Metodo Di Bella
Biological multitherapy of tumors
Scientific Evidence
Documentation in biomedical databases of the antitumor efficacy of the individual active ingredients of MDB and their simultaneous and synergistic use in cancer prevention and therapy
Documentation on Pub Med and ResearchGate.net of their synergistic use in various tumors related to over a thousand cases favorably treated with MDB updated to 25/09/19


2) **The Synergism of Somatostatin, Melatonin, Vitamins Prolactin and Estrogen Inhibitors Increased Survival, Objective Response and Performance Status In 297 Cases of Breast Cancer**, Dr. Giuseppe Di Bella Translational Biomedicine


6) **Solution of retinoids in vitamin E in the Di Bella Method biological multitherapy.** Di Bella L, Di Bella G. Neuro Endocrinol Lett. 2015 Dec;36(7):661-76.


Cellular multiplication protidosynthesis

**GH direct acting**
- On the respective plasma, ribosomal and nuclear membrane receptors (GHR)

**GH indirect-action**
- Induction of growth-angiogenesis factors
- Expression of oncogenes
- Epithelium-mesenchymal evolution
- Gene expression of protease and hyaluronidase
- Inhibition of the mechanisms of cellular senescence by action on telomerase

**Direct acting prolactin**
- Interactive D2R membrane receptors with GHR
Central function of the hormone GH in onset and tumor progression.

Mechanism of tumor action through activation of oncogenic GH–dependent growth factors EGF, IGF–1, VEGF.
ONCOGENI: TFF1 e 3: Trefoil factor; HOXA1: Homeobox 1; MAPK: protein chinasi attivate da mitogeno; MMP2 e 9: metalloproteasi 2 e 9; Fibronectina e Vimentina; JAK/STAT: proteine Janus chinasi e le proteine trasduttrici del segnale ed attivatore della trascrizione; Bcl-2: proteina pro-apoptotica; CHOP (gadd 153): C/EBP proteina omologa; SOD: superossido dismutasi; Catalasi; VEGF: fattore di crescita vascolare endoteliale; IGF-1: fattore di crescita insulina simile; EGF: fattore di crescita dell’epidermide; h-TERT: telomerasi

ONCOSOPPRESSORI: μ-catenina; TIMP-1: inibitore tissutale metalloproteasi; Occludina; PTGF-β: fattore di crescita placentare trasformante; Tsp-1: trombospondina
GH and oncogenic effect with positive (for oncogenes) and negative (for oncosuppressors) differential modulation.

<table>
<thead>
<tr>
<th>Promotion of the molecules that support tumour growth</th>
<th>Inhibition of the molecules that counter tumour growth</th>
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<tr>
<td>HOXA1</td>
<td>PTGF-β</td>
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<tr>
<td>JAK/STAT</td>
<td>μ-catenin</td>
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<td>Bcl-2</td>
<td>TIMP-1</td>
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<td>MMP2 e 9</td>
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<td>MAPK pathway</td>
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Survival

TME, Tumour invasion metastases

Angiogenesis

Activation of mitogenic growth factors

Unlimited replication potential

Insensitivity to anti-growth signals
Mitogenic effect inducing neoplastic cell proliferation

Angiogenesis creation of the blood vessel network that enables its nutrient supply

Cancer onset and progression the cancer cell overcomes all natural containment barriers

Fattori di crescita che attivano l’angiogenesi:

FGF  IGF1  HGF  PDGF  VEGF  TGF

Molecole promotrici che interagiscono con i fattori di crescita nell’attivazione dell’angiogenesi:

VIP e-Nos  CM  PGE2  Interl. 8 Anossia- Acidosi

Molecole MDB inibenti sinergicamente l’angiogenesi

MDB - Giuseppe Di Bella
Somatostatin-Octreotide

Therapeutic effect

STOP CELL CYCLE IN G0/G1 with tumor proliferation blocker

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PROLACTIN INHIBITORS

Inhibition of prolactin release by D2R receptor agonists

Bromocriptin
Cabergolin

D2R

α
β
γ

Ca²⁺

K⁺

Ca²⁺

PLC

IP₃

PIP₂

AC

cAMP

PKA

Cell Proliferation Block

Encoplastic Reticulum
Differentiating components of prevention that inhibit mutations

- Retinoids (group A)
- Vitamin B9
- Vitamin E
- Vitamin C
- Vitamin D3
- Condroitinsolfato
Vitamina E

Chemotassi macrofagi

Externalizzazione Fosfatidilserina

PS

PKC-alfa
LDH-A

Differenziazione

Pro-Caspasi 3

Pro-Caspasi 9

Caspasi 9

Cyt. c

ΔΨm

Bax

Bax/Bak

Arresto ciclo cellulare

c-myc

RAR

ROR

VDR

RXR

NF-kB
Acido *trans* retinoico (ATRA)
Ac. Ascorbico

Arresto ciclo cellulare
p21
p27
p53
Bax
Bcl2
Pro-Caspasi
Pro-Caspasi 9
Caspasi 9
Caspasi 3
Cyt. c
ΔΨm
Mitocondrio
Degradazione DNA
Vitamin D3

Effetto anti-proliferativo:
- IGFBP3
- C-myc oncogene
- Blocco EGF

Effetto pro-apoptotico:
- Livelli VEGF e inibizione angiogenesi
- BRCA1
- Fosfolipasi A2 e degradazione DNA
- E-caderine e altre molecole di adesione
- P21, 27 → chinasi ciclina-dipendenti
- Ciclina C e D1

Effetto anti-metastatico:
- ICAM-3 molecole di adesione inibenti
  degradazione barriere ECM
The mechanism of tumor cell mutations explains the temporary effects of oncology, its inability to eradicate solid tumors that become chemo-radio-immuno-resistent by mutation and the need for oncological surgery.

DEVELOPMENT OF LETTERATURE ON MUTATIONS

- **Radman M., Basic Life Sci–SOS, 1975:** *Escherichia coli* possesses an inducible DNA repair system ("SOS repair") which is also responsible for induced mutagenesis. Some characteristics of the SOS repair are (1) it is induced or activated following damage to DNA, (2) it requires *de novo* protein synthesis.

- **Israel L., Theor Biol., 1996:** Tumour progression: random mutations or an integrated survival response to cellular stress conserved from unicellular organisms?

- **Lambert G. et al., Nat Rev Cancer, 2011:** An analogy between the evolution of drug resistance in bacterial communities and malignant tissues.