and HPV vaccines against HPV-related cancers, and the field keeps growing.

ESTABLISHED CHEMOPREVENTION

Tamoxifen and Raloxifene, Aromatase inhibitors, HPV and Hepatitis B vaccine, HBV and HCV antivirals, Helicobacter pylori eradication and Aspirin.

BIOLOGICALS

Alkaloids. Polyphenols (EGCG, Curcumin, Resveratrol), Isothiocyanates, Carotenoids, Indoles, Flavonoids and Isoflavones.

UNDER CLINICAL INVESTIGATION

Metformin, mTOR inhibitors. GLP-1 agonists, Denosumab Eflornithine plus sulindac and Berberine.

NON-GENOTOXIC CHEMOPREVENTIVE ADVANCED NUTRITIONAL FORMULA

Four Bioscience formulas whose botanical and algal actives are grown in Vertical Farm clean-rooms, minimizing exposure to environmental genotoxic contaminants such as heavy metals, pesticides and microplastics.

BIOXAFE NGTX combines echinacea, zinc, vitamin D3, resveratrol and spermidine to support immune defence, antioxidant protection and cellular renewal.

CYTOXAFE NGTX combines curcuminoids, eugenol, selenium, astaxanthin and lycopene to protect cells from oxidative and inflammatory stress and lipid damage.

GENEXAFE NGTX combines NADH, B vitamins, choline, astaxanthin, Cistus polyphenols, Chlorella and vitamin D to support mitochondrial energy metabolism and function.

MYCROGENOX NGTX combines berberine, gingerols, silymarin and tyndallised lactobacilli to support digestive function, gut motility, microbiota balance and liver function.

PREVENTING CANCER RECURRENCE

Genomic instability drives both cancer and its recurrence. In survivors, the same process that built the first tumor can quietly resume, accumulating unrepaired DNA damage long before a new mass appears. **HELIXAFE** reads this process directly: it tracks somatic mutations in circulating DNA and measures whether instability is growing.

As a pathophysiological condition, the driver can be treated more successfully than cancer itself. **HELIXAFE** helps survivors prevent cancer recurrence by detecting the driver early and monitoring it over time. Always alongside the oncologist's follow-up, never instead of it.

HELIXAFE | HOW IT WORKS



BIOSCIENCE INSTITUTE



240 Longwood Avenue - Building C - Boston, MA 02115, USA

www.bioinst.com