

top ten

in gastroenterologia

14[^] EDIZIONE

24-25 NOVEMBRE 2023

BERGAMO

HOTEL EXCELSIOR SAN MARCO
Piazza della Repubblica, 6



**Prevenire il
cancro o
intercettare i
driver tumorali?**

Prevenire il cancro o intercettare i driver tumorali?

Giuseppe Mucci

CEO & Founder

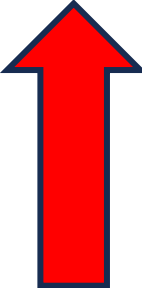
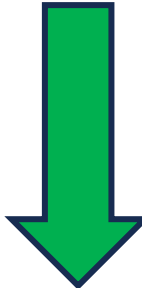
Bioscience Institute SpA – Bioscience Genomics srl

Presidente

Bioscience Foundation LTD

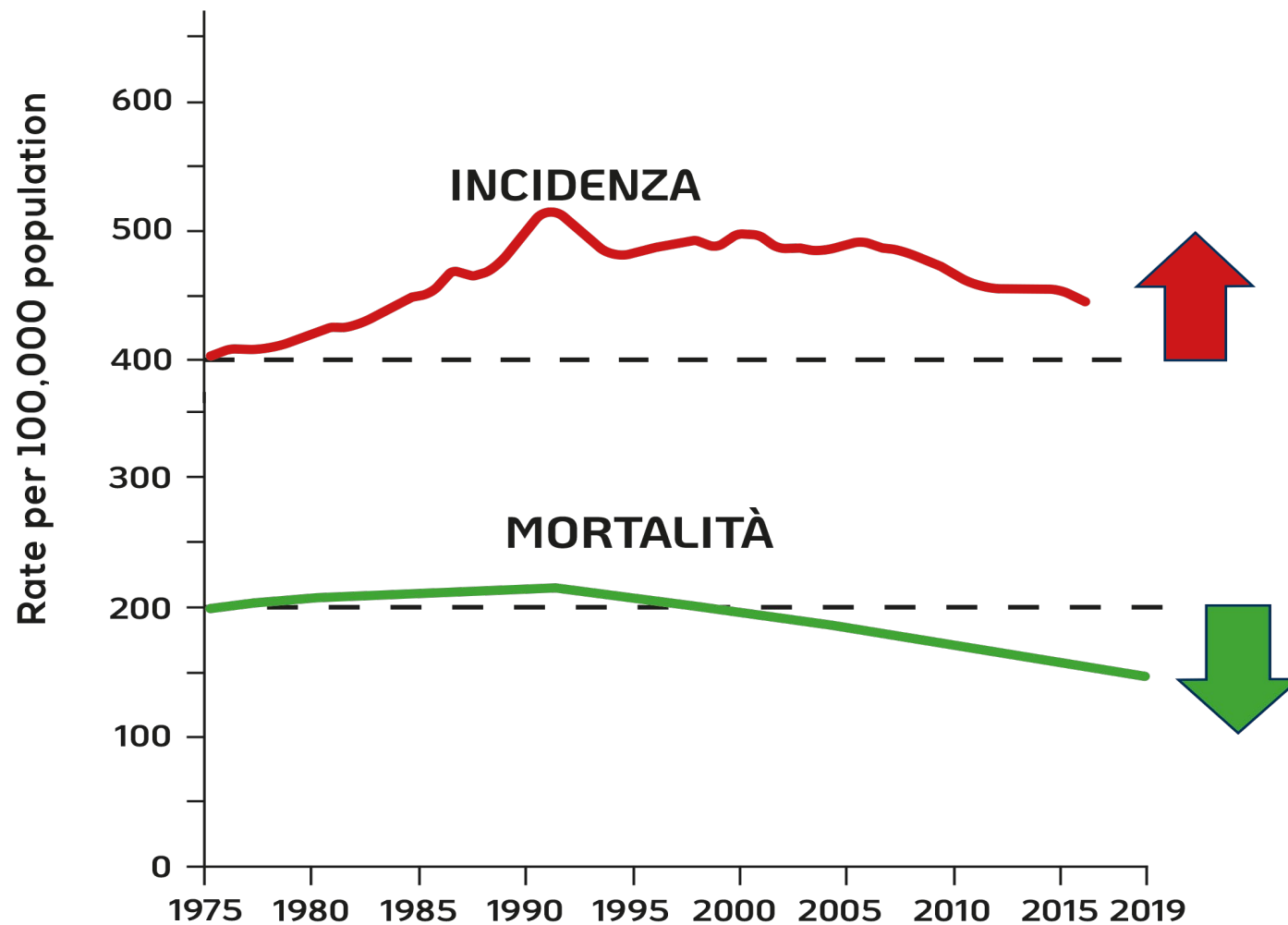
I NUMERI DEL CANCRO IN ITALIA 2022

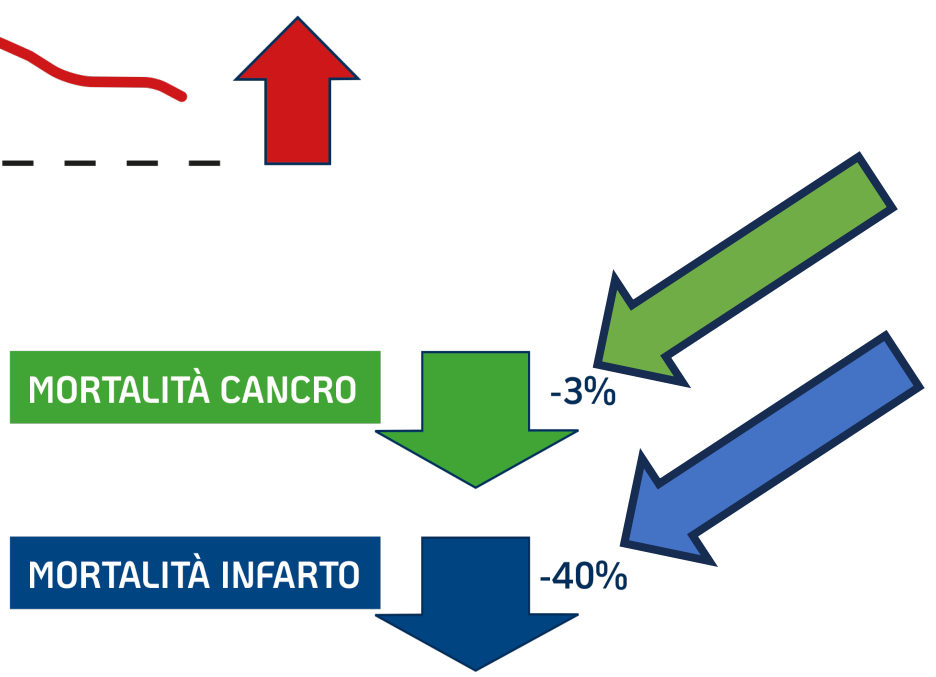
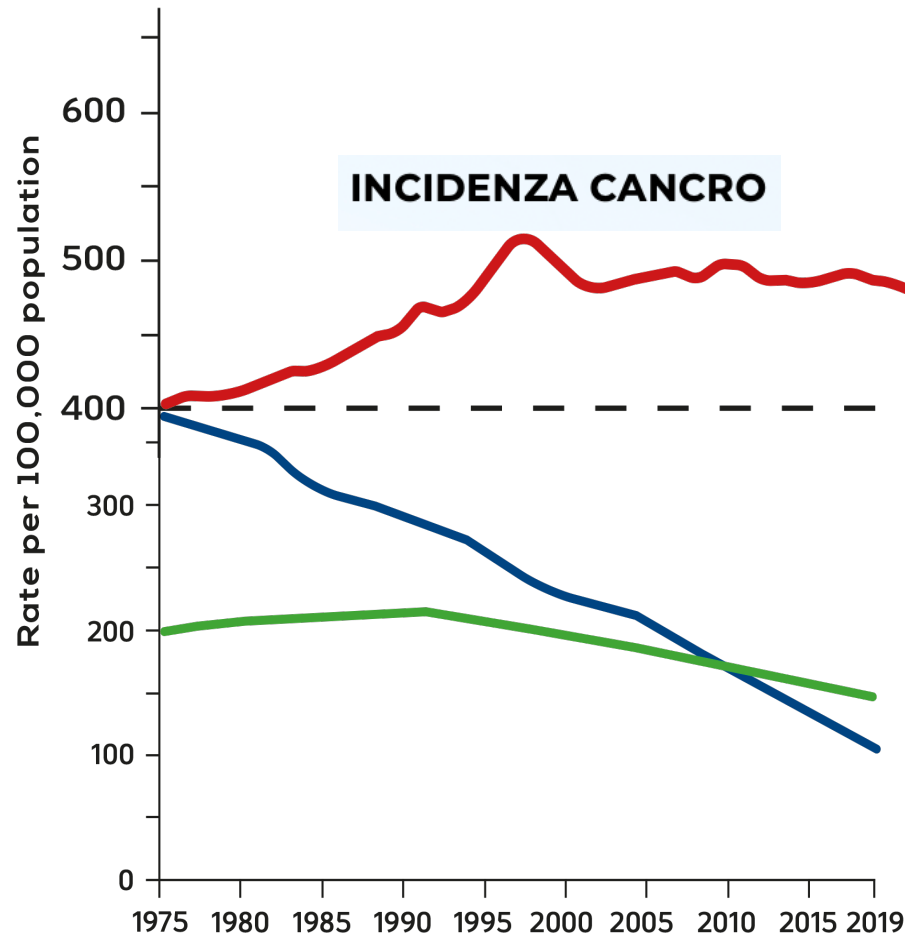
BIO SCIENCE
FOUN D A T I O N

	INCIDENZA	+ 0,7 %
	TENDENZA DI CRESCITA	+ 1,4 %
	MORTALITA'	-1,0 %
	TENDENZA DI CRESCITA	- 2,6 %





USA CANCER STATISTIC 2022





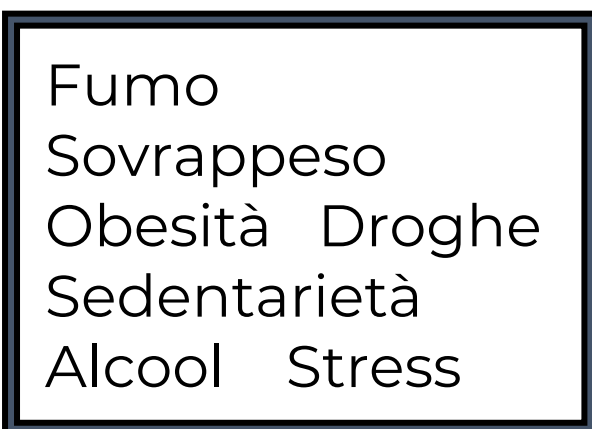
I FARMACI PIU' PRESCRITTI IN USA

	• <u>Blood Pressure</u>	• <u>19,4 %</u>
	• Antibiotic	• 13,7 %
	• <u>Cholesterol</u>	• <u>13,6 %</u>
	• Pain/Inflamm	• 13,6 %

PREVENZIONE DELLE PATOLOGIE CARDIACHE

BIO
SCIENCE
FOUN
DATION

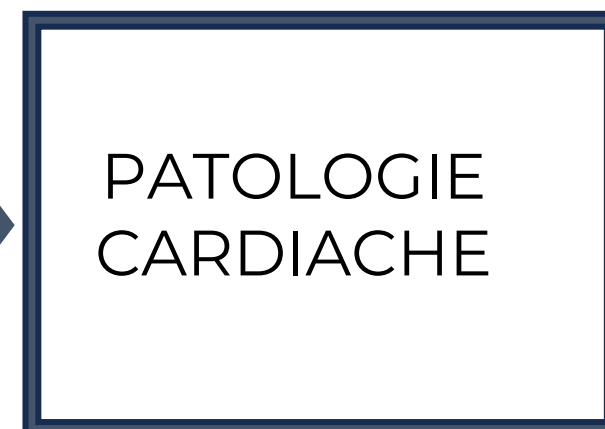
FATTORI COMPORTAMENTALI



CONDIZIONI FISIOPATOLOGICHE



MALATTIA



MORTALITA' - 40%

MODELLI DI PREVENZIONE : CARDIO vs CANCRO

1

FATTORI COMPORTAMENTALI

CONDIZIONI FISIOPATOLOGICHE

MALATTIA

CARDIO

Fumo
Sovrappeso
Obesità Droghe
Sedentarietà
Alcool Stress

IPERTENSIONE
IPERCOLESTEROLEMIA

PATOLOGIE
CARDIACHE

CANCRO

Fumo Sovrappeso
Obesità Radiazioni
Infezioni Droghe
Sedentarietà
Alcool Ormoni

?

CANCRO

causa del 44%
dei decessi globali

LA PREVENZIONE DEL TUMORE

*non indaga le condizioni
fisiologiche prodromiche*

*ricerca le lesioni precancerose
o diagnosi precoce*

**PREVIENE GLI SVILUPPI DELLA
MALATTIA**

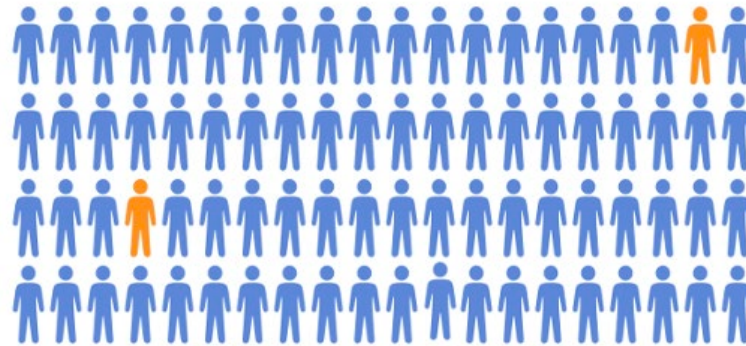
PROGRESSIONE DELLA MALATTIA

SCREENING

A-SINTOMATICI

DIAGNOSI PRECOCE

SINTOMATICI



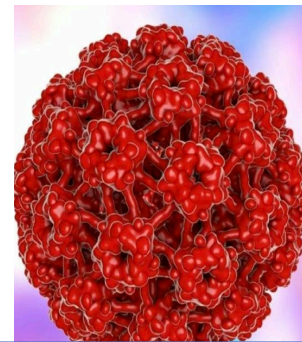
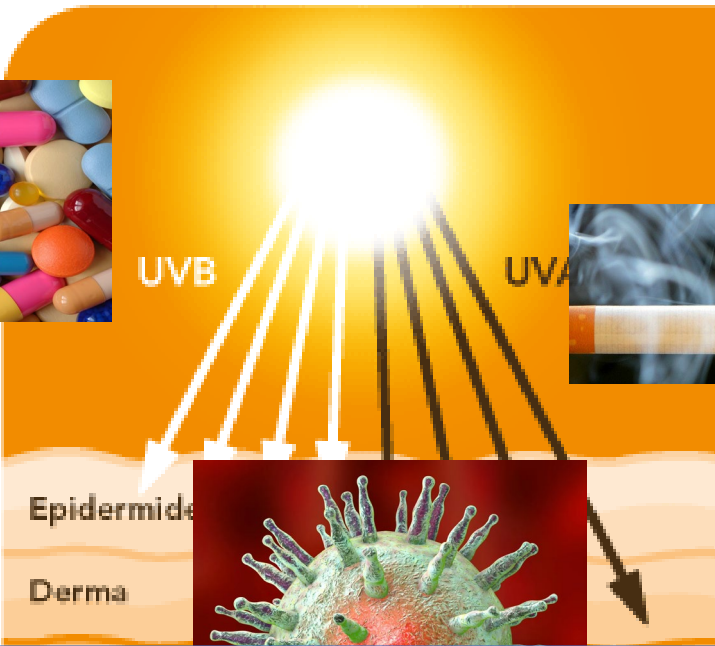
si identificano individui con
segni precoci di un tumore



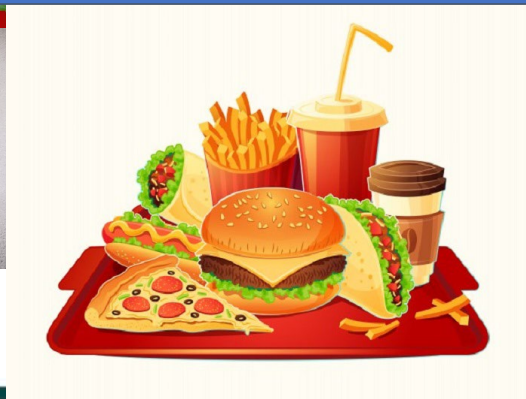
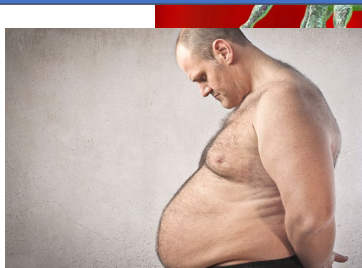
World Health
Organization

CANCER DRIVER INTERCEPTION

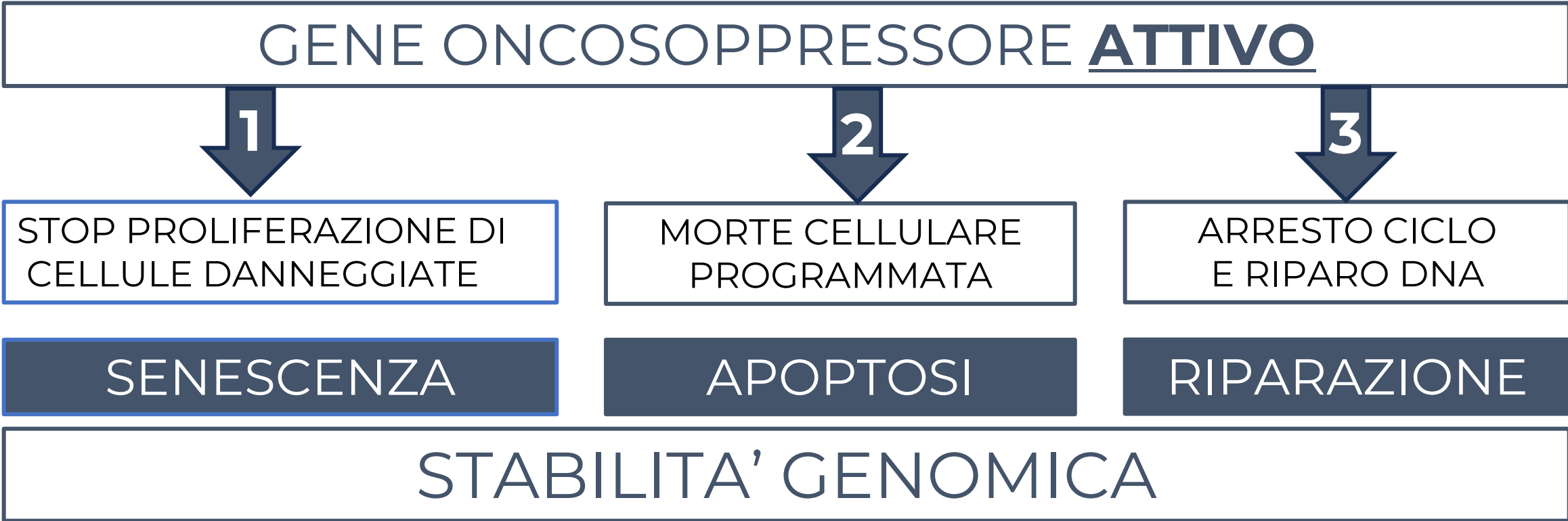
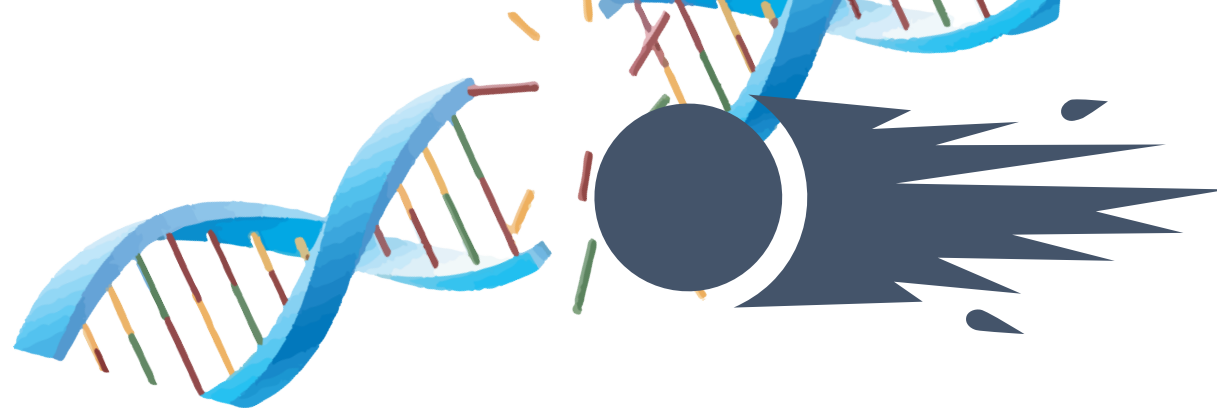
monitoraggio e gestione delle
CONDIZIONI FISILOGICHE
che, quando alterate, sono
PRODROMICHE DEL CANCRO

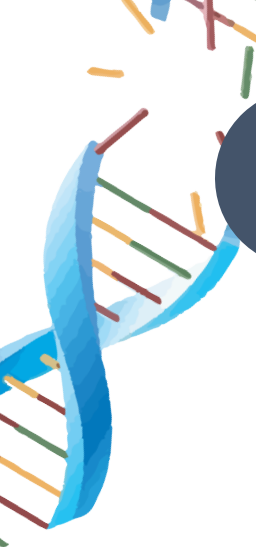


IL DNA RICEVE MIGLIAIA DI LESIONI AL GIORNO



	Fonte Danni	N _a LESIONI
RAGGI SOLARI	Peak hr sunlight	100,000/day ^d
FUMO	Cigarette smoke	45–1029 ^e
X-RAYS – IMAGING	Chest X-rays	0.0008 ⁱ
	Dental X-rays	0.0002 ⁱ
	Mammography	0.016 ⁱ
	Body CT	0.28 ⁱ
	Head CT	0.08 ⁱ
	Coronary angioplasty	0.88 ⁱ
	Tumor PET scan (¹⁸ F)	0.4 ⁱ
	¹³¹ I treatment	2.8–6 ⁱ
	External beam therapy	72–80
VOLO AEREO	Airline travel	0.0002/hr ⁱ
	Space mission (60 days)	2 ⁱ





GENE ONCOSOPPRESSORE INATTIVO

1° DANNO NON RIPARATO



MUTAZIONE SOMATICA

2° DANNO NON RIPARATO



MUTAZIONE SOMATICA

3° DANNO NON RIPARATO



MUTAZIONE SOMATICA

ACCUMULO **PROGRESSIVO** DI MUTAZIONI SOMATICHE

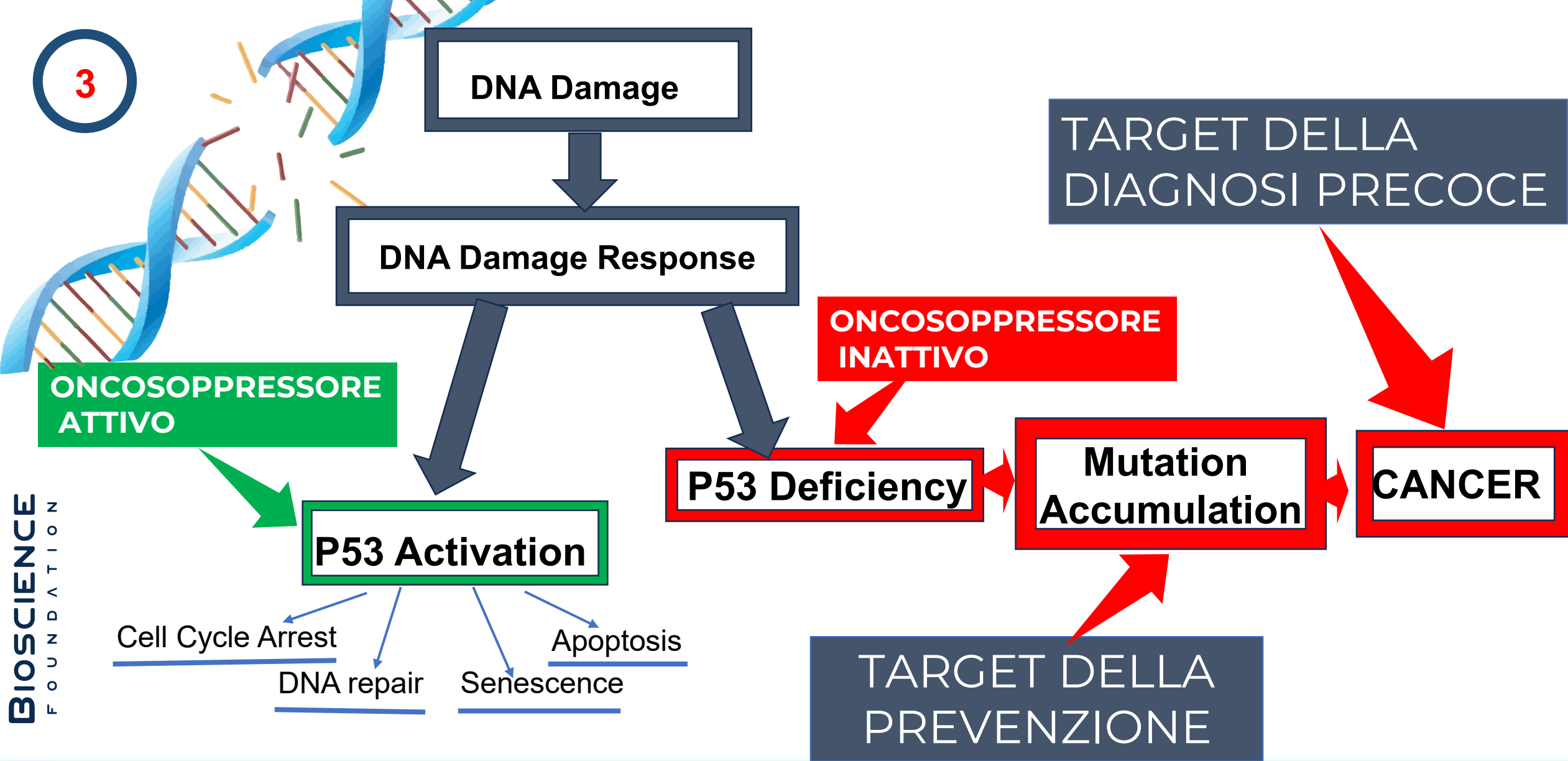


INSTABILITA' GENOMICA



CANCRO

3



BIO SCIENCE
F O U N D A T I O N

CELLULA
NORMALE

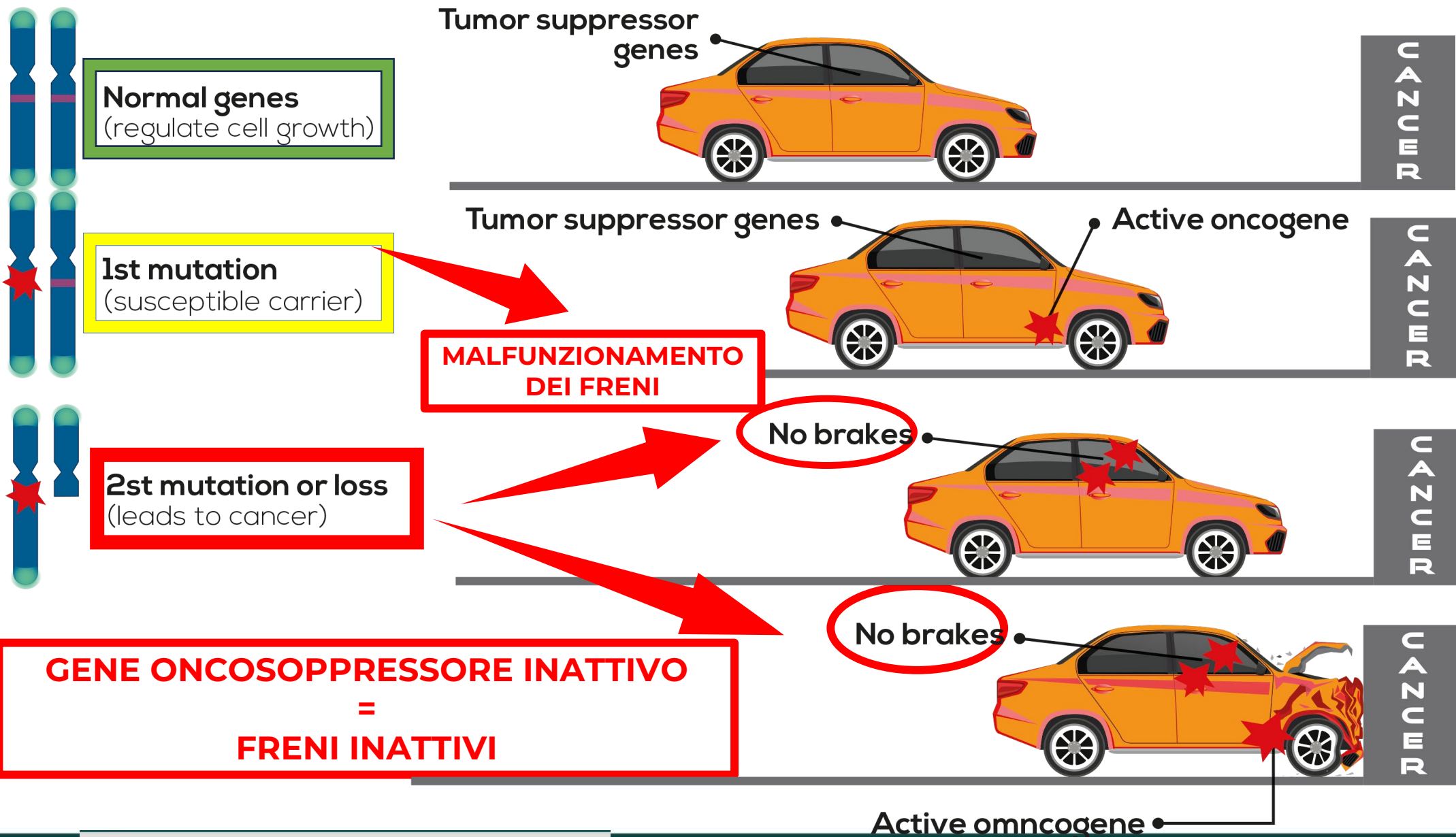
PREVENZIONE

ACCUMULO DI
MUTAZIONI SOMATICHE

DIAGNOSI
PRECOCE

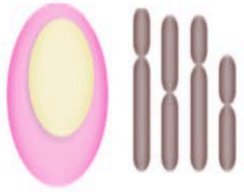
DIAGNOSI

PROLIFERAZIONE
INCONTROLLATA

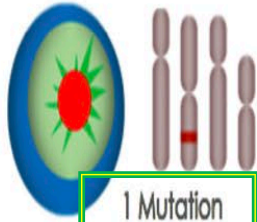


5

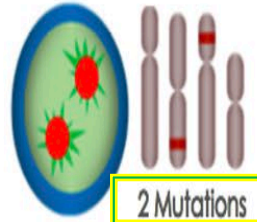
HEALTHY CONDITIONS WITHOUT SYMPTOMS



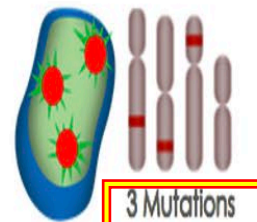
NORMAL CELL



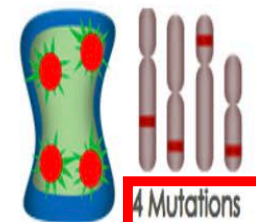
1 Mutation



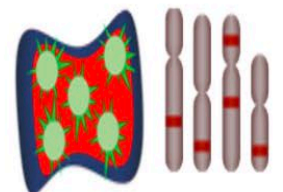
2 Mutations



3 Mutations



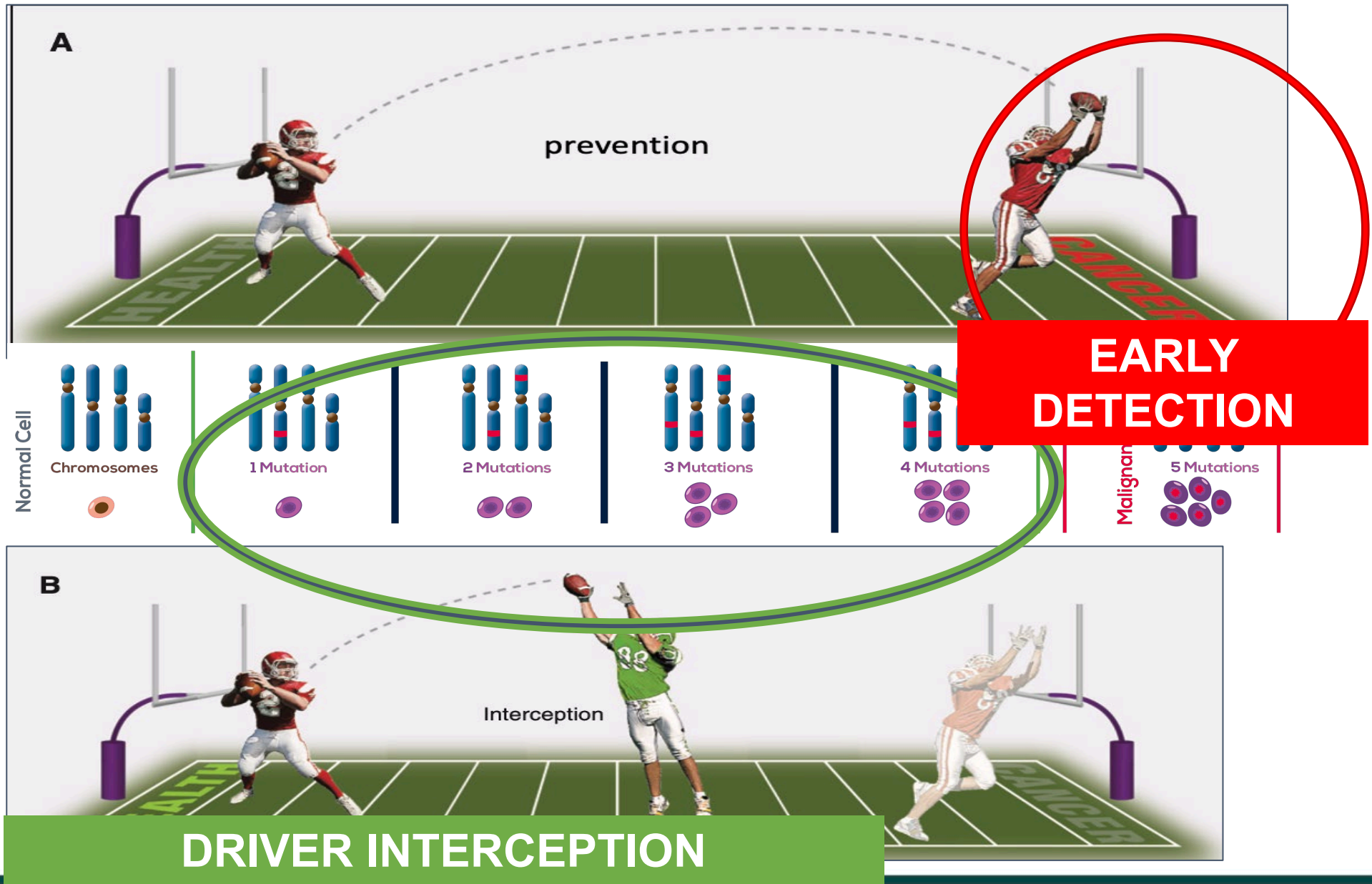
4 Mutations



CANCER CELL

PROGRESSIVE ACCUMULATION OF SOMATIC MUTATION

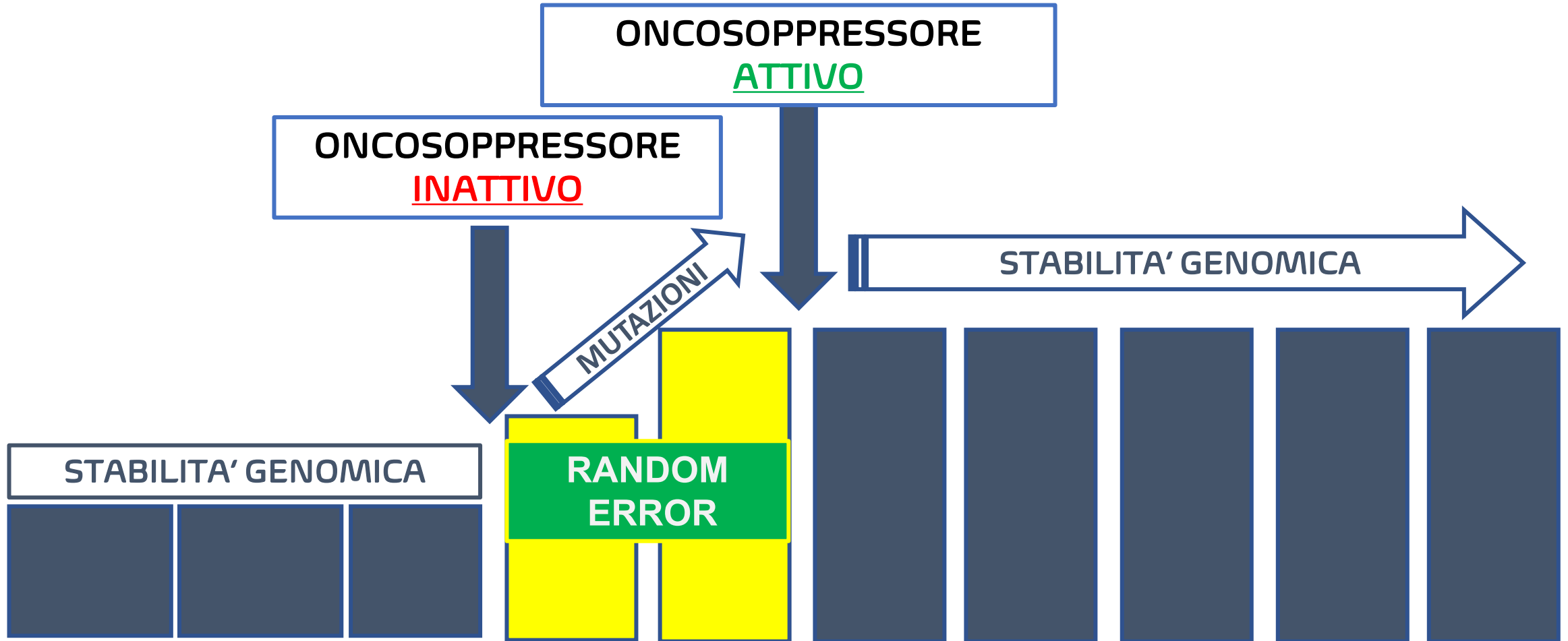
CANCER DRIVER CONDITIONS
GENETIC INSTABILITY



Adapted from: Blackburn EH. Cancer Prev Res (Phila). 2011 Jun;4(6):787-92.

STABILITA' GENOMICA

BIO
SCIENCE
FOUN
DATION



Grail Galleri testing proving to have high false positive rates

Sep 12, 2022 | Blog

Amid merger turmoil, Illumina's Grail unit reports downturn in accuracy of blood-based cancer test

Published Sept. 12, 2022

Last year, Grail reported that 44.6% of patients with positive test results on Galleri actually had cancer. Galleri is a multi-cancer early detection test. However, in the latest analysis, the figure, known as the positive predictive value, has fallen to 38.0%. This suggests that the diagnostic blood test is less accurate than previously reported.

REPORT

Stem cell divisions, somatic mutations, cancer etiology, and cancer prevention

Cristian Tomasetti^{1,2,*}, Lu Li², Bert Vogelstein^{3,*}

+ See all authors and affiliations

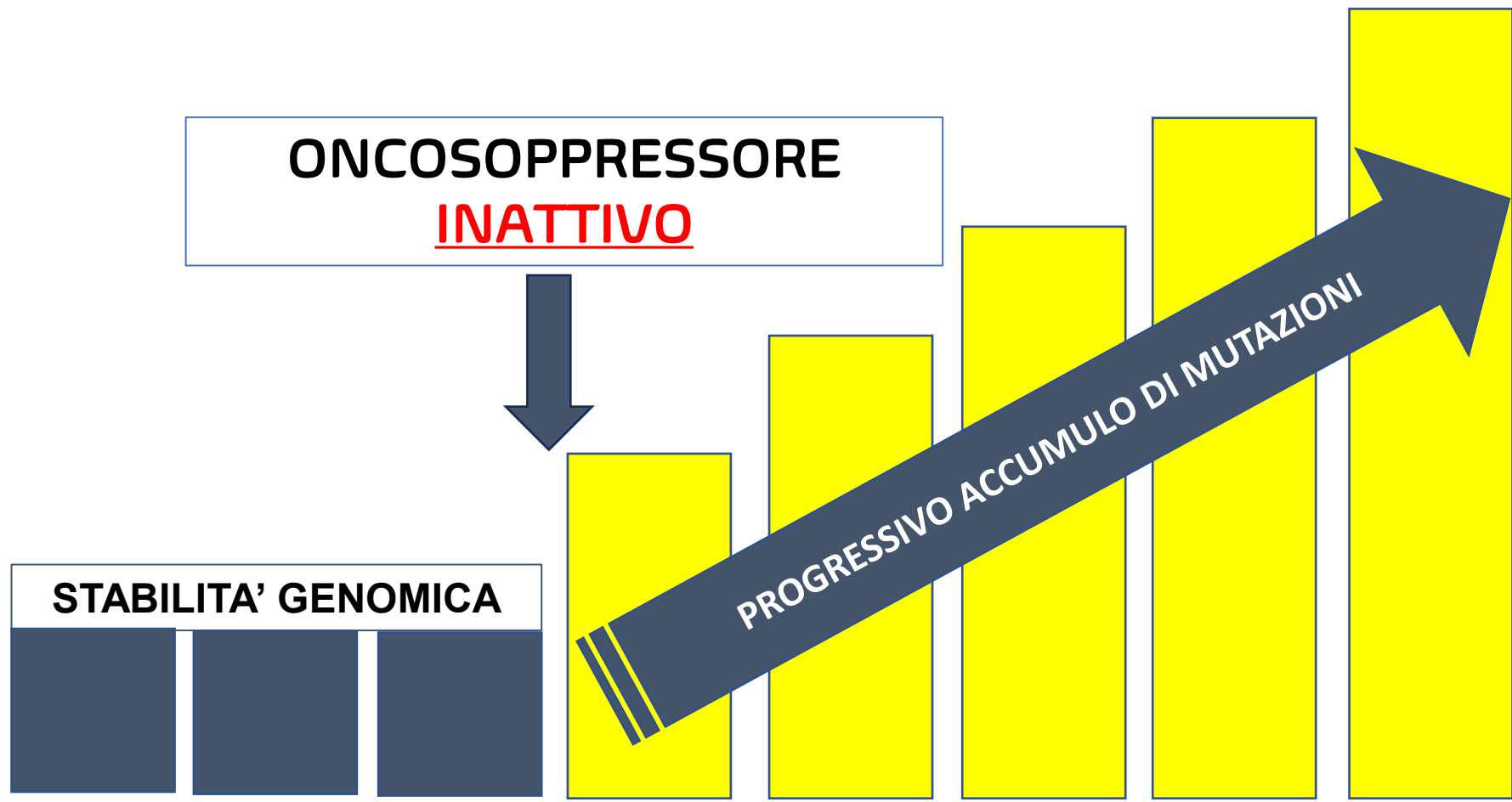
Science 24 Mar 2017:
Vol. 355, Issue 6331, pp. 1330-1334
DOI: 10.1126/science.aaf9011

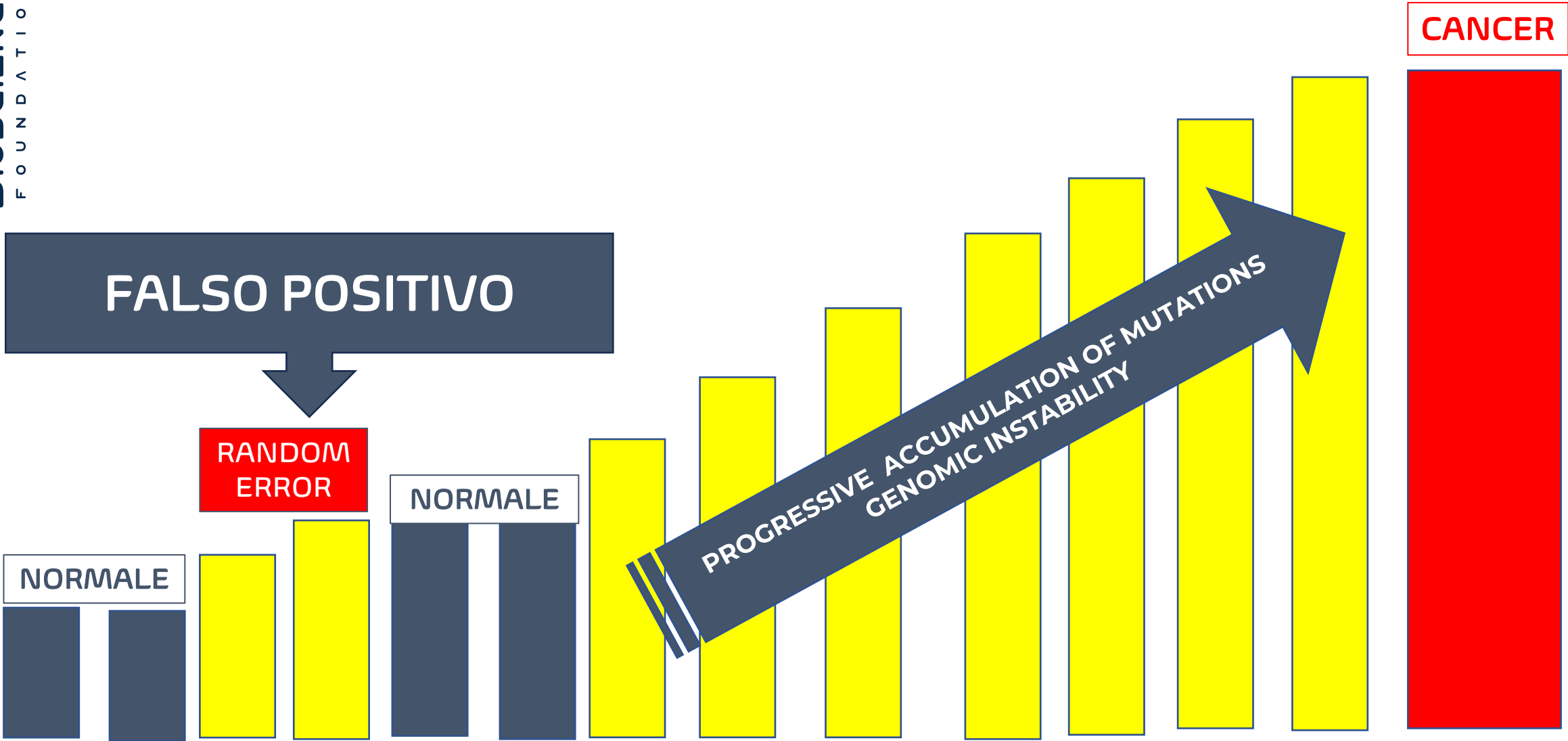
HIGH SINGLE SOMATIC MUTATION can be a simply random errors and is no helpful for cancer early detection

INSTABILITA' GENOMICA

CANCRO

BIO SCIENCE
FOUN D A T I O N





ARTICLE

Open Access

Cell-free DNA analysis in healthy individuals by next-generation sequencing: a proof of concept and technical validation study

Ilaria Alborelli¹, Daniele Generali^{2,3}, Philip Jermann¹, Maria Rosa Cappelletti², Giuseppina Ferrero², Bruna Scaggiante⁴, Marina Bortul³, Fabrizio Zanconati³, Stefan Nicolet¹, Jasmin Haegele^{1,11}, Lukas Bubendorf¹, Nicola Aceto⁵, Maurizio Scaltriti^{6,7}, Giuseppe Mucci⁸, Luca Quagliata^{1,12} and Giuseppe Novelli^{9,10}

- Institute of Pathology, University Hospital Basel, Switzerland
- Department of Medical Surgery, University of Trieste, Italy
- Cancer Metastasis Laboratory, University of Basel, Switzerland
- Memorial Sloan Kettering Cancer Center, New York, USA
- Bioscience Institute, San Marino
- Department of Biomedicine, University of Rome, Italy
- Novartis Institutes, Biomedical Research, Basel, Switzerland

BIOPSIA LIQUIDA

- ❑ cfDNA – DNA libero circolante

- ❑ ctDNA – DNA tumorale circolante

- ❑ CTC – cellule tumorali circolanti

GENOMICA NELLA PREVENZIONE DEL CANCRO

DNA



MUTAZIONI
GERMINALI
EREDITARIE



CONDIZIONE
PREDISPONENTE

cf DNA

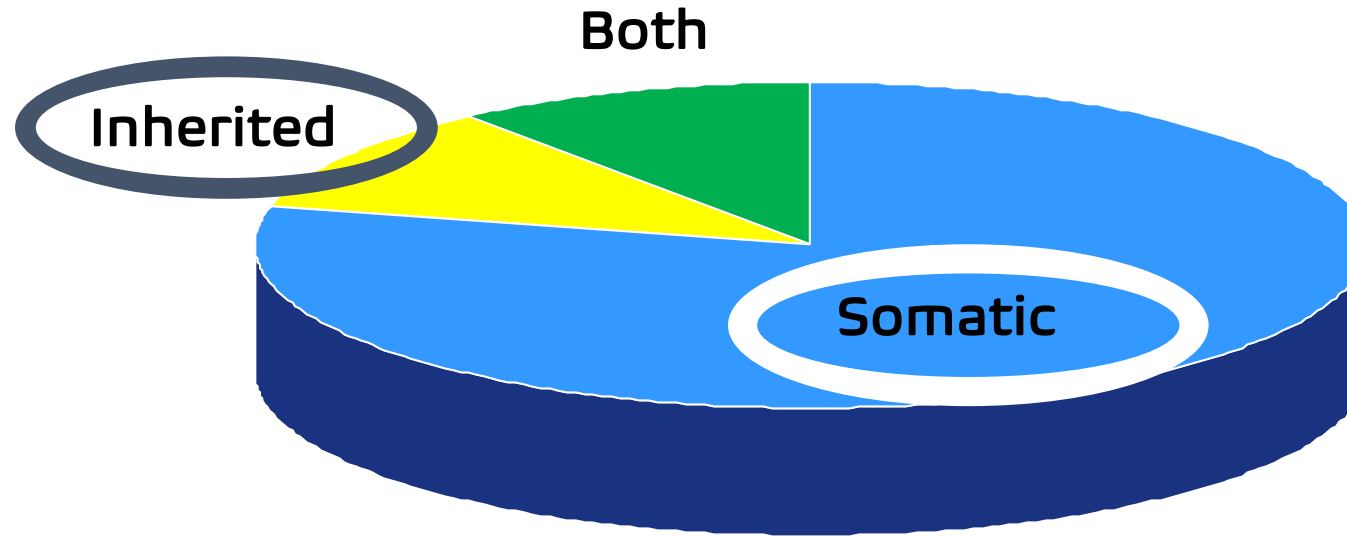


MUTAZIONI
SOMATICHE
ACQUISITE



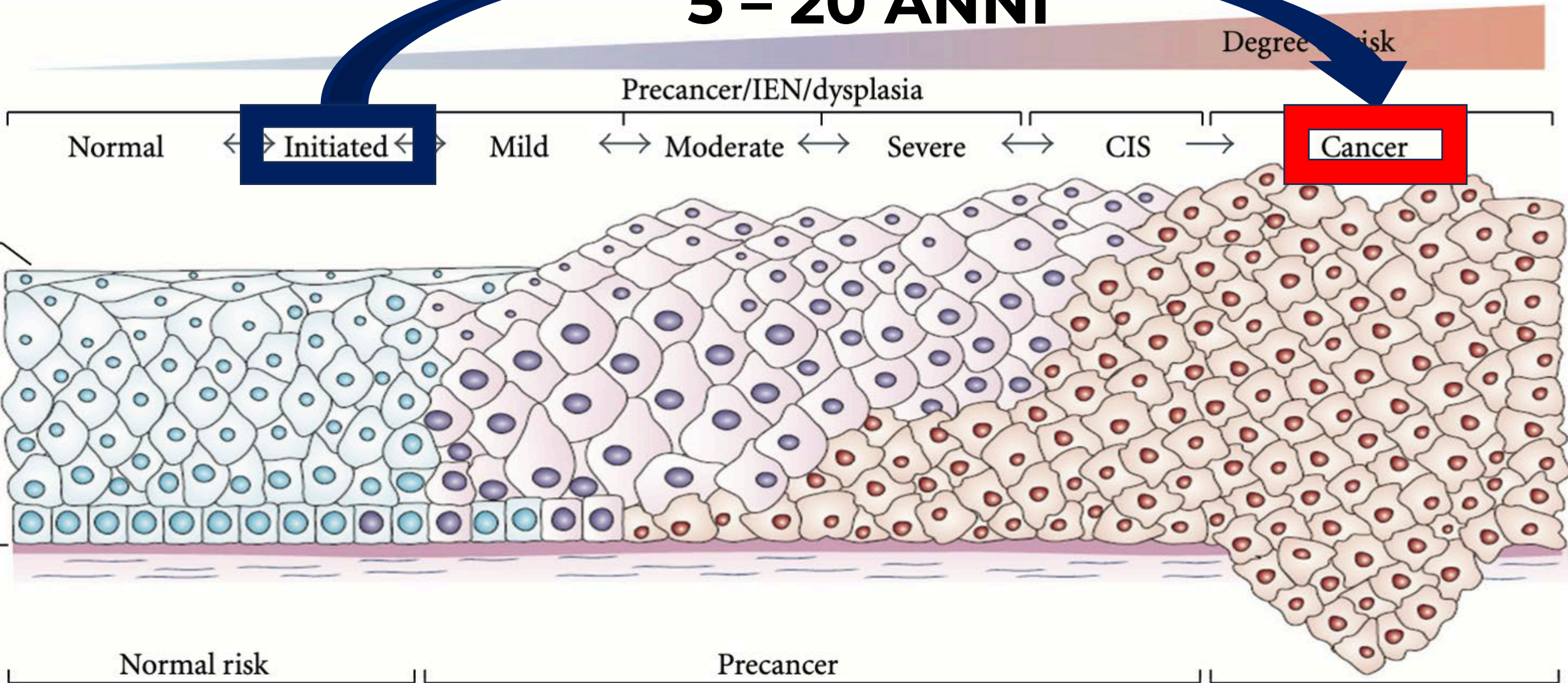
CONDIZIONE
DRIVER / PRODROMICA

MUTAZIONI SOMATICHE/GERMINALI E CANCRO

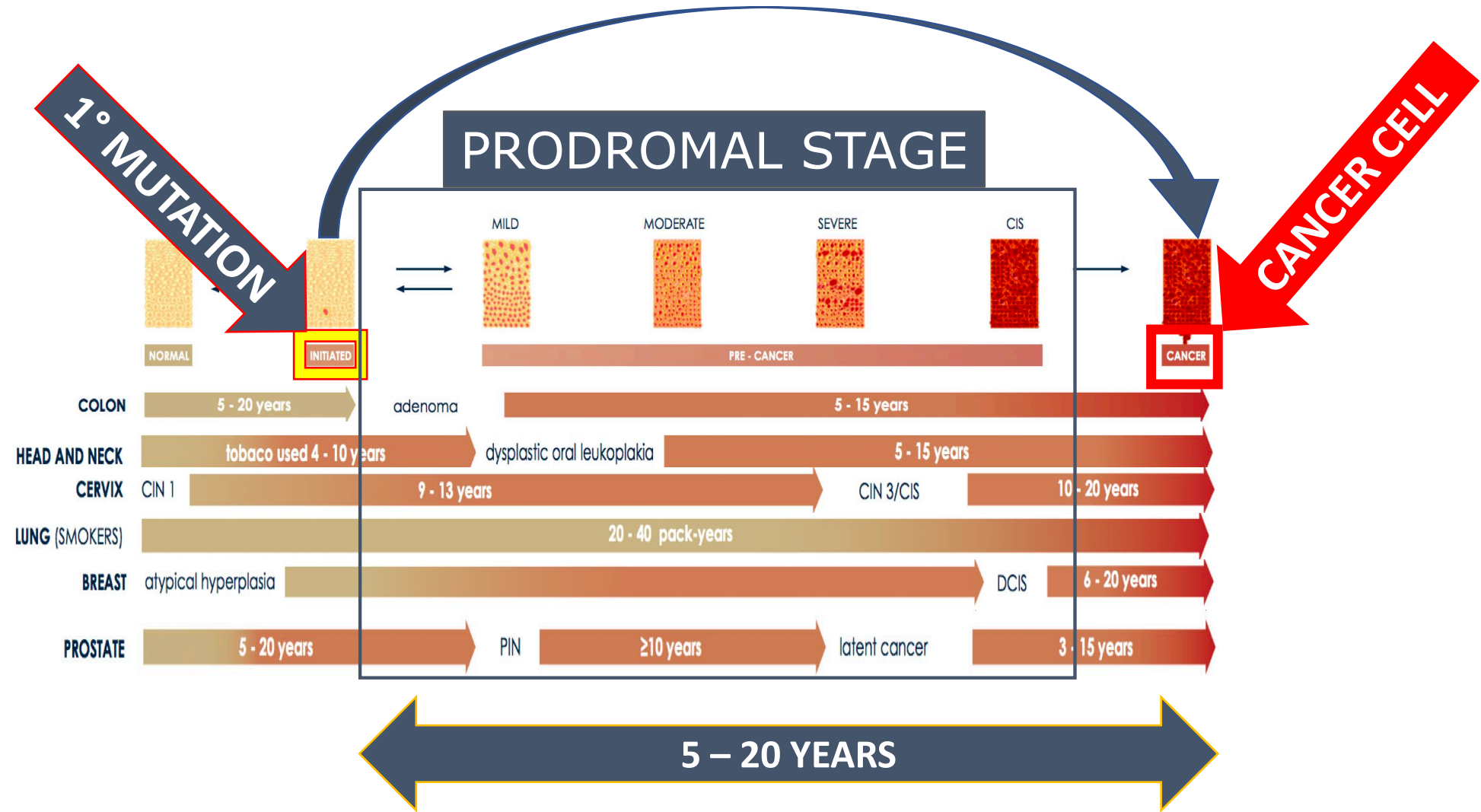


- ❑ 5 –10% DEI TUMORI HA COMPONENTE EREDITARIA
- ❑ LE MUTAZIONI SOMATICHE SONO INDISPENSABILI PER LO SVILUPPO DEL CANCRO

5 - 20 ANNI

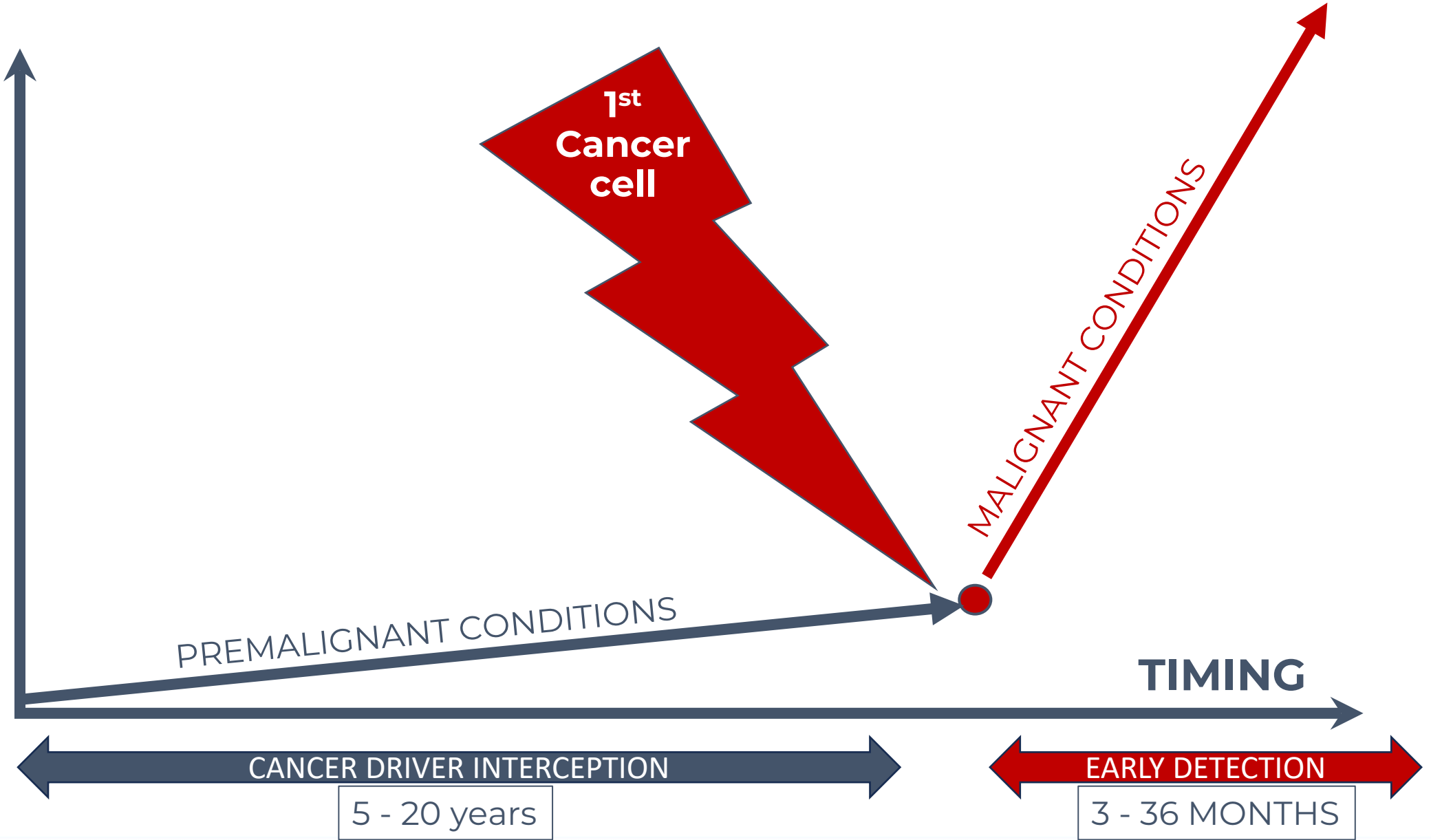


TIMING OF CANCER DEVELOPMENT



BIOSCIENCE FOUNDATION

CANCER DEVELOPMENT

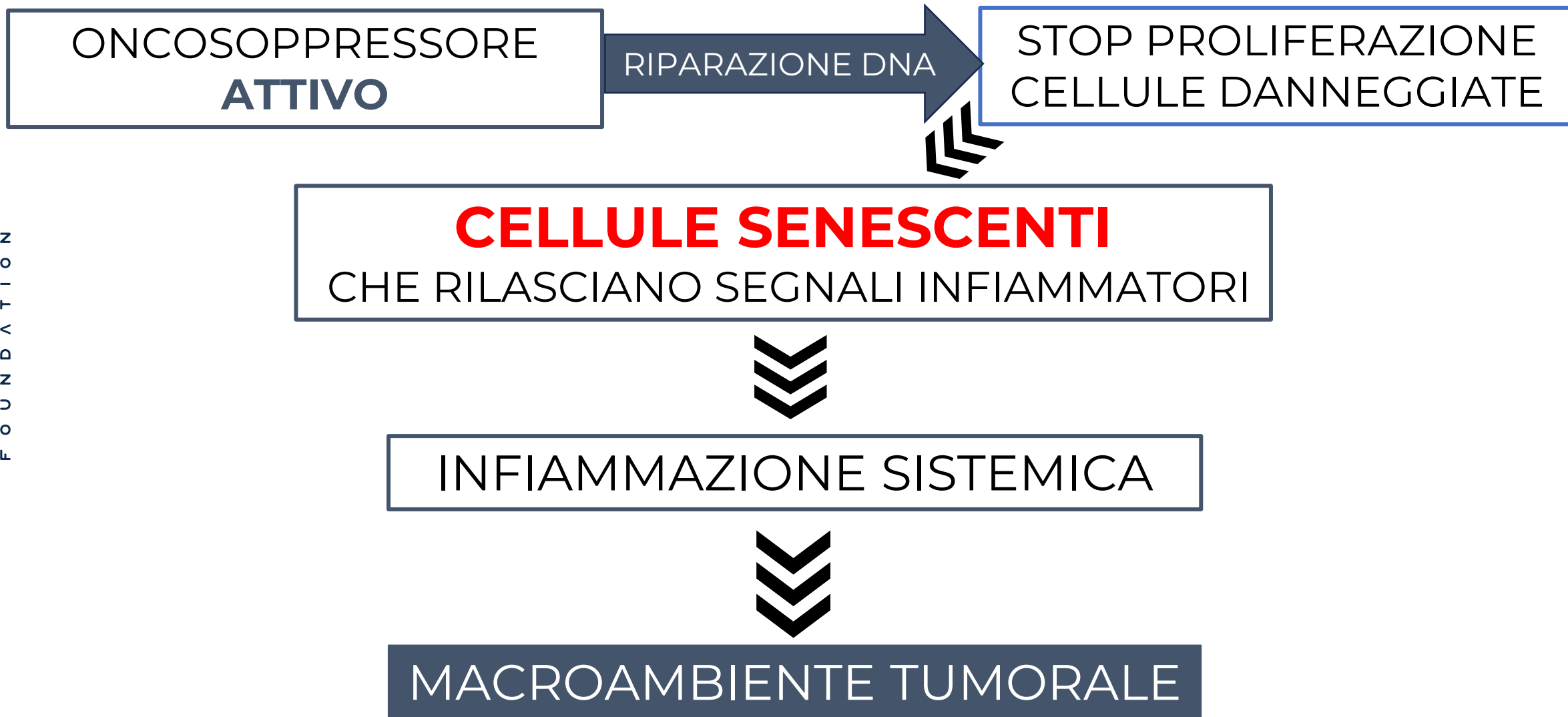


Instabilità Genomica

HELI  BALANCE

MACROAMBIENTE

L'interazione sistemica del
microambiente con altri organi e
sistemi dell'organismo



MANUTENZIONE DEL MACROAMBIENTE

RIMOZIONE DI CELLULE
SENESCENTI



*AZIONE SENOLITICA DEL
SISTEMA IMMUNITARIO*

VALUTARE PRESENZA DI
CELLULE SENESCENTI



*MISURAZIONE LIVELLO
INFIAMMAZIONE SISTEMICA*

VALUTARE EFFICIENZA
SISTEMA IMMUNITARIO



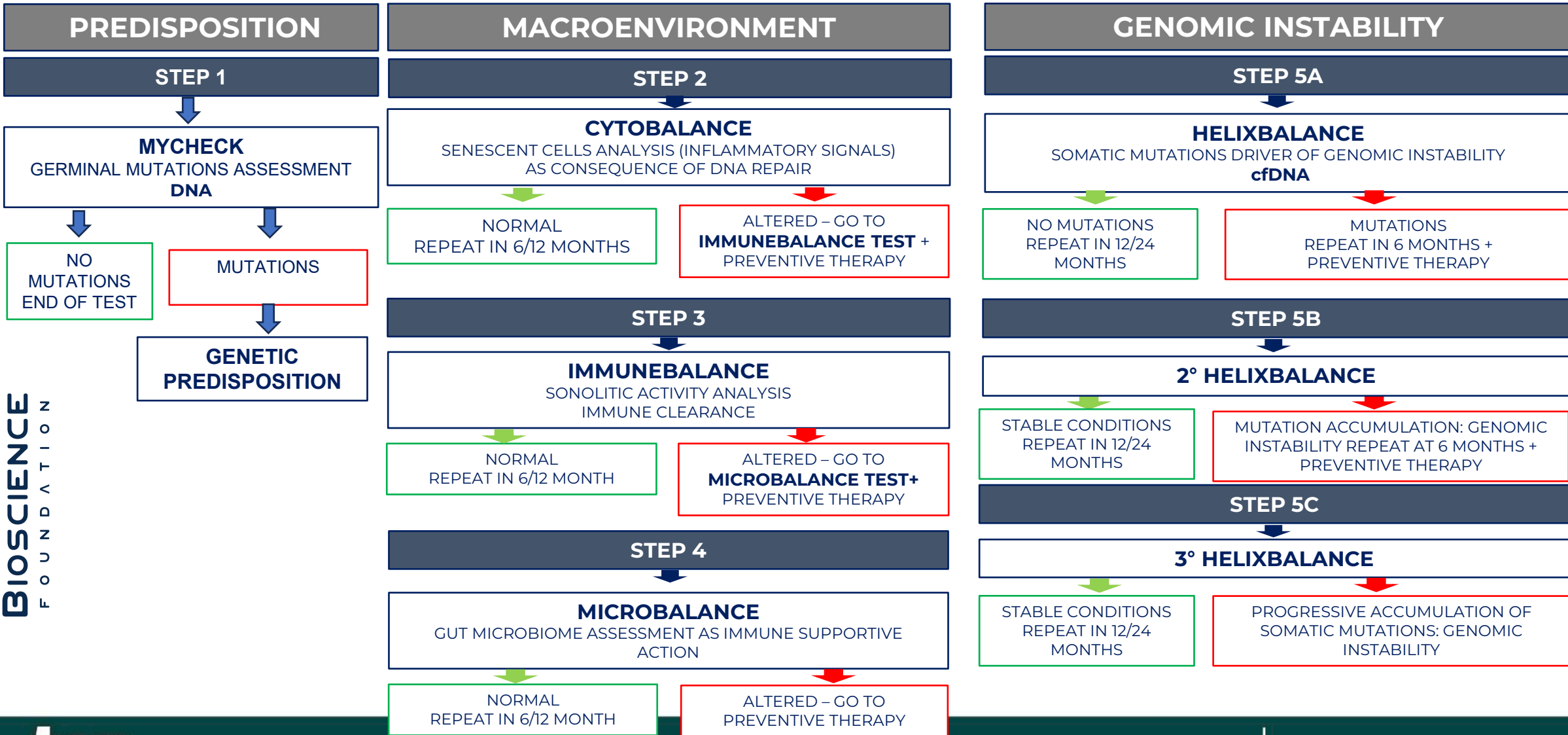
*MISURA BILANCIAMENTO
SISTEMA IMMUNITARIO*

VALUTARE SUPPORTO
SISTEMA IMMUNITARIO



*MISURA EQUILIBRIO
MICROBIOMA INTESTINALE*

FLOW CHART CANCER DRIVER INTERCEPTION



BIO SCIENCE
F O U N D A T I O N

8

BIOSCIENCE
FOUNDA T I O N

Immunodeficienza
IMMUNE BALANCE®

Infiammazione Cronica
CYTOBALANCE®

Instabilità
Genomica

HELI X BALANCE

Squilibrio Batterico
MICROBALANCE®

top
ten
in gastroenterologia

24-25 NOVEMBRE 2023
BERGAMO

9

CHRONIC INFLAMMATION

GENETIC INSTABILITY

IMMUNE DEFICIENCY

BACTERIAL IMBALANCE



SAFETY ZONE

BIO SCIENCE
FOUN D A T I O N

top
ten
in gastroenterologia

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BERGAMO

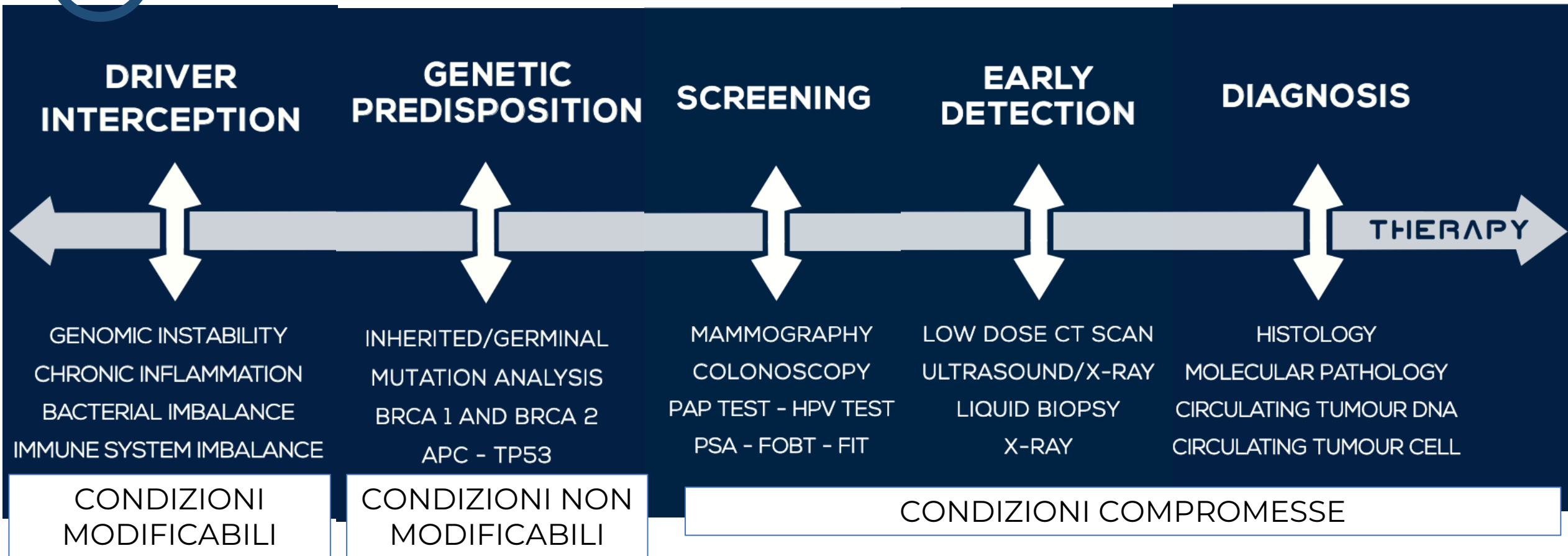
LAVORI SCIENTIFICI PUBBLICATI SU RIVISTE SCIENTIFICHE
PEER-REVIEWED



National Library of Medicine
National Center for Biotechnology Information



<input type="checkbox"/> GENOMIC INSTABILITY – CANCER	16.700
<input type="checkbox"/> INFLAMMATION – CANCER	86.800
<input type="checkbox"/> IMMUNE DEFICIENCY – CANCER	41.800
<input type="checkbox"/> MICROBIOME – CANCER	11.300

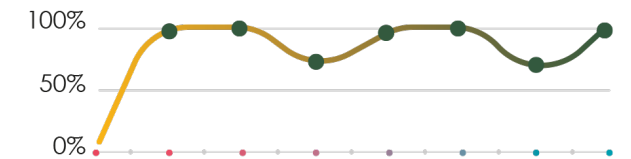
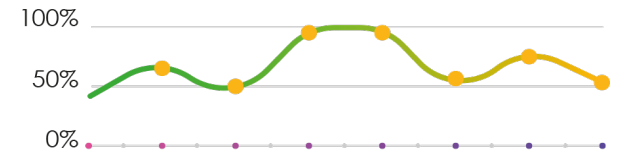
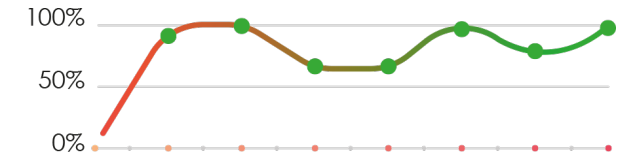
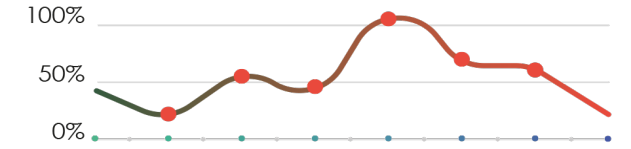


**INSTABILITÀ
GENOMICA**

**INFIAMMAZIONE
SISTEMICA**

**DISBIOSI
INTESTINALE**

**SQUILIBRIO
IMMUNITARIO**



CHEMOPREVENZIONE

uso di agenti chimici o biologici per prevenire o fermare la formazione di tumori maligni

REVIEW ARTICLE

[View Article Online](#)
[View Journal](#)



Cite this: DOI: 10.1039/c5cs00705d

The challenges for cancer chemoprevention

Lewis K. Penny and Heather M. Wallace*

Cancer chemoprevention: a rapidly evolving field

W P Steward^{*,1} and K Brown¹

Chemoprevention: First line of defence

Lauren Gravitz



National Library of Medicine
National Center for Biotechnology Information



❑ **CANCER CHEMOPREVENTION** - 24,586 RESULTS



National Library of Medicine
National Center for Biotechnology Information

ClinicalTrials.gov

❑ **CANCER CHEMOPREVENTION** - 355 STUDIES

- 226 Completed
- 38 Terminated

AGENTI CHEMOPREVENTIVI BIOLOGICI

- Berberina
- Coenzima Q10
- Cucrumina
- EGCG
- Glucosamine
- Glycine
- Lycopene
- Lithium
- Melatonina
- NAD+
- Nicotinamide Riboside
- NMN Nicotinamide M.
- OMEGA3
- Pterostilbene
- Puerarin
- Quercetina
- Resveratol
- Saponine
- Selenio
- Spermidine

US FDA APPROVED AGENTS FOR CANCER RISK REDUCTION

Table 1. US FDA approved agents for cancer risk reduction

Drug	Cancer type	Mechanism	Targeted cohort
Tamoxifen	Breast	SERM: Selective estrogen receptor modulator	Women with DCIS (ductal carcinoma in situ) after breast surgery and radiation Women at high risk for breast cancer ^a
Raloxifene	Breast	SERM	Postmenopausal women at high risk for invasive ^b breast cancer
Porfimer sodium + photodynamic therapy (PDT) & omeprazole	Esophageal	Production of oxygen-free radicals kills nearby cancer cells of precancerous tissues after exposure to light	Males and females with high-grade dysplasia in Barrett esophagus
Aspirin	Colorectal	Induces apoptosis and interrupts prostaglandin production through inhibition of cyclooxygenase enzymes	Adults ages 50-59 years ^c
Celecoxib	Colorectal	Induces apoptosis and interrupts prostaglandin production through selective inhibition of the cyclooxygenase-2 enzyme	Males and females ≥18 years with FAP (Familial adenomatous polyposis)
Bacillus Calmette-Guerin (BCG)	Bladder	Mechanism unknown; induces local immune reaction against tumor	Males and females with CIS (carcinoma in situ) of the urinary bladder
Valrubicin	Bladder	Interferes with DNA synthesis and leads to cell death	Males and females with BCG-refractory CIS
Fluorouracil	Skin	Interferes with DNA synthesis and leads to cell death	Males and females with multiple actinic keratoses
Diclofenac sodium 3%	Skin	Mechanism unknown	Males and females with actinic keratoses
5-aminolevulinic acid + PDT	Skin	Solution kills precancerous cell when exposed to light	Males and females with actinic keratoses of the face or scalp
Imiquimod	Skin	Enhances immune response and promotes apoptosis	Immunocompetent males and females with actinic keratoses of the face or scalp
Ingenol mebutate	Skin	Induces primary necrosis	Males and females with actinic keratoses on the face, scalp, trunk and extremities

^a"High risk" defined as women at least age 35 years with a 5-year predicted risk of breast cancer ≥ 1.67% as calculated by the Gail model.

^b"High risk" defined as at least one breast biopsy showing lobular carcinoma in situ (CIS) or atypical hyperplasia, one or more first-degree relatives with breast cancer, or a 5-year predicted risk of breast cancer ≥ 1.66% (based on the modified Gail model).

^cLow-dose aspirin use for the primary prevention of cardiovascular disease and colorectal cancer in adults ages 50-59 years who have a 10% or greater 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years.

TERAPIA PREVENTIVA

INSTABILITA' GENOMICA

NADH (SyncoZymes)
ES THE VERDE 94% EGCG (Teavigo®)
COLINA BITARTRATO
PLV SELENIO L-METIONINA
ACIDO FOLICO
VIT B3/PP/NICOTIN
VIT B12/CIANOCOBALAMINA
VIT D3
VIT E

INFIAMMAZIONE SISTEMICA

ES BERBERIS ARISTATA 97-85% BERBERINA gran
QUERCITINA GRANUALRE
SELENIO L METIONINA
Coenzima Q10

SISTEMA IMMUNITARIO

GLICINA
Miritto e.s. tit. 20% PTEROSTILBENE
ES RESVERATROLO 98% POLIGONUM
SPERMIDINA (98% sale, 57% sperimidina)
Vitamina C (Acido Ascorbico)

DISBIOSI

PLV BETAINE BASE ANIDRA (TRIMETILGLICINA)
ES BERBERIS ARISTATA 97-85% BERBERINA gran
ES CURCUMA 95%-CURCUMIN C3 COMPLEX DC (granulare)
GLUCOSAMINA
VITAMINA K2

CHEMOPREVENZIONE E' ANCHE SOMMINISTRAZIONE

Sia la carenza che l'eccesso di micronutrienti, come ad esempio:

- **Beta-carotene**
- **Acido folico**
- **Vitamina A e E**
- **Selenio**

possono causare danni al genoma equivalenti all'esposizione a dosi significative di agenti chimici cancerogeni, radiazioni ultraviolette e radiazioni ionizzanti.

GRAZIE

Giuseppe Mucci

top
ten

in gastroenterologia

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BERGAMO

HOTEL EXCELSIOR SAN MARCO
Piazza della Repubblica, 6

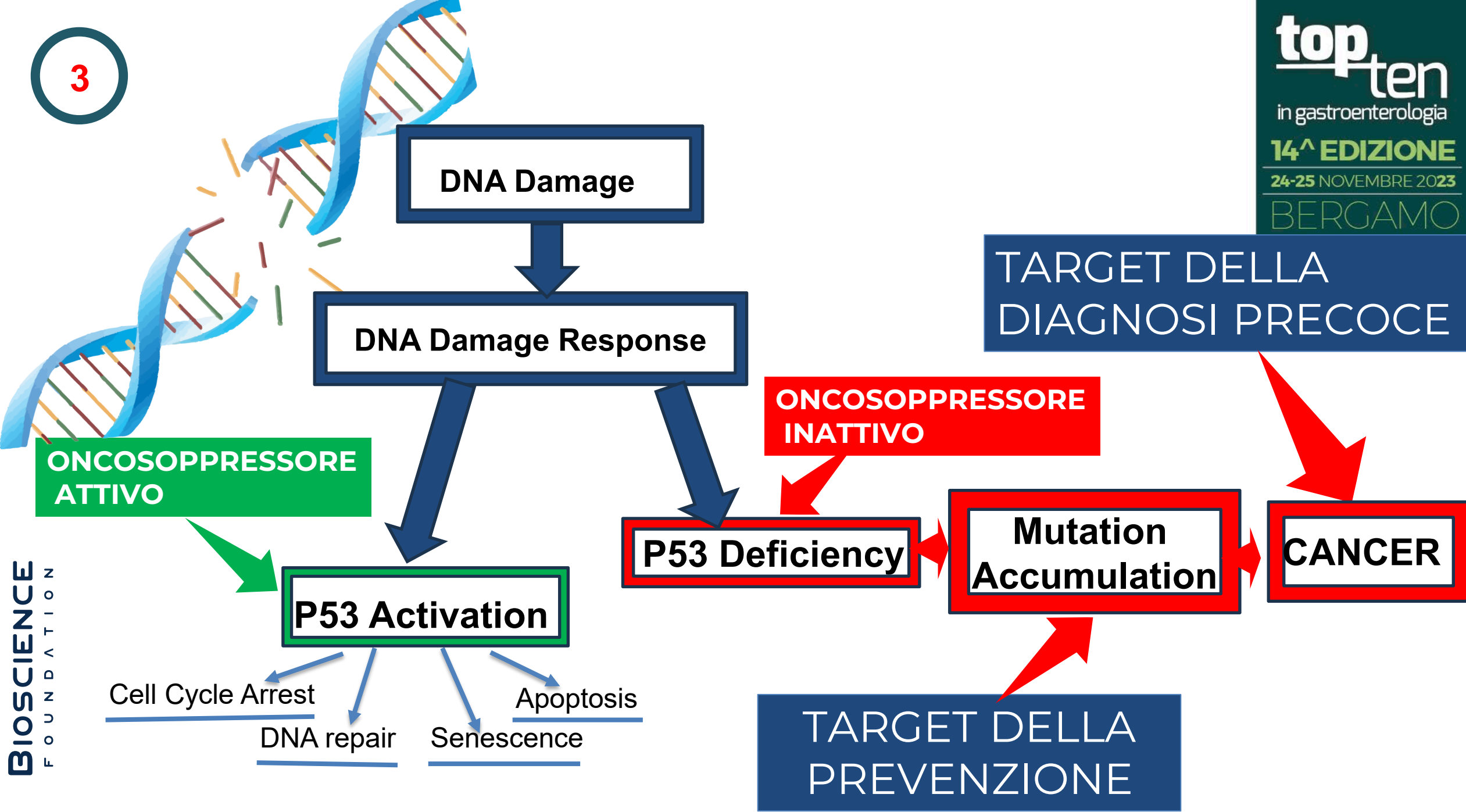
TOP TEN Slides

MODELLI DI PREVENZIONE : CARDIO vs CANCRO





3



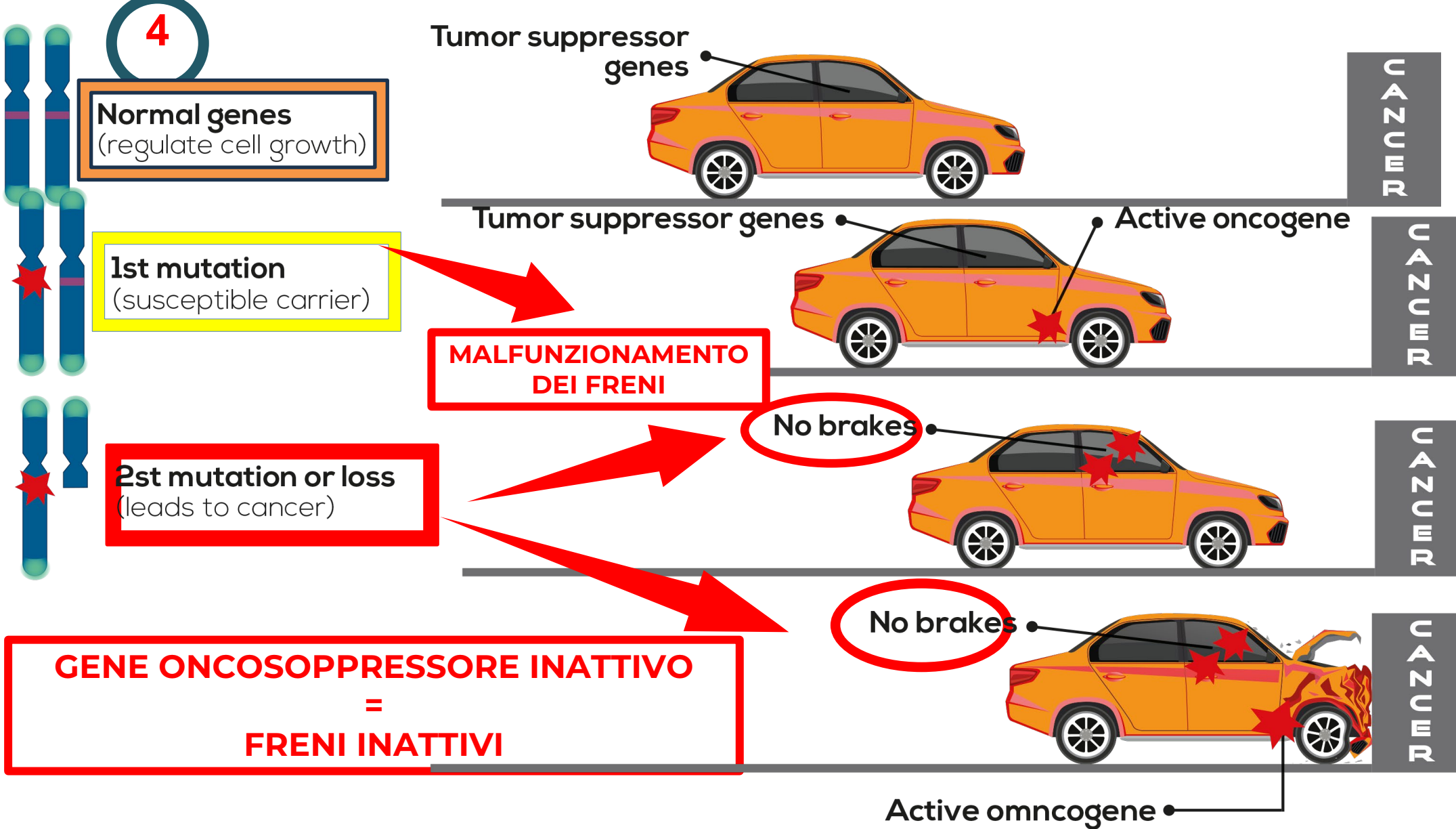
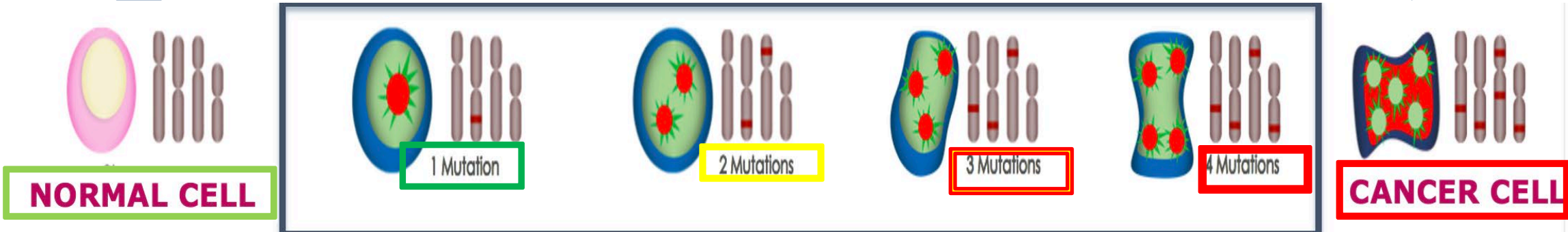


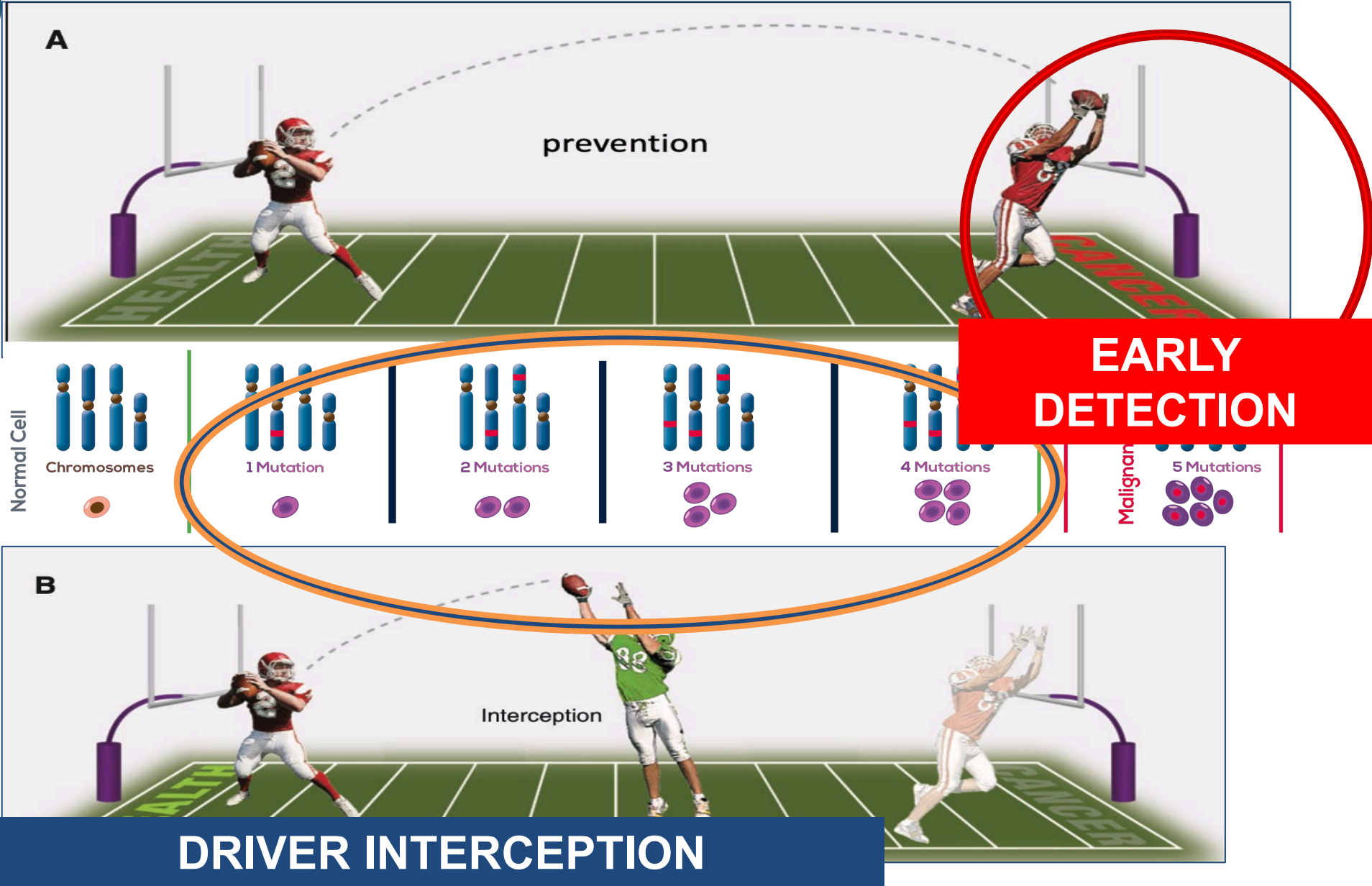
Image courtesy of the National Cancer Institute

HEALTHY CONDITIONS WITHOUT SYMPTOMS



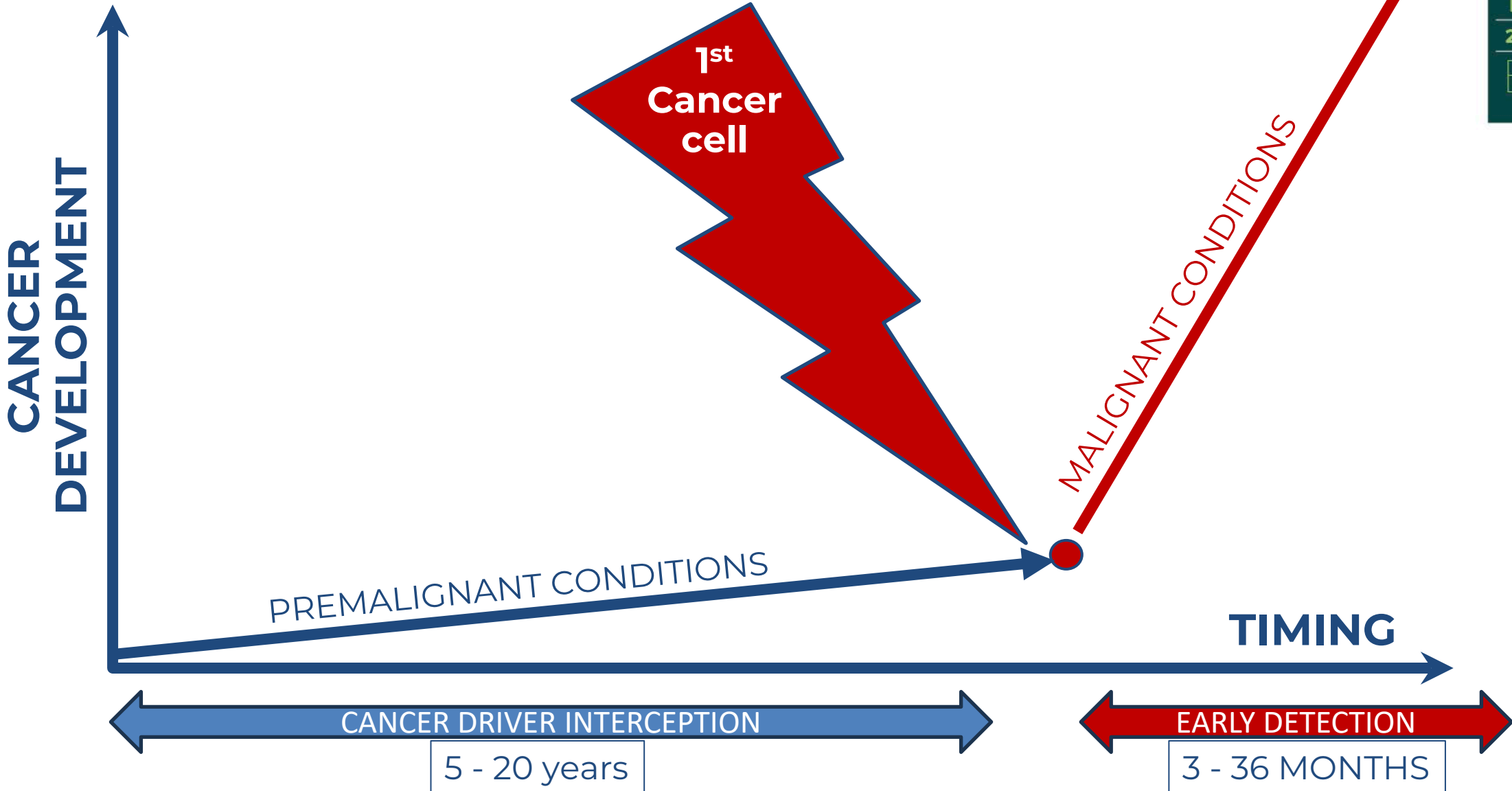
PROGRESSIVE ACCUMULATION OF SOMATIC MUTATION

CANCER DRIVER CONDITIONS
GENETIC INSTABILITY



Adapted from: Blackburn EH. Cancer Prev Res (Phila). 2011 Jun;4(6):787-92.

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