



Tomato-Derived Functional Foods with Enhanced Antitumor Activity

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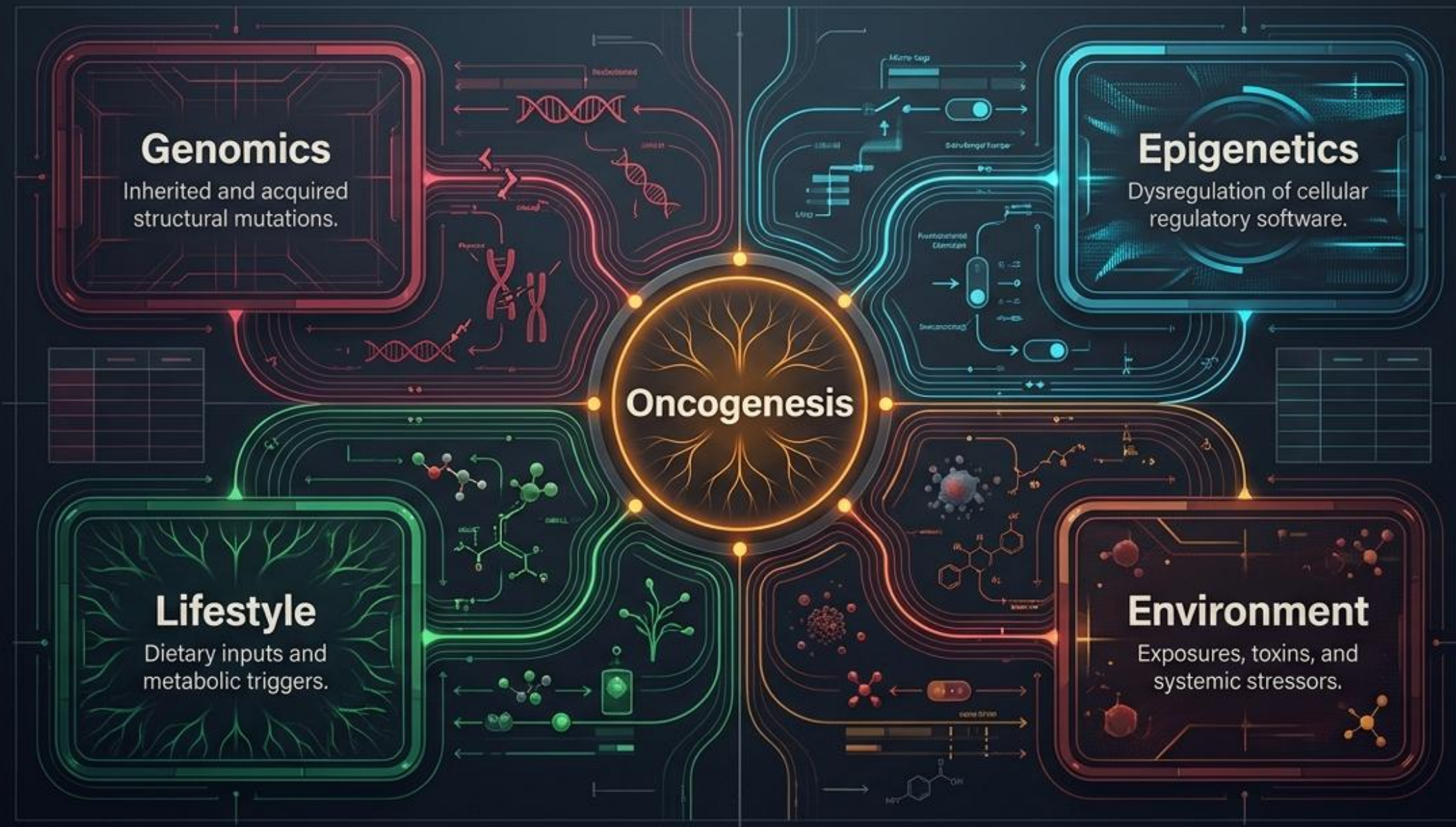
This project has received funding from the European Union's PRIMA Programme under grant agreement no. 2032



Genetic Basis of Cancer

Cancer is a multifactorial disease driven by genomic mutations, epigenetic dysregulation, lifestyle, and environmental exposures.

Oncogenesis is a System Failure

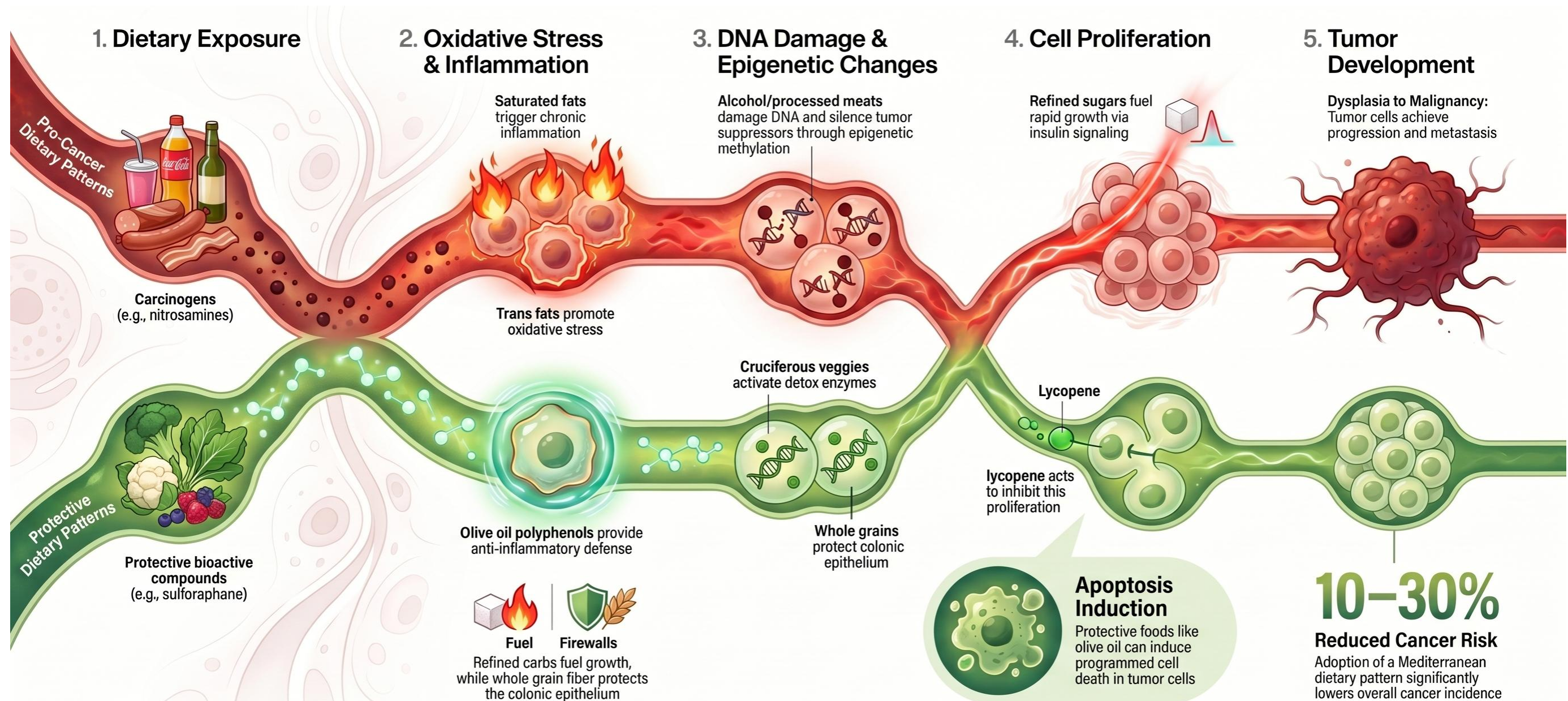


How Eating Habits Influence Cancer Development

Longevity and Wellness / Nutrigenetics and Nutrigenomics

Diet is one of the most modifiable risk factors in cancer development.

What we eat can either promote or suppress tumor initiation, progression, and metastasis through multiple biological mechanisms.



The Mediterranean Diet as a Functional Food Framework

A Complex Protective System

The Mediterranean Diet (MedDiet)—rich in fruits, vegetables, whole grains, legumes, nuts, olive oil, and moderate fish—is consistently linked to reduced risk of several cancers, neurodegeneration, and metabolic disease.

Its protection arises from the **synergistic interplay** of bioactive compounds rather than any single nutrient.

Functional foods enriched with Mediterranean bioactives represent a promising frontier in food science. Snack bars and fruit leathers—compact, ready-to-eat formats—offer versatile vehicles for delivering lycopene, flavonoids, and antioxidants with demonstrated protective effects against chronic diseases including cancer, neurodegeneration, and diabetes.

Key Bioactive Contributors

Tomatoes

Lycopene, flavonoids, vitamins C & E — potent antioxidants with anti-cancer evidence

Olives & Olive Oil

Polyphenols and oleocanthal — anti-inflammatory and neuroprotective

Herbs & Legumes

Gut-health support, mineral density, and bioactive peptides



FunTomP Project: Enriched Tomato Snack Products

Developed at Middle East Technical University (METU), the FunTomP project engineers Mediterranean-inspired functional snack bars and tomato leathers enriched with tomato peel powder, olive powder, and two novel plant-derived protein sources.

Optimized Formulation*

Ingredient	Amount (g)
Tomato juice	100
Pea Protein Isolate	10
Tomato powder	10
Olive powder	2
LMP (Low Methoxyl Pectin)	2
Rosemary	1
Thyme	1
Red pepper powder	1
Salt	1

**This formulation received the highest score in sensory testing (SELUZ panel).*

Leather Formulation (per 100 g tomato juice base)

Ingredient	Amount (g)
Tomato juice	100
Pea Protein Isolate	0.5
Olive powder	0.5
Salt	0.5
Basil (spice)	0.5

 RuBisCO is a plant protein which is stored in all green leaves. It is responsible for the process of photosynthesis and is considered to be the most abundant protein present on earth. It has high nutritional quality, antioxidant activity, and high digestibility

Project: Enriched Tomato Snack Products

Snack Bar:

Three formulation variants

- TS
- TS+O+P
- TS+O+R

were prepared to systematically evaluate the contribution of each enrichment ingredient.



Leather:

Four formulation variants

- TS
- TS+O,
- TS+O+P
- TS+O+R

were prepared to systematically evaluate the contribution of each enrichment ingredient.

Anti-Cancer Activity: MTT Cell Viability Assays

Cytotoxic potential of tomato leather and snack bar formulations was evaluated using MTT assays across four human cancer cell lines at 1–10 mg/mL over 24 hours.

Cell Lines Tested

HT-29

Colorectal adenocarcinoma

Caco-2

Colorectal carcinoma (intestinal model)

U87MG

Glioblastoma (brain tumor)

SK-MEL30

Melanoma



Caco-2 vs HT-29: Cell Line Comparison

Caco-2 — Highly differentiated · Enterocyte-like · Strong barrier

HT-29 — Poorly differentiated · Colonic/tumor-like · Mucus-producing

Genetic Profile

Feature	Caco-2	HT-29
BRAF mutation	Absent	Present (V600E)
PIK3CA mutation	Rare/absent	Frequent
TP53 status	Mutated	Mutated
Wnt signaling	Active	Active
Genetic stability	Stable	Heterogeneous

Morphology & Structure

Feature	Caco-2	HT-29
Differentiation	Highly differentiated	Poorly differentiated
Morphology	Polarized, columnar	Heterogeneous
Polarization	Strong	Weak-moderate
Microvilli	Well-developed	Poor/absent
Tight junctions	Robust	Less pronounced

Functional Properties

Feature	Caco-2	HT-29
Barrier (TEER)	High	Moderate/low
Mucus production	Minimal	High
Goblet cells	No	Yes (inducible)
Enzyme expression	High	Low
Drug transporters	Consistent	Variable

Typical Applications

Caco-2: Permeability · Absorption · Barrier models

HT-29: Mucus studies · Cancer biology · Inflammation

Ongoing Studies: Molecular Genetic Analyses

Building on cytotoxicity findings, ongoing studies aim to elucidate the molecular mechanisms underlying the anti-cancer activity of FunTomP formulations.

Cell Death Pathway Analyses

Apoptosis Detection: Annexin V/PI staining via flow cytometry to distinguish early/late apoptosis from necrosis

Caspase Activation: Caspase-3, -8, -9 activity assays to identify intrinsic vs extrinsic apoptotic pathways

Cell Cycle Analysis: PI-based flow cytometry to detect G1/S/G2-M arrest induced by formulations

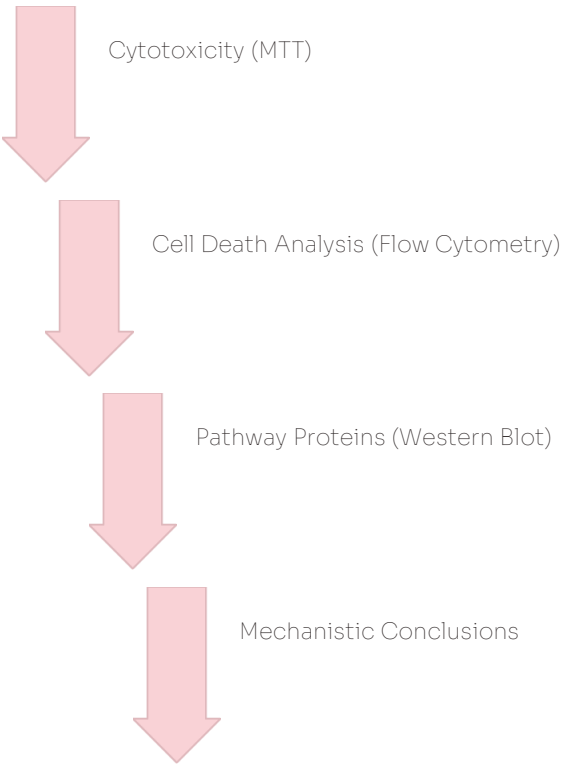
Protein Expression: Western Blot (WB)

Pyroptotic Proteins: GSDMD NLRP3

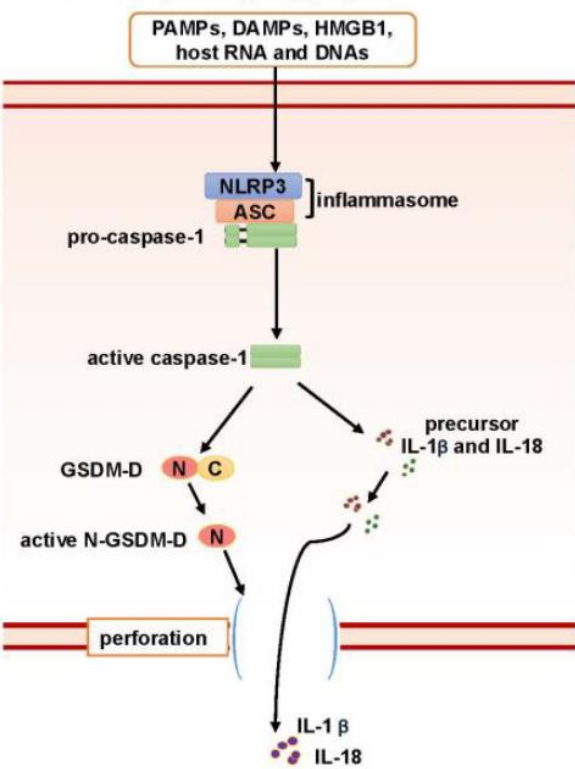
Cell Cycle Regulators: p21, p53, Cyclin D1, CDK4/6 expression changes

Caspase Cascade: Cleaved caspase 3, -1

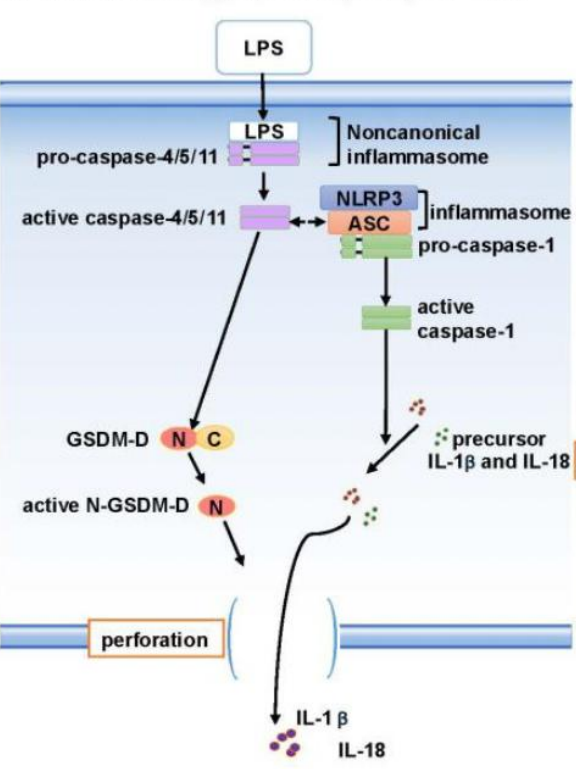
Survival Pathways: PI3K/AKT/mTOR and MAPK/ERK phosphorylation status



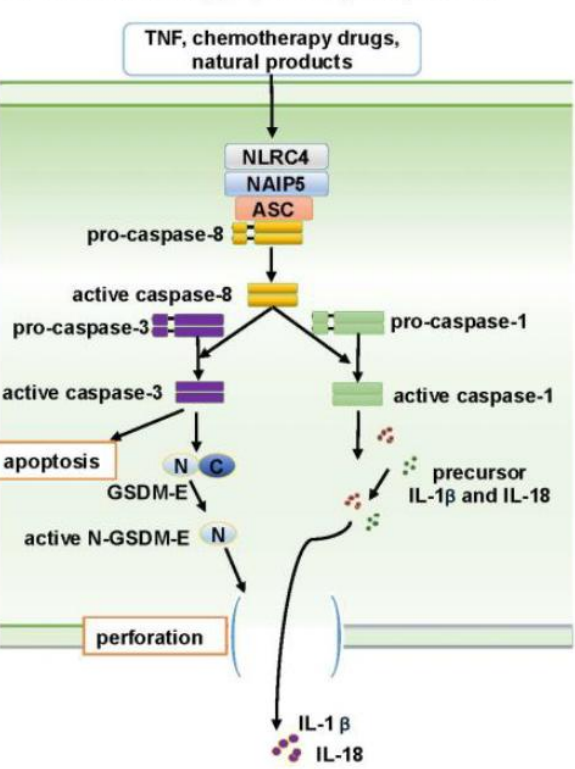
A. Canonical pathway of pyroptosis



B. Noncanonical pyroptosis by caspase-4/5/11



C. Noncanonical pyroptosis by caspase-3/8



Jhonson ED et al. , 2025, Biomolecules

Key Takeaways & Future Directions



Mediterranean Ingredients Work

Tomato, olive, and herb enrichment delivers measurable anti-cancer bioactivity in food matrices



RuBisCO Shows Promise

The R+O snack bar was most cytotoxic across all four cancer lines — a compelling case for RuBisCO as a functional ingredient



Molecular Targets and Bioactive Molecules

Further molecular analyses should be performed to clarify the molecular signaling pathways which are associated with the cell death mechanisms.





Thank You for Your Attention!

Questions & Discussion

Functional Foods & Cancer Research