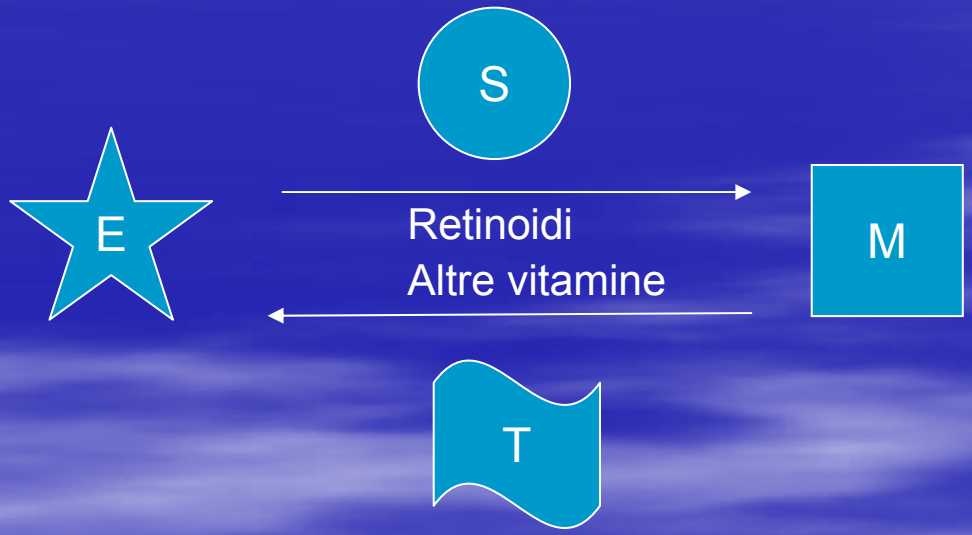
Il Metodo Di Bella

DEFINIZIONE DEL CONCETTO DI VITA

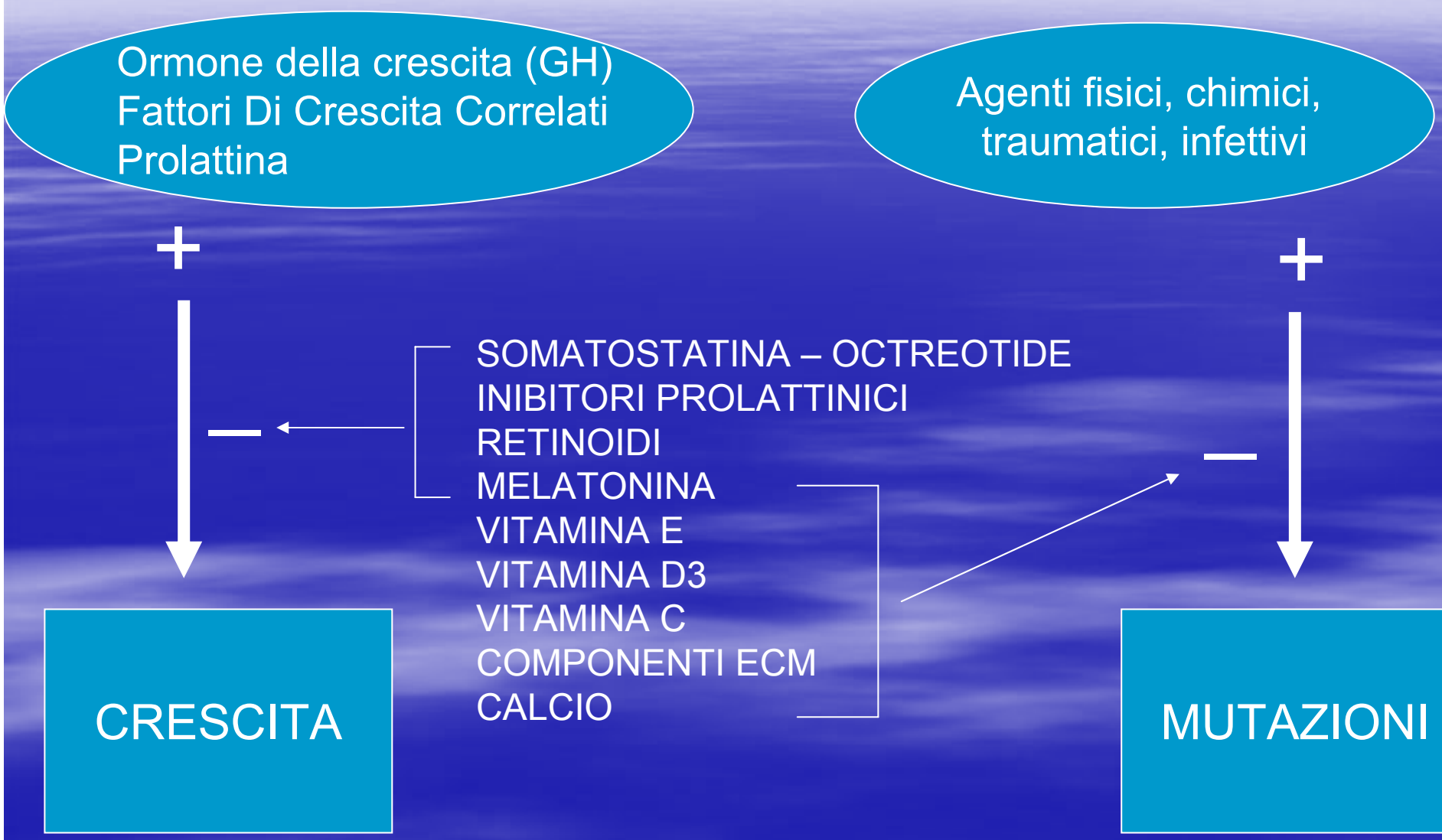
$$\text{Vita} = K \frac{E\ (\text{energia})}{M\ (\text{materia})} \bullet S\ (\text{spazio}) \bullet T\ (\text{tempo})$$

Vita = Equilibrio biologico



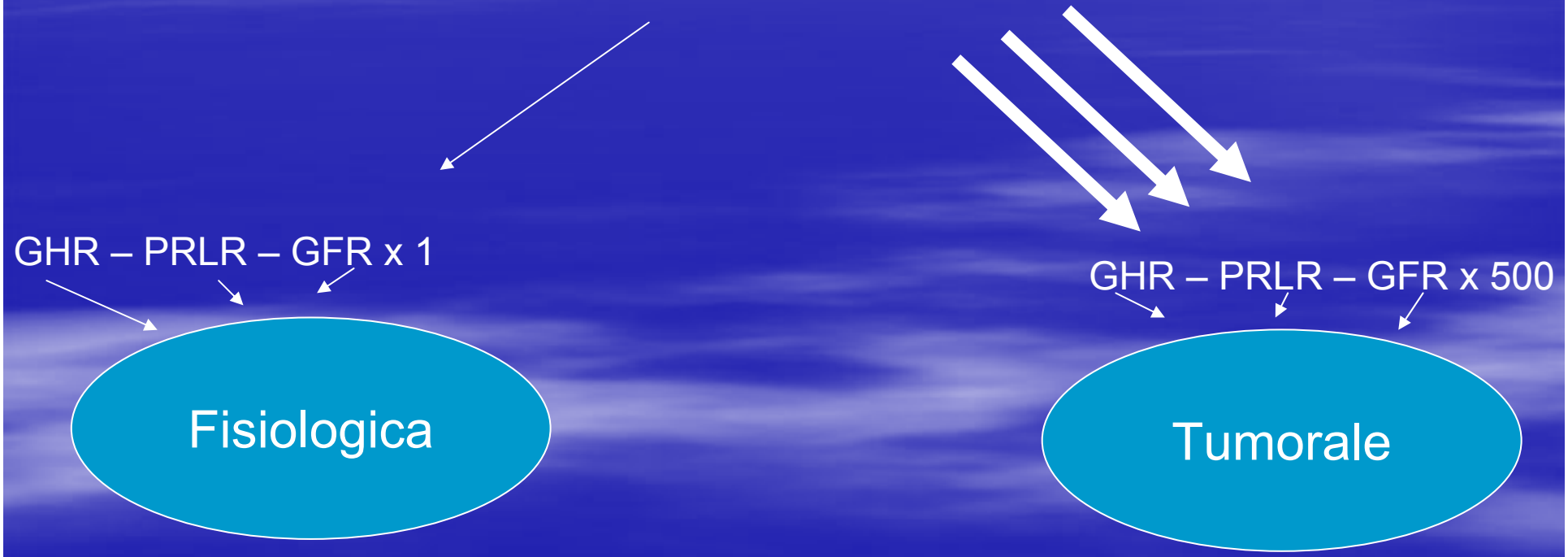
MDB regolazione dell'equilibrio, materia ed energia su cui poggia la vita. Equilibrio biologico realizzato dal rapporto finemente modulato e gradualmente regolato tra composizione materiale e contenuto energetico.

Caratteristiche comuni ai tumori



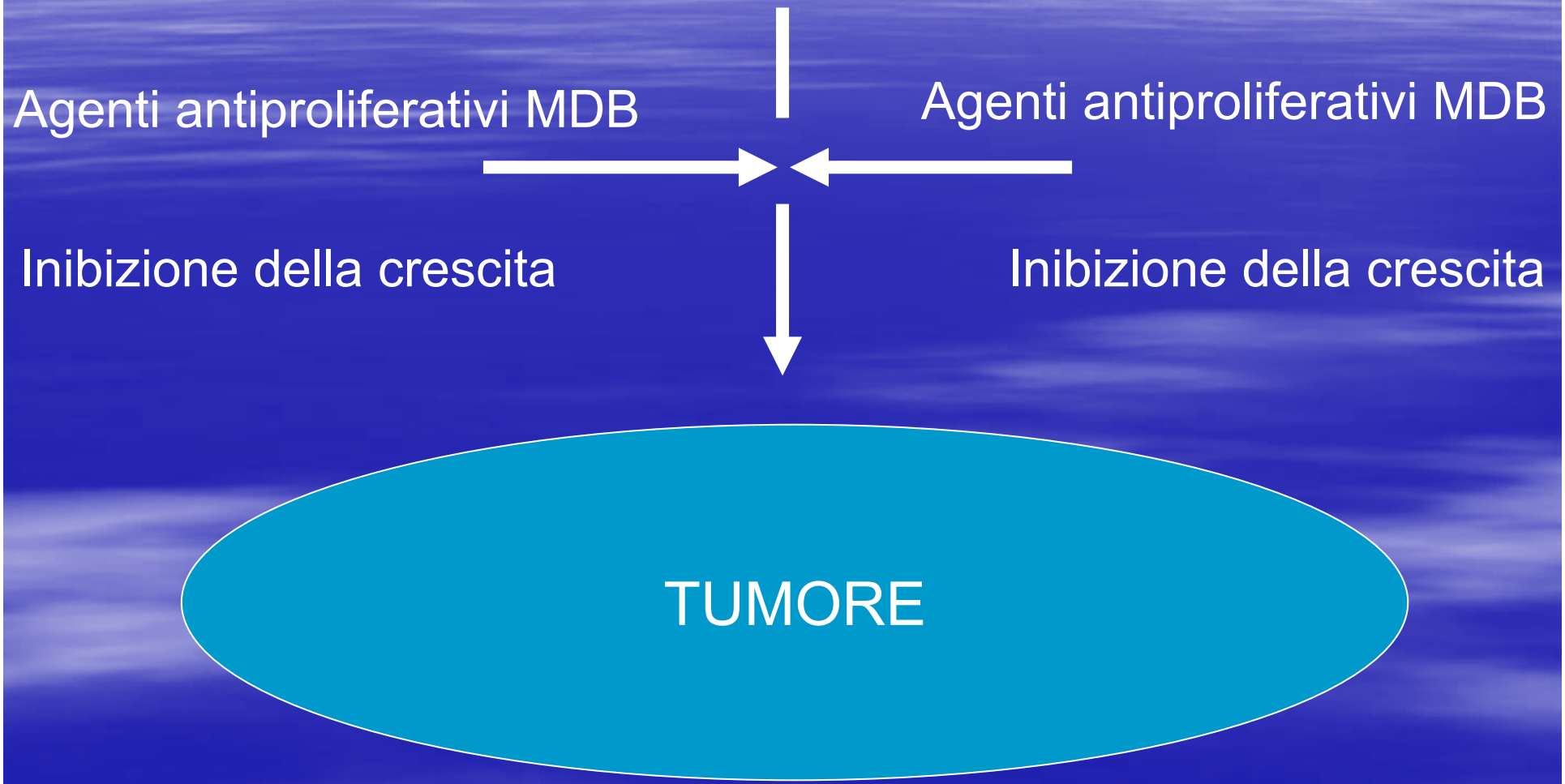
Crescita

GH
PRL
GF (growth factors)



Crescita tumorale

GH – PRL - GF



Histochem Cell Biol. 1998 Feb;109(2):141-59.

Growth hormone receptor expression in the nucleus and cytoplasm of normal and neoplastic cells.

Lincoln DT, Sinowatz F, Temmim-Baker L, Baker HI, Kölle S, Waters MJ.

Department of Medical Science, Faculty of Allied Health, Kuwait University, Sulaibikhat.

Growth hormone (GH) exerts its regulatory functions in controlling metabolism, balanced growth and differentiated cell expression by acting on specific receptors which trigger a phosphorylation cascade, resulting in the modulation of numerous signalling pathways dictating gene expression. A panel of five monoclonal antibodies was used in mapping the presence and somatic distribution of the GH receptor by immunohistochemistry in normal and neoplastic tissues and cultured cells of human, rat and rabbit origin. A wide distribution of the receptor was observed in many cell types. Not all cells expressing cytoplasmic GH receptors displayed nuclear immunoreactivity. In general, the relative proportion of positive cells and intensity of staining was higher in neoplastic cells than in normal tissue cells. Immunoreactivity showed subcellular localisation of the GH receptor in cell membranes and was predominantly cytoplasmic, but strong nuclear immunoreaction was also apparent in many instances. Intense immunoreactivity was also observed in the cellular Golgi area of established cell lines and cultured tissue-derived cells in exponential growth phase, indicating cells are capable of GH receptor synthesis. The presence of intracellular GH receptor, previously documented in normal tissues of mostly animal origin, is the result of endoplasmic reticulum and Golgi localisation. Heterogeneity of immunoreactivity was found in normal and neoplastic tissue with a variable range of positive cells. The nuclear localisation of immunoreactivity is the result of nuclear GH receptor/binding protein, identically to the cytosolic and plasma GH-binding protein, using a panel of five monoclonal antibodies against the GH receptor extracellular region. The expression of GH receptors, not only on small proliferating tumour cells such as lymphocytes, but also on well differentiated cells including keratinocytes, suggests that GH is necessary not only for differentiation of progenitor cells, but also for their subsequent clonal expansion, differentiation and maintenance.

Publication Types:

- Research Support, Non-U.S. Gov't

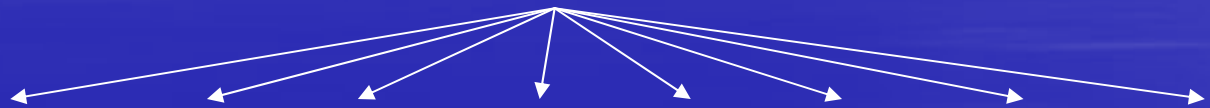
PMID: 9504775 [PubMed - indexed for MEDLINE]

Ormone della crescita [GH]

Funzione centrale dell'ormone **GH** nell'insorgenza e progressione tumorale

Lincoln DT et al. – Histochem Cell Biol 1998 Feb;109(2):141-59

Fattori di crescita satelliti GH-dipendenti decisivi per l'oncogenesi X X



EGF FGF IGF1 HGF NGF PDGF VEGF TGF COLECISTOCHININA VIP GASTRINA

Effetto mitogeno X [induzione alla proliferazione cellulare neoplastica]

Angiogenesi [creazione della rete di vasi sanguigni che consente il suo apporto nutritivo]

Metastatizzazione X[la cellula tumorale supera tutte le barriere naturali, di contenimento]

Prolattina [PRL]

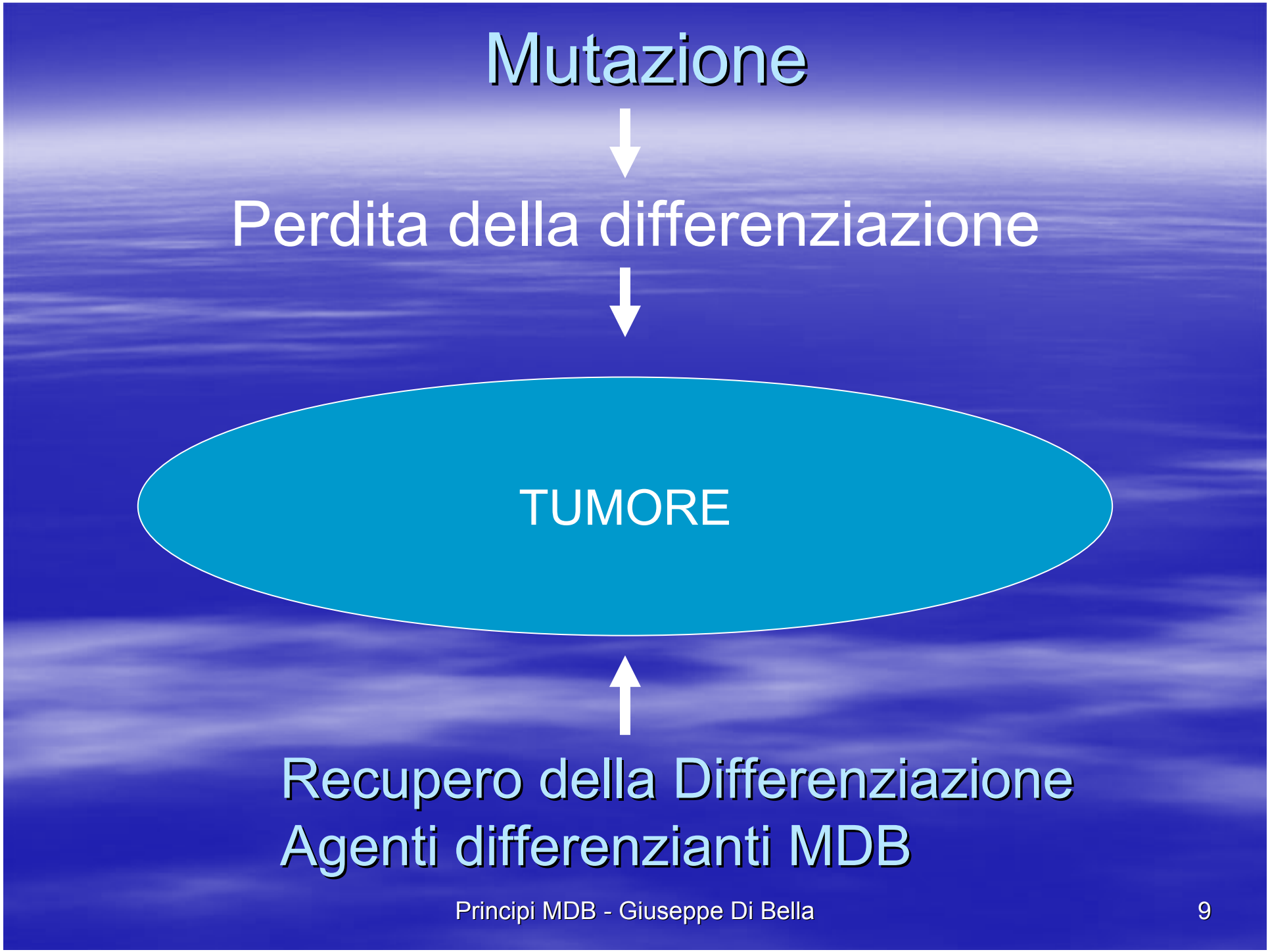
Funzione ubiquitaria dell'ormone **PRL** nell'insorgenza e progressione tumorale

Ben-Jonathan N et al Trends Endocrinol Metab. 2002; **13**(6):245-250.

Effetto mitogeno [induzione alla proliferazione cellulare neoplastica]

Angiogenesi [creazione della rete di vasi sanguigni che consente il suo apporto nutritivo]

Metastatizzazione [la cellula tumorale supera tutte le barriere naturali, di contenimento]


Mutazione
Perdita della differenziazione
TUMORE
Recupero della Differenziazione
Agenti differenzianti MDB

Definizione dell' M.D.B.

- Sintesi delle acquisizioni mediche documentate ed evidenze scientifiche con una clinica affrancata da inquinamenti politico finanziari
- Bio-politerapia oncologica razionale con interazione sinergica fattoriale di componenti singolarmente dotati di documentata attività antiblastica
- Prima formulazione risalente al 1965

Componenti dell' M.D.B. (I)

- **Modulo Fisso**
  - Somatostatina o Octreotide
  - Retinoidi
  - Melatonina
  - Vitamina E
  - Vitamina D
  - Vitamina C
  - Dosaggi minimali di chemioterapici
  - Inibitori della prolattina

Componenti dell' M.D.B. (II)

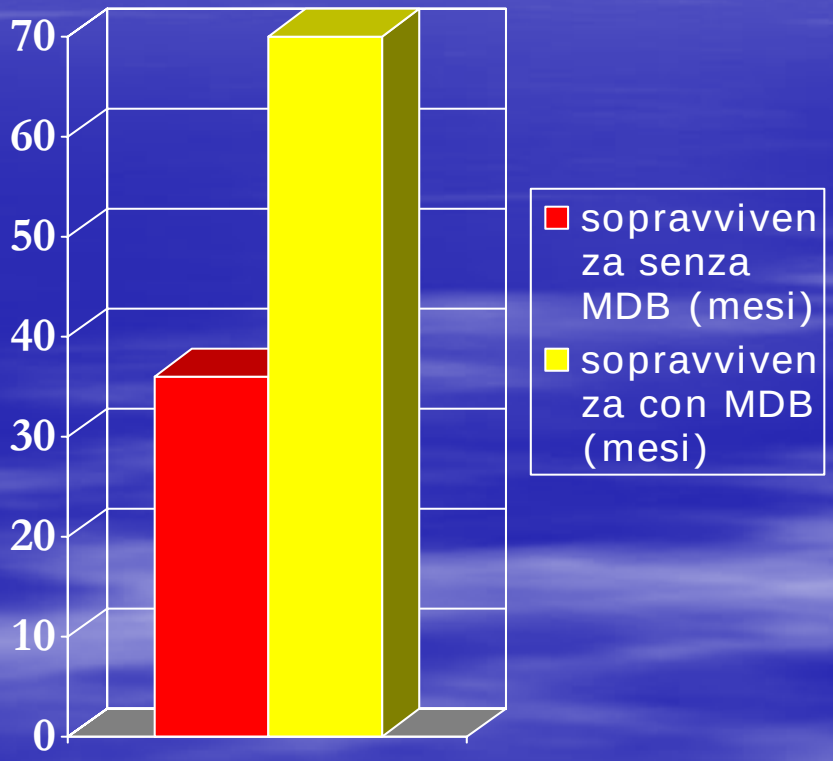
- **Modulo Variabile**
  - ACTH di sintesi
  - Inibitori degli estrogeni
  - Inibitori degli androgeni
  - Calcio
  - Glucosammina solfato
  - Glifosina
  - Galatturoglicano solfato
  - Anidrometilencitrato-esametilentetramina
  - Dibromomannitolo
  - Isoniazide
  - Anidrometilencitrato-esametilentetramina
  - Eritropoietina
  - Citochine (Granulokine)
  - Albumina umana 25%
  - Lisozima
  - Immunoglobulina

Dott. Mauro Todisco:
Linfomi Non-Hodgkin basso grado stadio avanzato (pubblicato su Cancer Biotherapy and Radiopharmaceuticals)

- Pazienti arruolati: **20**
- Tasso di risposta (completa o parziale) con MDB:

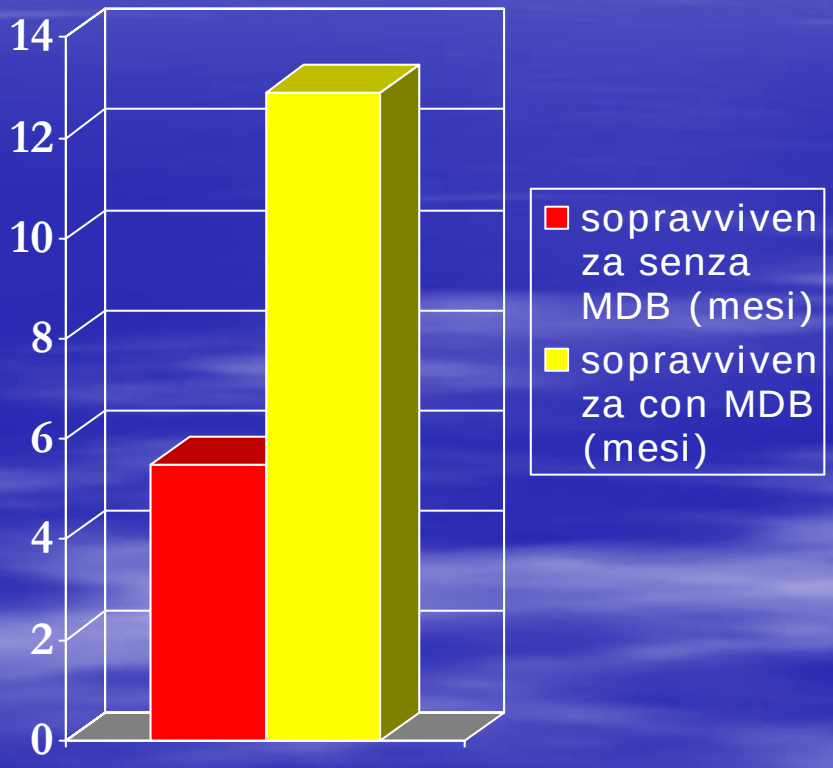
  70% (14 pazienti)
- Mediana di riferimento (senza MDB):

  36%



Dott. Achille Norsa:
Cancro del polmone non a piccole cellule metastatico – basso performance status (pubblicato su Cancer Biotherapy and Radiopharmaceuticals)

- Pazienti arruolati: **28**
- Sopravvivenza mediana con MDB:
  12,9 mesi
- Mediana di riferimento (senza MDB):
  5,5 mesi



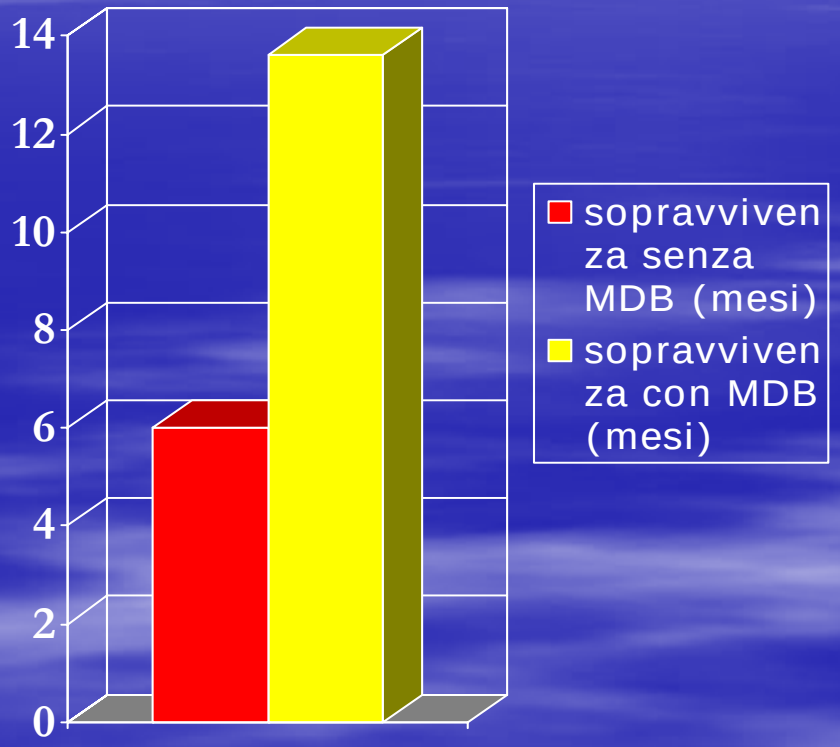
Dott. Mauro Madarena 1° Congressso nazionale MDB 2004- Bo Carcinoma esocrino del pancreas metastatico con MDB

- Pazienti totali arruolati:

  17
- Sopravvivenza mediana con MDB:

  13,6 mesi
- Mediana di riferimento (senza MDB):

  6 mesi

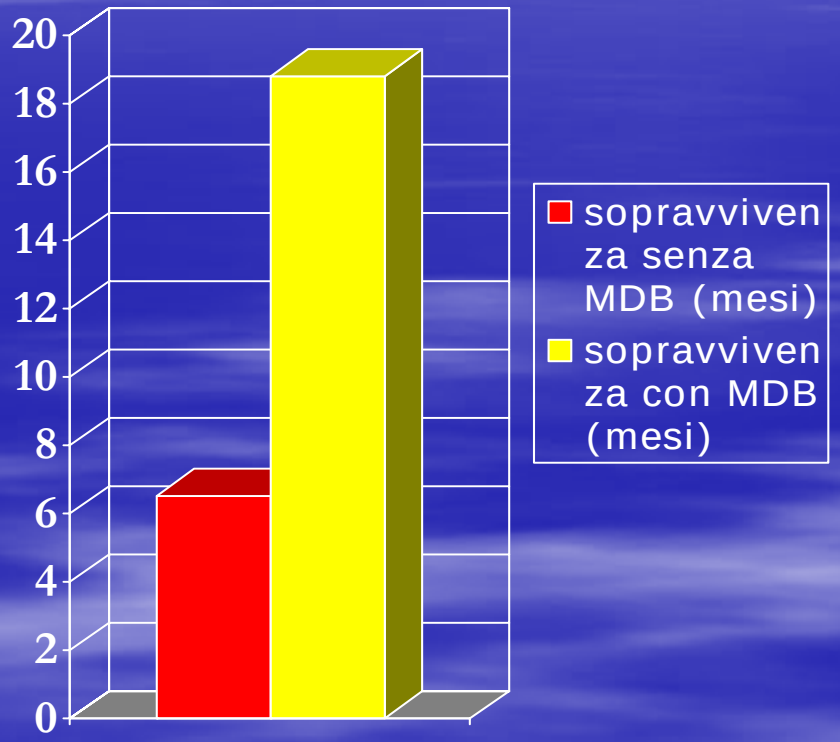


Dott. Mauro Madarena:
Carcinoma esocrino del pancreas metastatico con MDB
N° pazienti totali arruolati: 17 Sopravvivenza mediana: 13,6 mesi

- Pazienti non pretrattati con chemio: **6**
- Sopravvivenza mediana con MDB:

  18 mesi
- Mediana di riferimento (senza MDB):

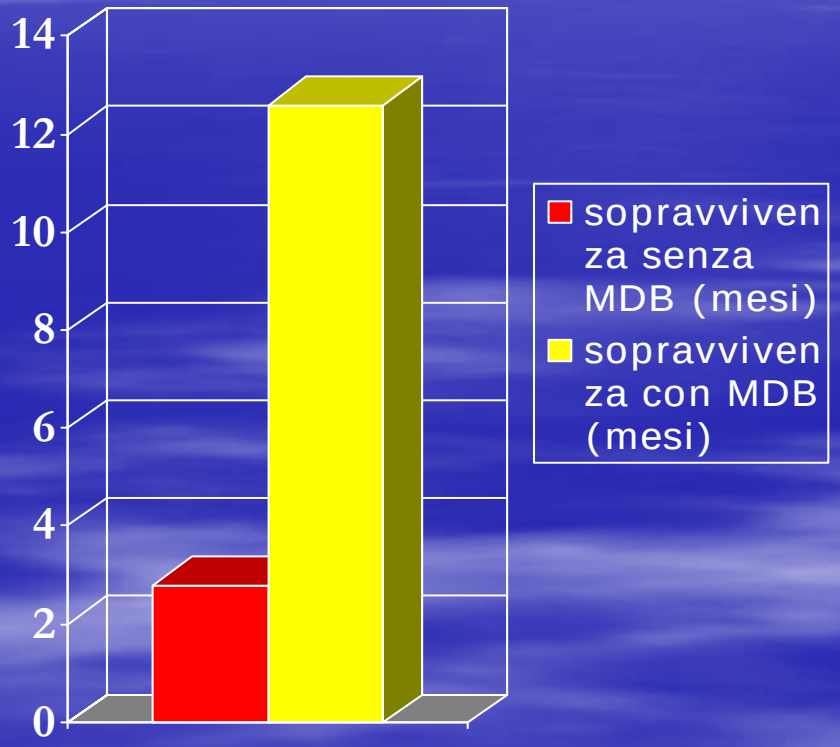
  6,5 mesi



Dott. Mauro Madarena:
Carcinoma esocrino del pancreas metastatico con MDB
N° pazienti totali arruolati: 17 Sopravvivenza mediana: 13,6 mesi

- Pazienti pretrattati con chemio: **11**
- Sopravvivenza mediana:

  12,6 mesi
- Mediana di riferimento: **2,8 mesi**



Proc Soc Exp Biol Med. 1998 Feb;217(2):143-52.

Related Articles, Links

Mechanisms of antineoplastic action of somatostatin analogs.

Pollak MN, Schally AV.

Department of Medicine, Lady Davis Research Institute, McGill University, Montreal, Quebec, Canada. MD49@MUSICA.MCGILL.CA

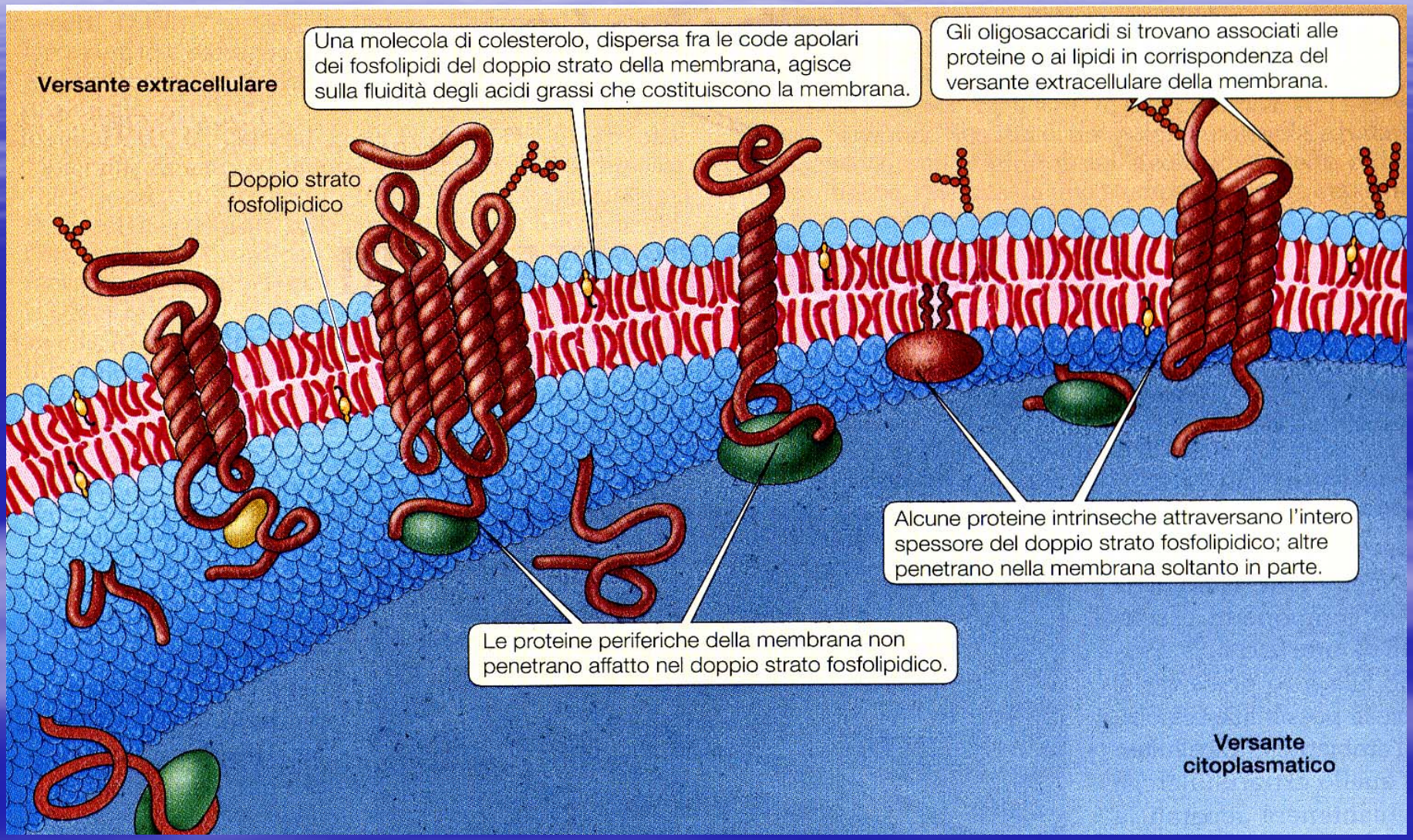
Over the past decade, impressive antineoplastic activity of somatostatin analogs has been demonstrated in many tumor models. More recent research has provided information regarding mechanisms underlying the antiproliferative and apoptosis-inducing actions of these compounds. These include both 'direct' mechanisms that are sequellae of binding of somatostatin analogs to somatostatin receptors present on neoplastic cells and 'indirect' mechanisms related to effects of somatostatin analogs on the host. The upregulation of intracellular tyrosine phosphatase activity triggered by binding of ligands to the type II somatostatin receptor has received considerable attention as a direct mechanism, not only because this activity is the converse of the tyrosine kinase activity associated with many peptide mitogen receptors, but also because the type II somatostatin receptor is frequently expressed by common human neoplasms, including breast cancer. The potential importance of indirect mechanisms of action of somatostatin analogs, such as alterations in host insulin-like growth factor physiology, is emphasized by the in vivo antineoplastic activity of these compounds against somatostatin receptor-negative neoplasms. Clinical efficacy and a favorable toxicity profile of somatostatin analogs in the treatment of relatively uncommon conditions such as acromegaly and neuroendocrine tumors have already been demonstrated. Preclinical data now are sufficient to justify controlled clinical trials in breast, prostate, and pancreatic cancer. The development of monthly depot formulations will facilitate the clinical evaluation of somatostatin analogs for these and other indications.

Publication Types:

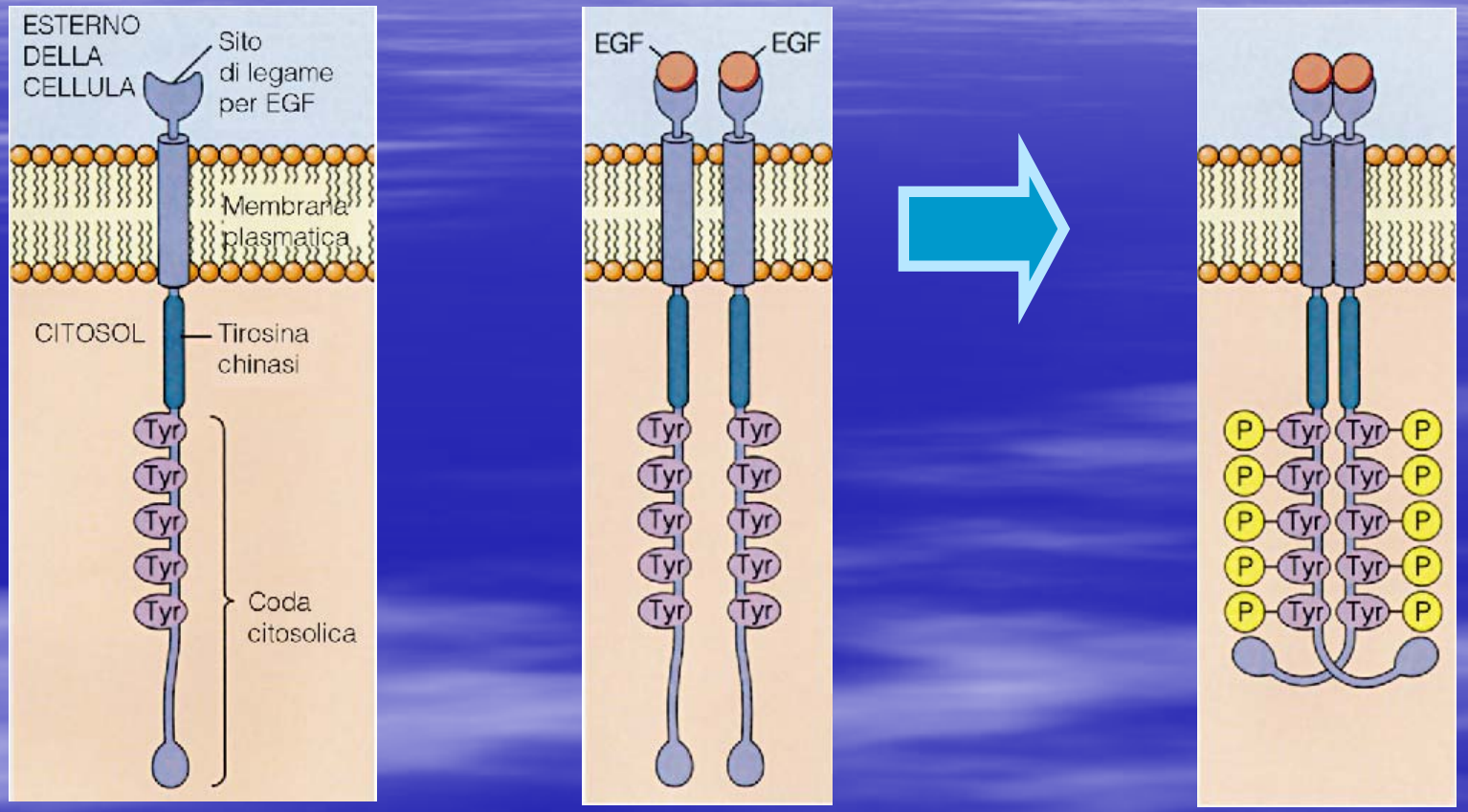
- Research Support, Non-U.S. Gov't
- Research Support, U.S. Gov't, Non-P.H.S.
- Review

PMID: 9452137 [PubMed - indexed for MEDLINE]

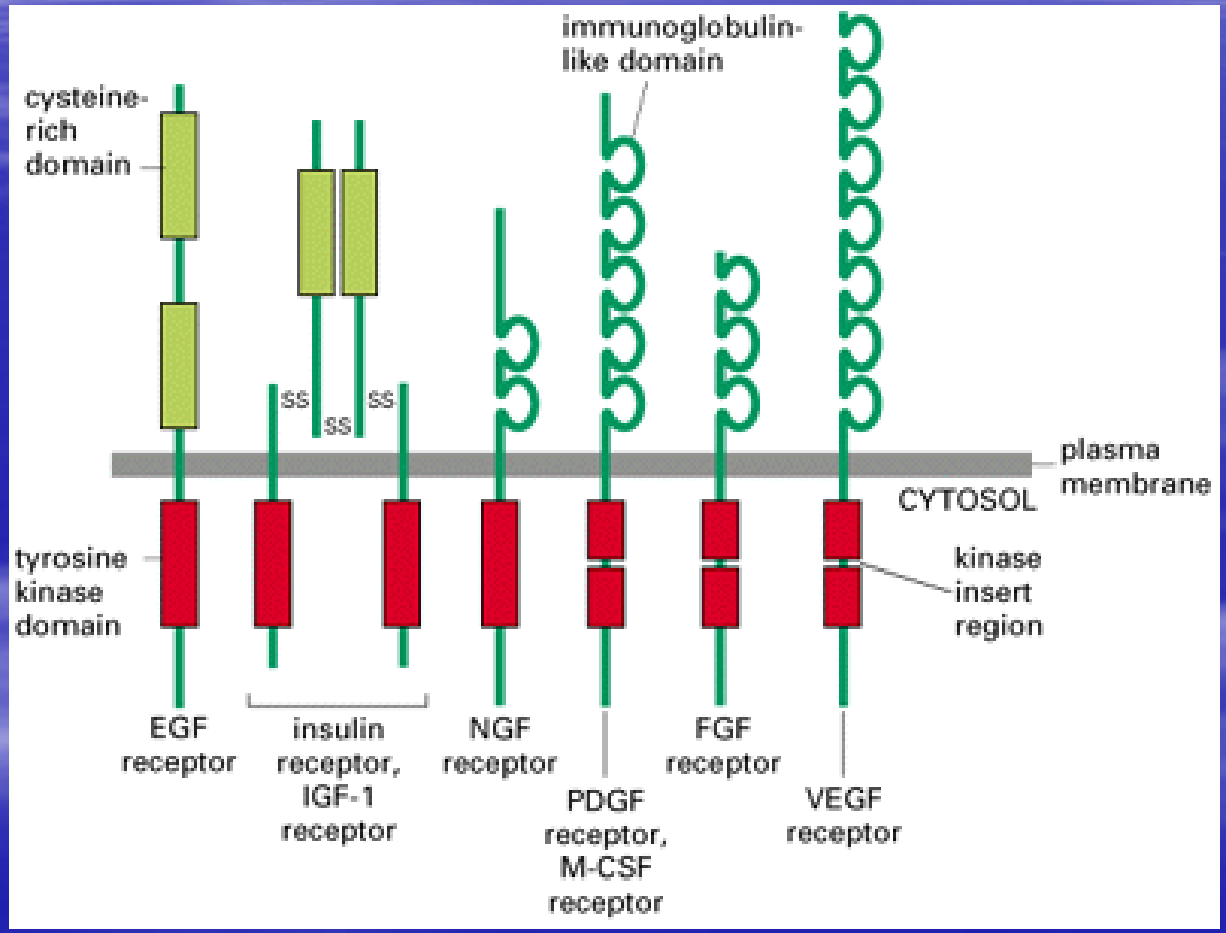
Membrana cellulare



Recettori Tirosino Chinasici

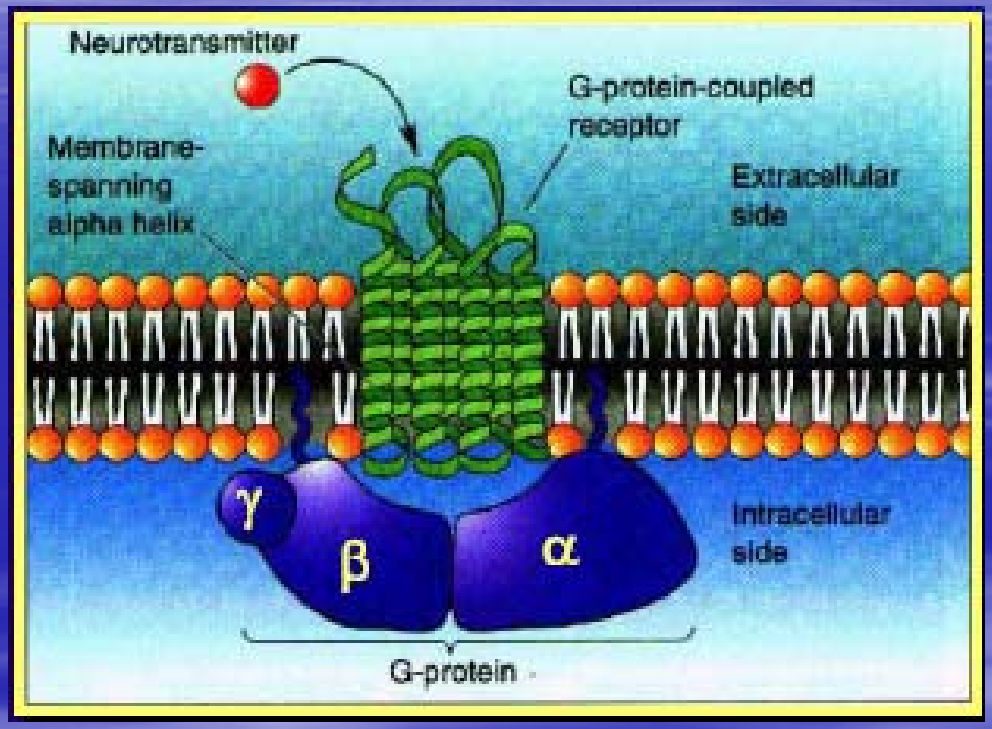


Recettori tirosino chinasici



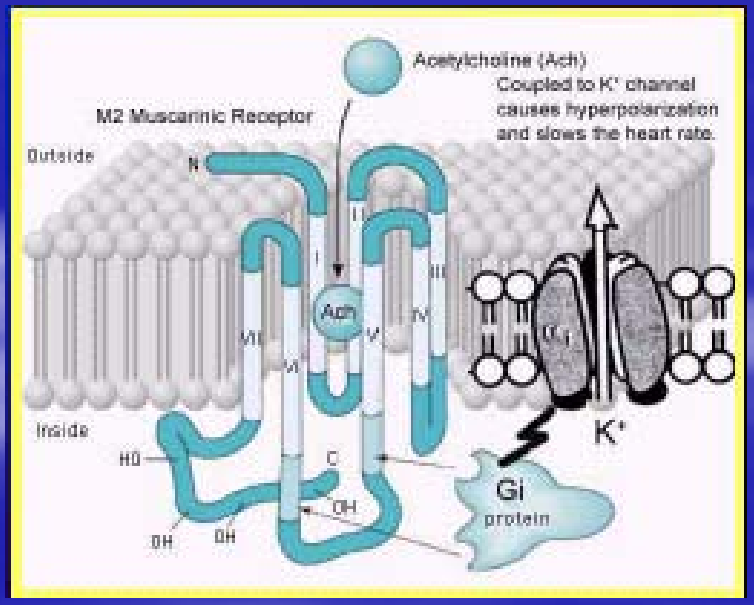
Proteine G

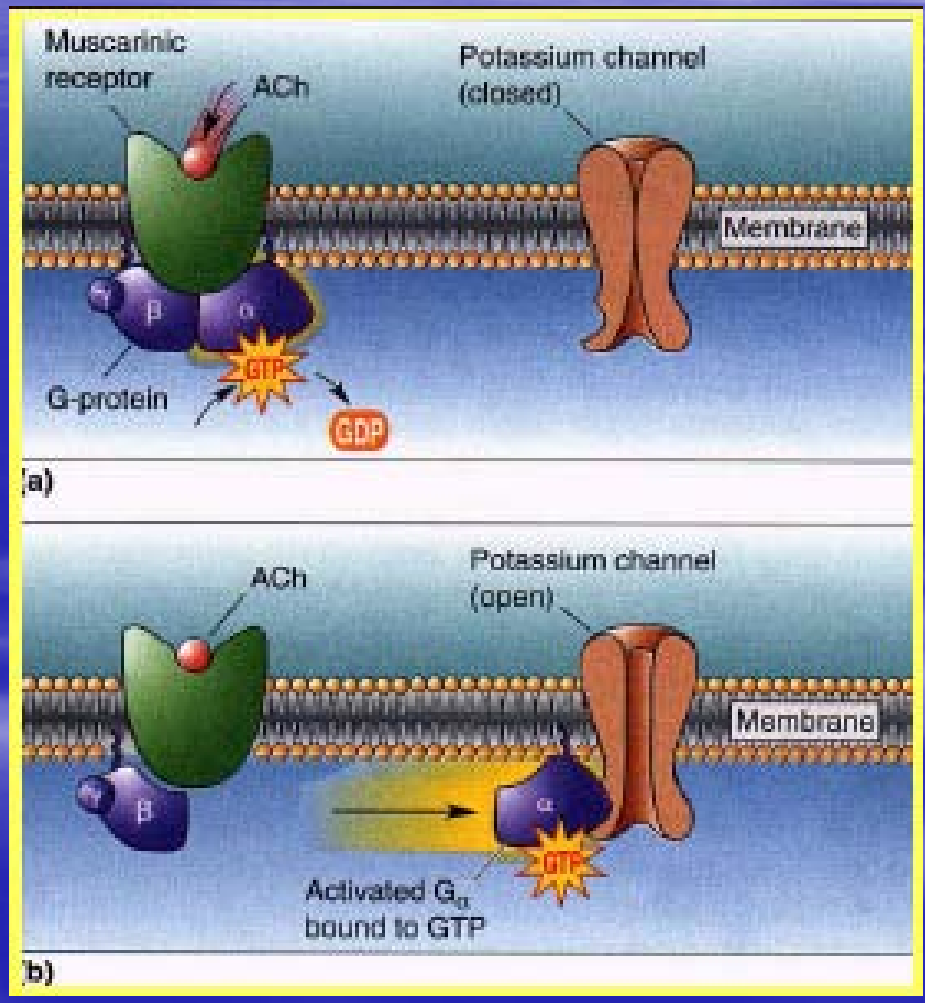
- Eterotrimeri costituiti da 3 subunità: α, ß, γ.
- α è in grado di legare il GTP e di idrolizzarlo grazie a una attività GTPasica intrinseca
- Le proteine G trasferiscono informazioni dai recettori alle molecole effettrici attraverso un ciclo di attivazione-deattivazione governato dal legame e dall'idrolisi del GTP.



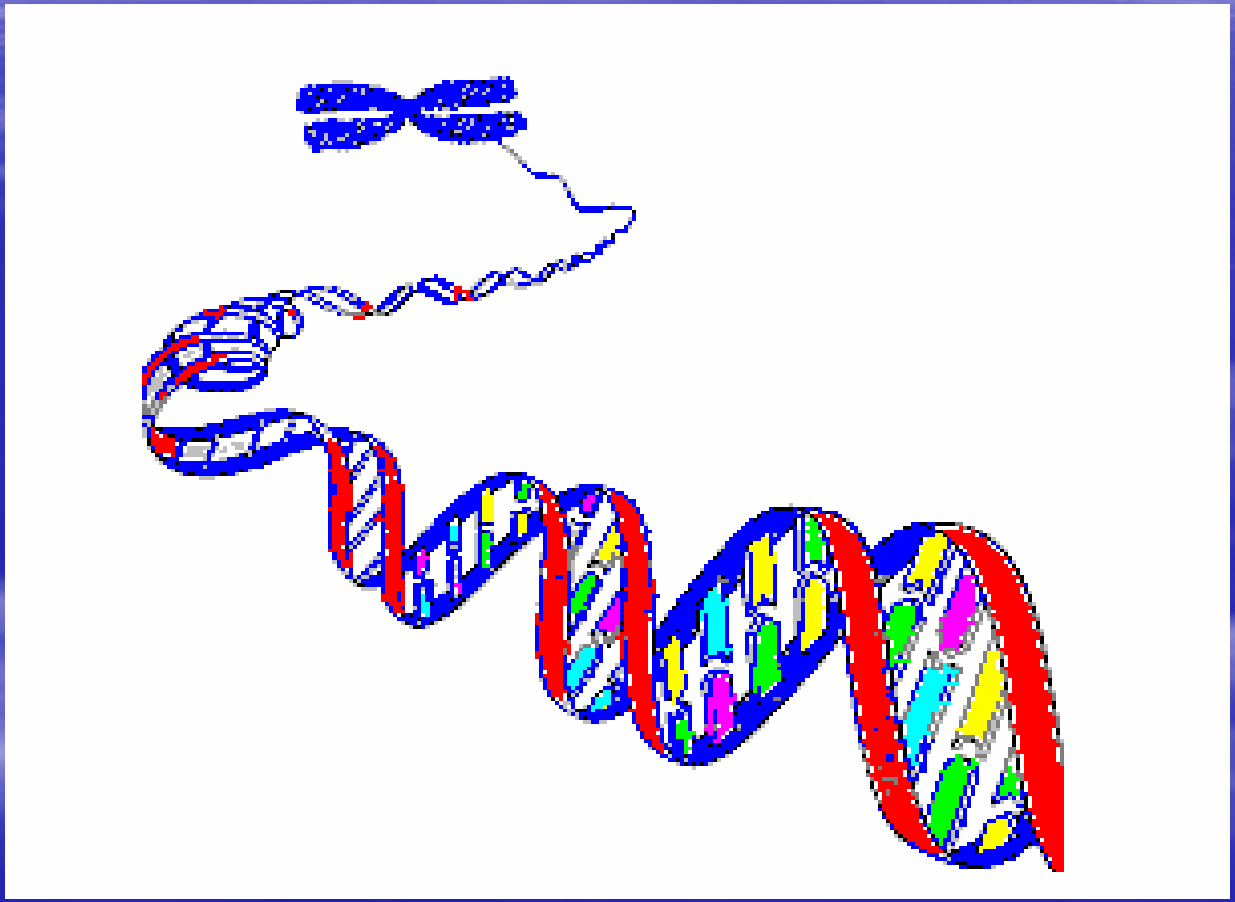
EFFETTORI DELLE PROTEINE G CON FUNZIONI DI CANALE IONICO

I più studiati sono i canali al calcio operati da proteina G e un numero sempre più crescente di canali al potassio





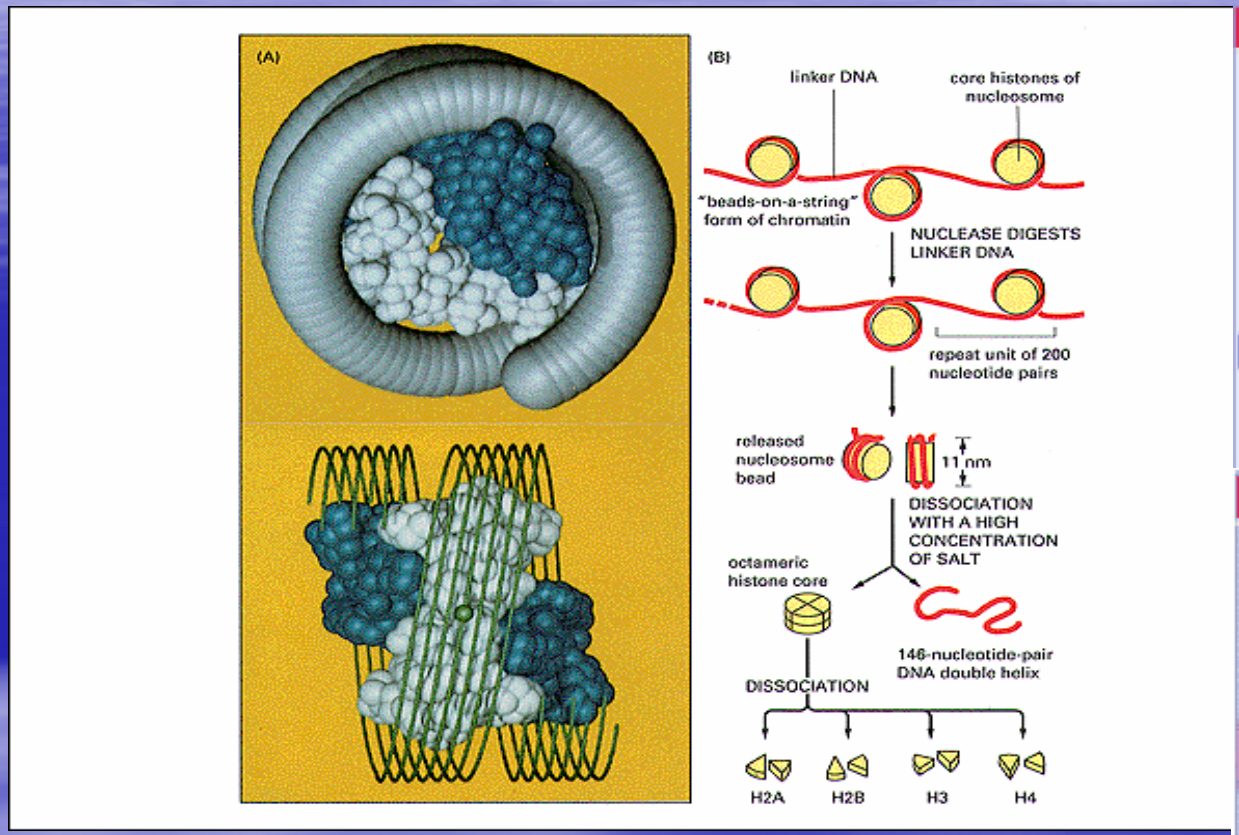
Struttura del DNA

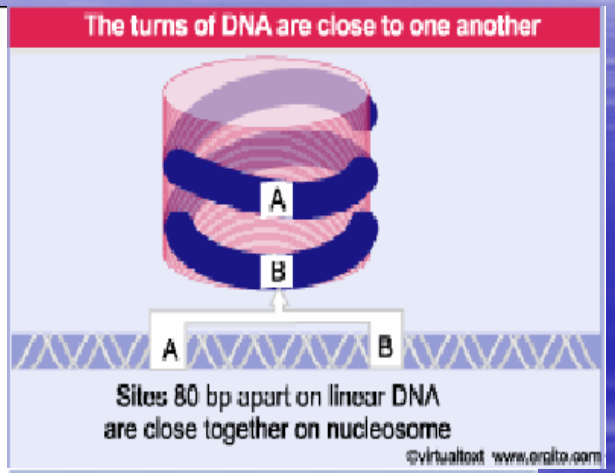


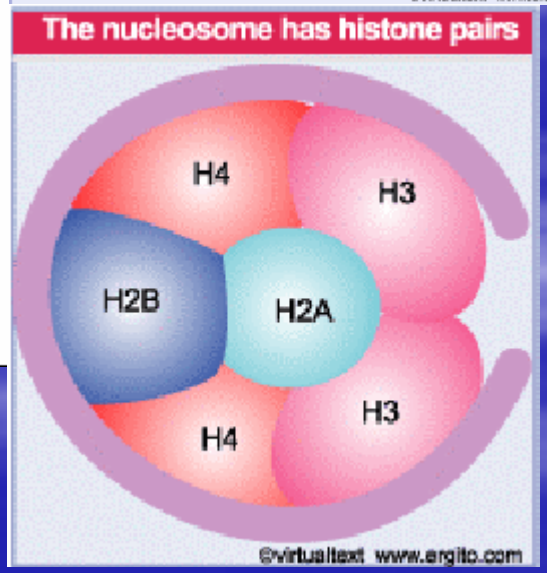
Proteine cromosomiche

- Proteine Istoniche
- H1
- H2a
- H2b
- H3
- H4
- Proteine non Istoniche
- Enzimi
- Proteine di trascrizione
- Proteine di replicazione

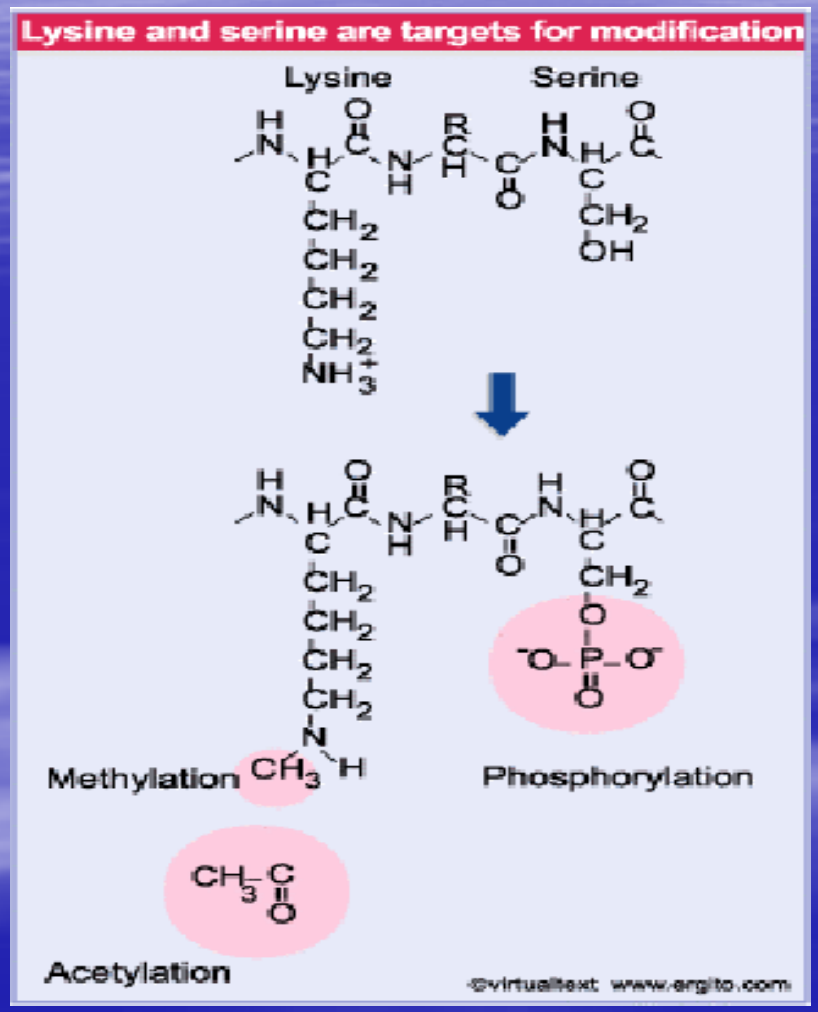
Struttura degli Istoni

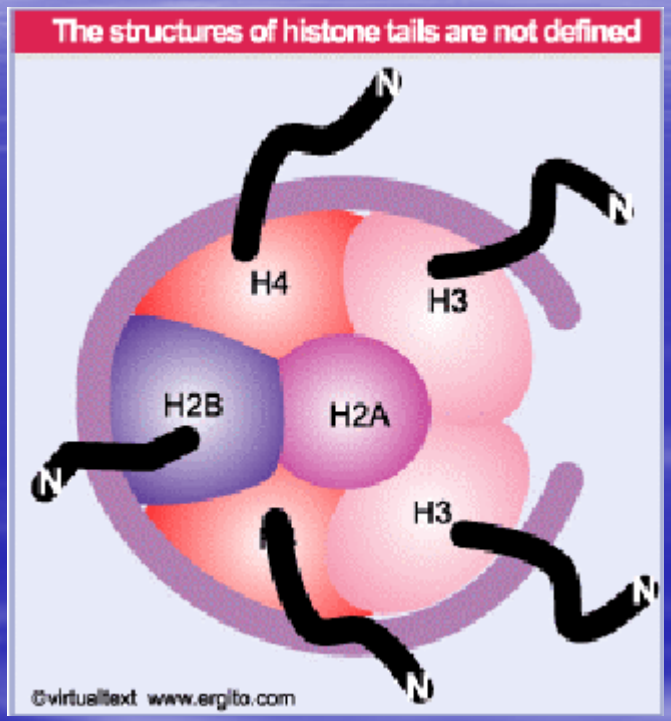






Struttura del nucleosoma





Meccanismi d'azione dei retinoidi: Betacarotene

- Stabilizza le membrane cellulari
- Inibisce la perossidazione lipidica
- Incrementa il glutatione intracellulare
- Esercita un effetto antiproliferativo diretto indipendentemente dalla conversione in acido retinoico
- Attraverso l' apertura degli otto doppi legami insaturi della catena di carbonio fornisce energia necessaria alla crescita differenziata

Meccanismi d'azione dei retinoidi: Vitamina A

- Provoca la morte della cellula neoplastica per apoptosi:
  1. Attraverso l'attivazione delle caspasi
  2. Attraverso la degradazione del fattore della trascrizione generale Sp-1
- Azione prodifferenziante
- Epitelio-protettiva
- Immuno-stimolante

Meccanismi d'azione dei retinoidi: Acido Retinoico

- Ridifferenzia i blasti e le cellule tumorali
- Azione antiangiogenetica
- Inibisce la trascrizione genica di fattori oncogeni promuovendo l' effetto antiproliferativo
- Effetto antimetastatico inibendo l' espressione di VnR correlata all' organizzazione della fibronectina e all' adesione ed espansione cellulare
- Antiossidante
- Proapoptotico

La Melatonina (I)

- Azione **antiproliferativa** attraverso:
  - Inibizione della trascrizione del recettore dell' estrogeno
  - Sopprime il recettore del fattore di crescita epidermico (EGFR)
  - Inibizione increzione e azione della prolattina
  - Diffusione ubiquitaria degli esteri fosforici di AMP, ADP, ATP
  - Azione omeostatica antitumorale
  - Inibisce l' azione della proteina N-Ras

La Melatonina (II)

- Agisce come molecola chiave del sistema paracrino per la coordinazione distrettuale delle relazioni intercellulari
- Regola messaggeri secondari: cAMP, cGMP, e diacilglicerolo, inositolo, acido arachidonico, Ca2+ intracellulare
- Regola la fosforilazione della proteina legante e l'espressione del C-Fos
- Tasso ematico MLT invers. proporz. all' indice proliferativo

La Melatonina (III)

- Azione **antimetastatica**
  - Riduce l' attrazione per la fibronectina
  - Attiva l' espressione delle proteine di adesione cellulare E-Cadherin e beta(1)integrin
  - Agisce sugli spazi di giunzione intercellulare inducendo la proteina dello spazio di giunzione CX32
  - Polimerizza il tubulin e incrementa i microtubuli delle cellule tumorali

La Melatonina (IV)

- Azione **antiossidante, antiradicali-liberi, radioprotettiva**
  - Protegge il DNA nucleare dal danno ossidativo e dalle radiazioni ionizzanti
  - Come componente principale DNES agisce su tutti i sistemi d'organo in forma fisiologica, omeostatica, antiradicali liberi, antiossidante
  - Esercita azione radioprotettiva e radiomodificante
  - Somministrata prima della radioterapia riduce il danno epatico delle radiazioni ionizzanti e inattiva i radicali liberi da questi prodotti

La Melatonina (V)

- **Azioni varie**:
  - Antiaggregante piastrinico
  - Fattore primario della piastrinogenesi
  - Regola la formula leucocitaria in senso granulocitico
  - Incrementa la sintesi Hb e la sua degradazione, la resistenza globulare con indicazioni fondamentali nelle talassiemie
  - Azione prodifferenziante
  - Azione proapoptotica
  - Regolazione circadiana e circanuale
  - Modulazione neuro-immuno-endocrina

Somatostatina e Octreotide (I)

- **Azione antiproliferativa** mediante:
  - Inibizione dei percorsi non ossidativi del fosfato pentosio
  - Inibizione del riciclo del carbonio del glucosio tramite PC con incremento del 20% in combinazione con l' ossitiamina
  - Modulazione dei canali ionici e inibizione dell' adenilciclasi, della chinasi, e fosfatasi della serina/treonina e tiroxina
  - Inibizione della sintesi del DNA
  - Induce l'espressione di p21Cip, e P27
  - Inibisce l' incorporazione della (<3>H)Timidina nel DNA

Somatostatina e Octreotide (II)

- Attivazione della traslocazione del PTP1C intracellulare alla membrana della cellula neoplastica
- Inibizione dell' espressione di EGFR
- Attivazione mediante SSTR di Fosfatasi della Tirosina
- Riduzione dell' espressione di EGF
- Inibizione della fase S del ciclo cellulare dose-dipendente
- Incremento dell' attività del gene soppressore P53
- Inibizione dell' attività di chinasi della proteina mitogenoattivata MAB
- Soppressione dell' attivazione della RAS
- Induzione di aberrazione (CA) cromosomica con rottura cromosomica
- Riduzione dell' espressione del gene C-FOS

Somatostatina e Octreotide (III)

- Effetto **proapoptotico**:
  - Induzione di una forte espressione della proteina BCL-2
  - Intensa attività fosfatasica
  - Abbattimento della concentrazione plasmatica di fattori di crescita tumorale
  - Aumento della perossidazione lipidica intracellulare neoplastica
  - Condensazione nucleare delle CHromatine con frammentazione, restringimento, formazione di corpi apoptotici
- Effetto **antiangiogenetico:**
  - Inibizione dell' espressione di VEGF e di VEGFR
- Effetto **antimetastatico**

Vitamina D3 (I)

- Azione **prodifferenziante** (sinergica a retinoidi, vit. E, mlt):
  - Sia mediante interazione con recettore ma anche con meccanismi extrarecettoriali mediati dalla membrana
- Azione **proapoptotica**:
  - Induzione dell' espressione di mRNA della proteina BRCA1
  - Inibizione della segnalazione del fattore di crescita dei cheratinociti e diminuzione dell' espressione basale di *bcl2*
  - Determina l' accumulo di cellule tumorali in G0 e G1
  - Abbatte le concentrazioni di cyclin C e D1

Vitamina D3 (II)

- Disattiva l' effetto anti apoptotico dell' inibitore delle caspasi ad ampio spettro z-VAD-fmk
- Attiva una via apoptotica caspasi indipendente mediante il coinvolgimento della cerammide e fosfolipasi A-2
- Induce una elevata espressione di P21, P27
- Promuove il clivaggio della molecola che attiva la promozione della sopravvivenza e della crescita attivata dal mitogeno
- L' apoptosi avviene attraverso il clivaggio selettivo caspasidipendente del MEK-1 ed è mediata dal p38 MAPK
- Inibizione dell' angiogenesi e dello sviluppo e crescita indotti da VEGF con meccanismo apoptotico

Vitamina D3 (III)

- Effetto **antimetastatico**
  - Induce e-camerin ed altre molecole di adesione
  - Promuove l' espressione in forma dose-dipendente delle molecole di adesione ICAM-3
  - Inibisce l' invasività della matrice extracellulare mediante il blocco della degradazione delle sue barriere mediante collagenolisi da parte delle cellule tumorali
  - Diminuisce l' adesione e la migrazione delle cellule dalla membrana basale legato a una diminuzione dell' espressione degli integrins alfa6 e beta4, recettori della laminina, responsabili dell' incremento della migrazione invasione cellulare e tumorale

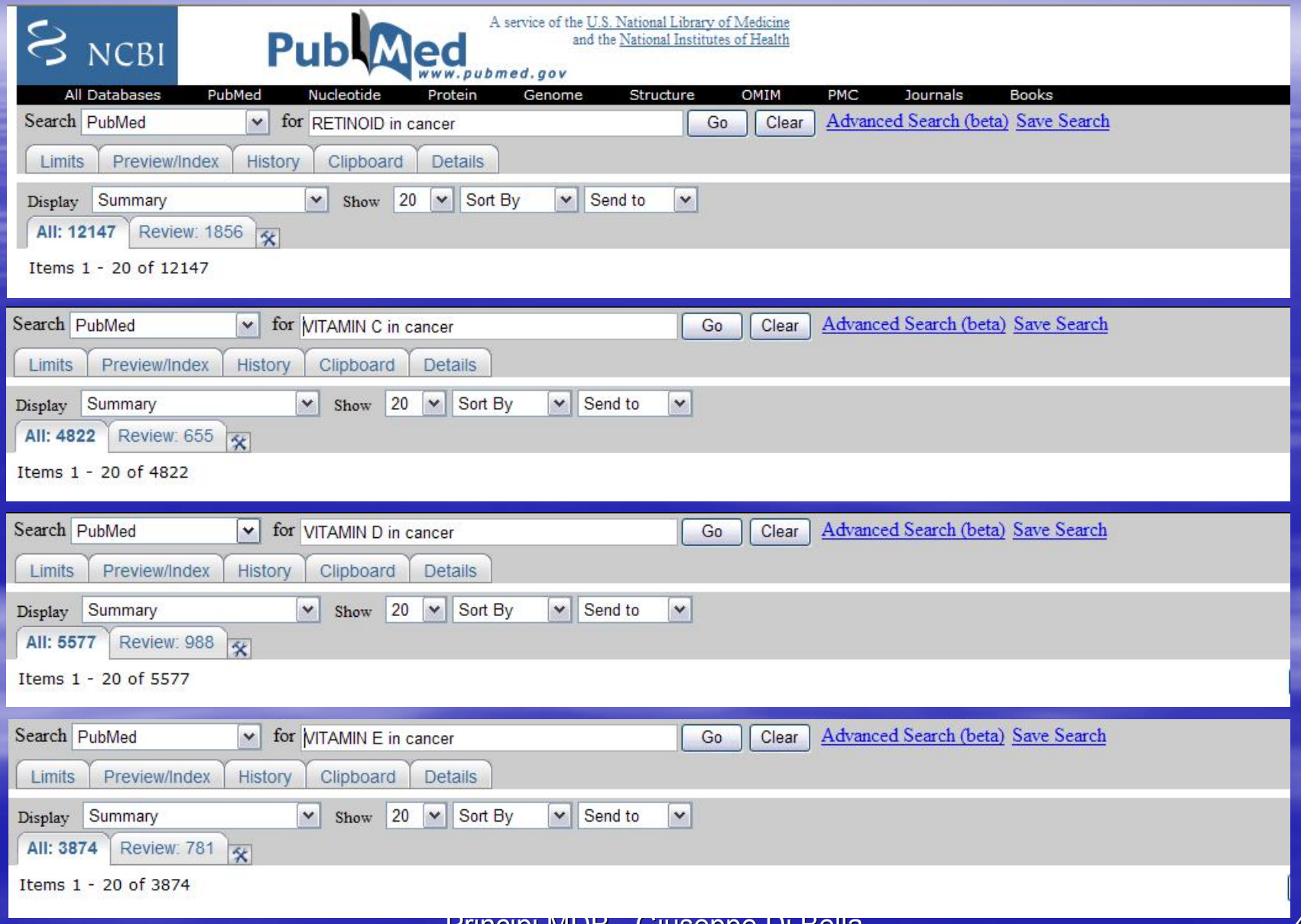
Vitamina D3 (IV)

- Effetto **antiproliferativo**:
  - Blocca l' espressione di EGFR mediante inibizione della sua fosforilazione con defosorilazione dei polipeptidi 17 e 66-kDa
  - Incrementa l' espressione nucleare di p27
  - Abbatte i livelli della proteina c-MIK
  - Blocca in fase G1 il ciclo cellulare neoplastico abbattendo le concentrazioni di cyclin C e D1
  - Incrementa l' espressione della proteina 3 legante IGF (IGFBP3), indispensabile per la realizzazione dell' effetto antiproliferativo della D3

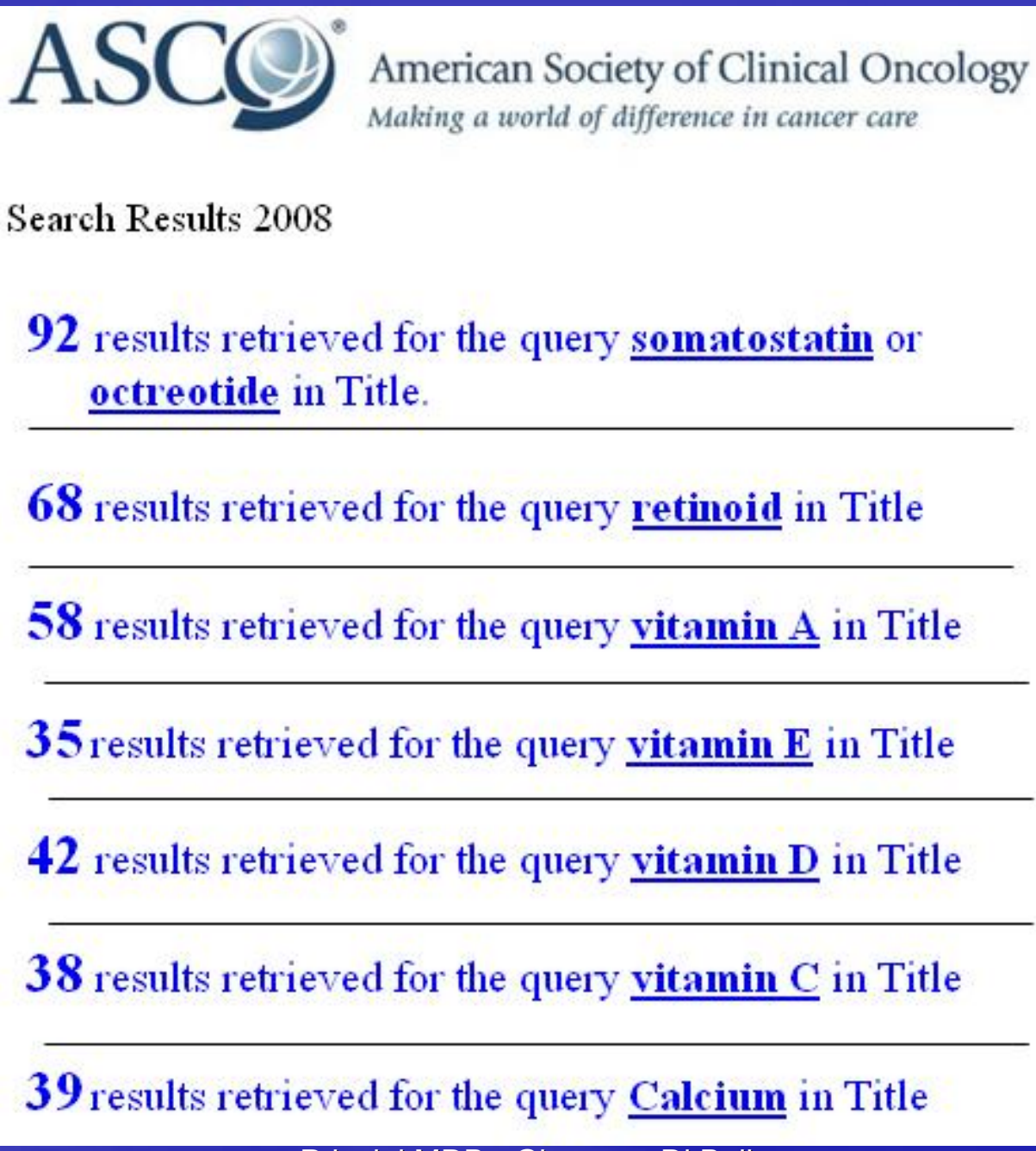
Meccanismi sinergici dei componenti dell' MDB

- Antiangiogenetica (MLT, SST, ATRA, D3)
- Antiproliferativa (MLT, SST, ATRA, D3)
- Antimetastatica (MLT, SST, D3)
- Prodifferenziante (MLT, ATRA, B.car, D3, A, E)
- Proapoptotica (MLT, SST, ATRA, D3, A, E)
- Antiossidante – Antirad. Liberi (RET, MLT, E, C, D3)
- Immunomodulante (MLT, RET, C, D, E)
- Omeostatica - Antiblastica (MLT, SST, RET, D3, E)

Articoli molecole MDB - PUBMED



Articoli molecole MDB - PUBMED


ASCO
American Society of Clinical Oncology
Making a world of difference in cancer care
Search Results 2008
92 results retrieved for the query somatostatin or octreotide in Title.
68 results retrieved for the query retinoid in Title
58 results retrieved for the query vitamin A in Title
35 results retrieved for the query vitamin E in Title
42 results retrieved for the query vitamin D in Title
38 results retrieved for the query vitamin C in Title
39 results retrieved for the query Calcium in Title

MDB nel cancro del polmone (I)

Cancer Biother Radiopharm. 2006 Feb;21(1):68-73. Related Articles, Links

Mary Ann Liebert,

Somatostatin, retinoids, melatonin, vitamin D, bromocriptine, and cyclophosphamide in advanced non-small-cell lung cancer patients with low performance status.

Norsa A, **Martino V**.

Thoracic Surgery Unit, Ospedale Maggiore Azienda Ospedaliera, Verona, Italy. norsaachille@yahoo.it

BACKGROUND: The prognosis of low performance status (PS) patients with advanced non-small-cell-lung cancer (NSCLC) is dismal. In these patients, we have determined the survival, clinical benefits, and toxicity of a multidrug regimen, based on cyclophosphamide and biotherapeutical agents. METHODS: Patients with a diagnosis of stage IIIB or stage IV NSCLC, no previous surgery or chemoradiotherapy, and an Eastern Cooperative Oncology Group (ECOG) PS equal to or greater than 2 received a daily combination of somatostatin, retinoids, melatonin, vitamin D, bromocriptine, and cyclophosphamide. RESULTS: Twenty-eight (28) patients were enrolled. The median age was 64 years (range, 35-74). The PS was 2 and 3 in 78.6% and 21.4% of patients, respectively. The median overall survival (intent-to-treat analysis) was 12.9 months (range, 1.5-33.5 months), The overall survival rates at 1 and 2 years were 51.2% and 21.1%, respectively. The side-effects were very mild, mostly consisting of diarrhoea, nausea/vomiting, and drowsiness of grade 1-2. Most patients experienced an improvement of both respiratory (cough and dyspnoea) and general (pain, fatigue, and insomnia) symptoms. CONCLUSIONS: Low PS patients with advanced NSCLC may benefit from a combination of somatostatin, retinoids, melatonin, vitamin D, bromocriptine, and cyclophosphamide, in terms of survival and quality of life, with very low side-effects.

Publication Types:
- Clinical Trial

PMID: 16480333 [PubMed - indexed for MEDLINE]

MDB nel cancro del polmone (II)

Cancer Biother Radiopharm. 2007 Feb;22(1):50-5. Related Articles, Links

Mary Ann Liebert,

Somatostatin, retinoids, melatonin, vitamin D, bromocriptine, and cyclophosphamide in chemotherapy-pretreated patients with advanced lung adenocarcinoma and low performance status.

Norsa A, **Martino V**.

Division of Thoracic Surgery, Ospedale Maggiore Azienda Ospedaliera, Verona, Italy. norsaachille@yahoo.it

BACKGROUND: We previously reported on an improvement in survival and quality of life in chemotherapy-naïve patients with advanced non-small-cell lung cancer and low performance status (PS) treated with a combination of biotherapeutical agents and cyclophosphamide. In this study, we assessed the survival, clinical status, and toxicity of this multidrug regimen in chemotherapy-pretreated patients with advanced lung adenocarcinoma and low PS. METHODS: Patients with stage IIIB or IV lung adenocarcinoma, who had progressed after prior standard chemotherapy, and with an Eastern Cooperative Oncology Group PS > or = 2, received a daily combination of somatostatin, retinoids, melatonin, vitamin D, bromocriptine, and cyclophosphamide. RESULTS: Twenty-three (23) patients were enrolled. The median age was 59 years (range, 42-75). The PS was 2 and 3 in 73.9% and 26.1% of patients, respectively. The median overall survival (intent-to-treat analysis) was 95 days (range, 19-214). The side-effects were mild, mostly consisting of diarrhea, nausea and vomiting, and drowsiness of Grade 1-2. There was an improvement in both respiratory and general symptoms, which was more evident in patients surviving more than 95 days. CONCLUSIONS: The combined regimen of somatostatin, retinoids, melatonin, vitamin D, bromocriptine, and cyclophosphamide is well tolerated and can improve disease-related symptoms in heavily pretreated patients with late-stage lung adenocarcinoma and poor PS.

Publication Types:
- Clinical Trial

PMID: 17627413 [PubMed - indexed for MEDLINE]

MDB nei linfomi non-Hodgkin (I)

Cancer Biother Radiopharm. 2001 Apr;16(2):171-7. Related Articles, Links

Mary Ann Liebert,

Cyclophosphamide plus somatostatin, bromocriptin, retinoids, melatonin and ACTH in the treatment of low-grade non-Hodgkin's lymphomas at advanced stage: results of a phase II trial.

Todisco M, **Casaccia P**, **Rossi N**.

ASL13, Sondrio. todmau@tin.it

PURPOSE: Somatostatin, prolactin, retinoids, melatonin and ACTH have been shown to influence the lymphatic growth, and the action of the cyclophosphamide in lymphoproliferative disorders is well known. This provided the rationale to conduct, in patients with low-grade non-Hodgkin's lymphomas (NHL), a phase II trial of a combined association of cyclophosphamide, somatostatin, bromocriptin, retinoids, melatonin and ACTH. PATIENTS AND METHODS: Twenty patients with a diagnosis of low-grade NHL, stage III or IV, were included in this study. Patients received for one month the following treatment: cyclophosphamide, somatostatin, bromocriptin, retinoids, melatonin, and ACTH. The therapy was continued for two additional months in patients with stable or responding disease. After three months, the responding patients continued the therapy for three months and more. RESULTS: Twenty patients were assessable for toxicity and response; 70% (14 of 20 patients; 95% confidence interval [CI], 50% to 90%) had a partial response; 20% (4 of 20) had stable disease, and 10% (2 of 20) progressed on therapy. Going on with the treatment, none of the 14 patients with partial response had a disease progression (average follow-up time of 21 months, range, 7 to 25), and 50% of these patients had a complete response; among 4 patients with stable disease, 25% (1 of 4) had a partial response and 75% (3 of 4) progressed on therapy (mean time to progression [TTP] 14.3 months, range, 7 to 21). The toxicity was very mild, the most common side effects being drowsiness, diarrhea and hyperglycemia. CONCLUSIONS: The association of cyclophosphamide, somatostatin, bromocriptin, retinoids, melatonin, and ACTH is well tolerated and effective in treatment of low-grade NHL at advanced stage.

Publication Types:
- Clinical Trial
- Clinical Trial, Phase II
- Evaluation Studies

PMID: 11385964 [PubMed - indexed for MEDLINE]

MDB nei linfomi non-Hodgkin (II)

Am J Ther. 2006 Nov-Dec;13(6):556-7. Related Articles, Links

Wolters Kluwer | Lippincott Williams & Wilkins

Relapse of high-grade non-Hodgkin's lymphoma after autologous stem cell transplantation: a case successfully treated with cyclophosphamide plus somatostatin, bromocriptine, melatonin, retinoids, and ACTH.

Todisco M.

ASL 11, Local Health Department of National Health Service, Fermo, Italy. todmau@tin.it

Patients with relapse of high-grade non-Hodgkin lymphoma (NHL) after autologous stem cell transplantation (auto-SCT) generally have a poor prognosis. Only a minority of these patients can be cured by a second myeloablative chemotherapy, and conventional salvage treatments are often associated with severe toxicities. With a combination of cyclophosphamide, somatostatin, bromocriptine, retinoids, melatonin, and ACTH, we already reported 100% global response in 8 patients with relapse of low-grade NHL after single or combined chemotherapy and a therapy-free period of > or = 6 months. This provided the rationale to evaluate the same pharmacological association in a patient with relapse of high-grade NHL after auto-SCT performed 2 years before. The patient was treated for at least 2 months. At the end of this period, if he had stable or responding disease, he received additional 3 months of treatment, and if he was stable or responding after 5 month, he was treated for 3 months and more. After 2 months, patient had a partial response, and after 5 months, he achieved a complete response. Today, 14 months after beginning treatment, patient is in complete remission. Treatment had very good tolerance, and patient carried on at home doing his normal activities. Our result and severe toxicities associated with conventional salvage treatments suggest in a relapse of high-grade NHL after auto-SCT, further clinical trials using the pharmacological association we employed in this case.

Publication Types:
- Case Reports

PMID: 17122540 [PubMed - indexed for MEDLINE]

MDB nei linfomi non-Hodgkin (III)

Am J Ther. 2007 Jan-Feb;14(1):113-5.

Wolters Kluwer | Lippincott Williams & Wilkins

Low-grade non-Hodgkin lymphoma at advanced stage: a case successfully treated with cyclophosphamide plus somatostatin, bromocriptine, retinoids, and melatonin.

Todisco M.

ASL 11, Local Health Department of National Health Service, Fermo, Italy. todmau@tin.it

Low-grade non-Hodgkin lymphomas (NHLs) at advanced stage are still incurable, and treatment may include chemotherapy with a single drug or a combination of different drugs. With a combination of cyclophosphamide, somatostatin, bromocriptin, retinoids, melatonin, and adrenocorticotropic hormone, we already reported 100% of global response (50% complete response and 50% partial response) in 12 patients with low-grade NHL at advanced stage: 4 previously untreated patients and 8 with relapse of disease after single or combined chemotherapy and therapy free time >or=6 months. This provided the rationale to treat a patient affected by low-grade NHL stage 4, with cyclophosphamide, somatostatin, bromocriptin, retinoids, and melatonin (adrenocorticotropic hormone was not administered for high blood pressure). The patient was treated for at least 2 months. After this period, if he had stable or responding disease, he received an additional 3 months of treatment, and if he was stable or responding after 5 months he was treated for 3 months and more. After 2 months the patient had a partial response, and after 5 months he achieved a complete response. Today, 18 months after the beginning of treatment, the patient is in complete remission. Treatment had very good tolerance, and the patient carried on at home doing his normal activities.

Publication Types:
- Case Reports

PMID: 17303979 [PubMed - indexed for MEDLINE]

Review su Melatonina

Neuro Endocrinol Lett. 2006 Aug;27(4):425-32. Related Articles, Links

Neuro endocrinology letters.

Key aspects of melatonin physiology: thirty years of research.

Di Bella L, **Gualano L**.

Private Laboratory of Physiology Prof Luigi Di Bella, Modena, Italy.

Numerous studies of melatonin, by now widely acknowledged as a circadian rhythm-affecting neurohormone, also describe its anti-oxidant, anti-cytotoxic or immune-modulating activity. While emphasizing the multifunctional aspect of melatonin action, this review presents the results of our thirty years of research, which point to the following conclusions: melatonin is capable of promoting platelet production by megakaryocytes, of acting on the latter's ion channels by way of the outward currents, and of performing a physiological anti-aggregation function thus lengthening platelet life span. Melatonin can be transported everywhere by platelets and, thanks to its lipophilicity, can cross cellular membranes easily, thus regulating blood-tissue exchanges and ensuring an improved haematic crisis. It interacts with endothelial cells by regulating their release of both relaxing-factor and contracting-factor, and with platelets by affecting their discharge of dense-body components. Finally, platelets could behave as mobile and itinerant serotonergic and/or melatonergic elements, a function comparable to the release of neurotransmitters by neurons of the central nervous system. This dynamism in melatonin physiology could prove to be a key in approaching tumour aetiopathogenesis.

Publication Types:
- Review

PMID: 16892002 [PubMed - indexed for MEDLINE]

Neuro Endocrinol Lett. 2007 Jun 12;28(3):219-220 [Epub ahead of print]Links

Luigi Di Bella MD. PhD. Homage.

Gualano L.

Private Laboratory of Physiology "Prof Luigi Di Bella", Modena, Italy.

Luigi Di Bella was born on July 17, 1912 at Linguaglossa, a small Sicilian village near Catania (Italy). So poor was his family that, after completing his secondary education, it was only by virtue of the several scholarships he had won that he could attend the faculty of Medicine at the University of Messina. He was noted and sought after as an intern by Prof. Pietro Tullio, Medicine Nobel prize candidate 1930 and 1932. At age nineteen, Luigi Di Bella associated his name to his master's in his first joint paper, and prior to graduating in 1936, he had already published nine works and won four national contests. During the Autumn of 1936 he initiated teaching physiology and biochemistry at the University of Parma. In 1937 he was presented with a scholarship by the acclaimed scientist Guglielmo Marconi, then president of CNR (National Research Council). In 1938 he earned his second University degree, in Pharmacology, and the third one, in Chemistry.

PMID: 17627252 [PubMed - as supplied by publisher]

2nd INTERNATIONAL SYMPOSIUM OF SOMATOSTATIN

Athens, June 1-3, 1981

L. Di Bella, L. Gualano, M.T. Rossi & G. Scalera

(Cattedra di Fisiologia Generale, Istituto di Fisologia, Via Campi 287 Modena)

Somatostatin in cancer therapy.

We are employing Somatostatin, associated with dl-*-bromocriptin, melatonin and cyclophosphamide in breast-, lung-, stomach-, bowel cancers, in Hodgkin and non-Hodgkin lymphomas, in malignant hystiocytosis, in bone- and smooth muscle sarcomas, in neuroblastomas, in melanomas. The dosages have been moderate (250 µg i.m./day, to the highest degree); apart from some temporary and tolerated trouble, no drawback has been met with, even after several years of unbroken therapy. It is difficult or even impossible to state the role of Somatostatin, in a compound treatment of several remedies, but we have become convinced that Somatostatin plays an important although not yet exactly defined role. Somatostatin has proved useless in the last, quickly progressive stages of malignancies.

In neuroblastoma Somatostatin has been poorly tolerated. In some case of cerebral metastasis from breast cancer a clinically complete recovery has been reached since more than four years. The goodness of the results includes both the possibility of patients continuing their normal social and family life, and a significantly longer survival. Urinary bladder irritation may lead to temporary discontinuance of cyclophosphamide.

Good results have been obtained in those cases of chronic lymphatic leukemia which cannot anylonger be treated with common antiblastic remedies owing to the dangerously low blood platelet count. Malignant histiocytosis has been equally well treated by a continued treatment with Somatostatin.

The treatment of cancer with Somatostatin, melatonin, prolactin incretion blocking agents and ACTH is probably the most physiological among the proposed and applied official therapies for cancer. It demonstrated no toxicity, is well tolerated, allows the common duties and performances of everyday social life to be undertaken. The combined remedies converge in blocking the incretion of adenohypophyseal hormones that impinge on tissue growth, and probably also act on their receptive peripheral action sites, without provoking any rebound action or adaptation or counterbalancing reaction.

FUNZIONI DELLA PINEALE, PROSPETTIVE

L. Di BELLA, M.T. ROSSI and G. SCALERA
(Cattedra di Fisiologia Generale, Università di Modena. 41100 Modena Italy)

già edito in:
The Pineal Gland of Vertebrates including Man (Progress in Brain Research, Vol. 52)
Editors: J. Ariens Kappers and P. Pevet 1979, Elsevier/North-Holland Biomedical Press

In pazienti cancerosi l'influenza regolatoria di MLT sulla crescita cellulare è fortemente accentuata dal simultaneo abbassamento dei livelli del GH circolante (attraverso la somministrazione di somatostatina o p-ossipropiofenone) e di prolattina. I risultati di una simile terapia combinata sembrano essere molto buoni. Tuttavia risultano meno favorevoli quando la massa neoplastica è molto estesa e scarsamente vascolarizzata o se le cellule neoplastiche si moltiplicano in tessuti poco vascolarizzati perché danneggiati da precedenti interventi. Dato che né la MLT né il GH presentano una qualche citotossicità, l'effetto di piccole quantità di sostanze antiblastiche può essere simultaneamente utilizzato nel tentativo di accelerare la riduzione o la scomparsa della massa neoplastica. Si possono trarre le seguenti conclusioni: Probabilmente il cancro può essere correlato con uno sbilanciamento tra MLT , GH e prolattina. Gli agenti eziologici, virali, fisici e chimici del cancro probabilmente agiscono interferendo con le stesse reazioni di crescita che vengono promosse dalla copresenza di GH e MLT. La MLT probabilmente estende la sua azione a tutte le cellule dell'organismo così come si verifica con il GH. Il GH ha ampi effetti sulla sintesi delle proteine e degli acidi nucleici (Kostyo e Isaksson, 1977), mentre le indolamine (Da Prada et al., 1971, 1978) e MLT (Di Bella et al., 1976) interferiscono con il metabolismo degli acidi nucleici. Esistono meccanismi biochimici in comune tra le due specie di sostanze a livello dei processi di crescita di ogni cellula somatica.

Med Sci Monit. 2002 Dec;8(12):BR527-31. Related Articles, Links

INDEX COPERNICUS FULL TEXT ARTICLE

Melatonin effects on megakaryocyte membrane patch-clamp outward K+ current.

Di Bella L, **Bruschi C**, **Gualano L**.

Private Laboratory of Physiology, Modena, Italy. luigidibella@libero.it

BACKGROUND: This study was carried out to evaluate the influence of melatonin concentration on rat bone marrow megakaryocyte outward K+ current and its implications with regard to platelet production. It is the Authors' view that the greatly extended development of megakaryocyte membrane, together with its ion channels, makes the choice of this topic particularly pertinent. MATERIAL/METHODS: Megakaryocytes from fresh Wistar rat bone marrow were clampaged with patch-clamp technique and the examination of membrane outward current was performed when melatonin dissolved in external or internal standard solution was used. RESULTS: On the basis of this study, melatonin does reduce outward K+ current intensity, the more the higher the melatonin concentration. In quantitative terms, whereas no change is noticed when dissolved melatonin concentration in external standard solution is smaller than 25 mM, at 50 mM only a delayed outward current decrease appears. The effect on the outward current intensity is reversible at least until melatonin concentration reaches 500 mM; when melatonin concentration is higher than 1000 mM the effect is demonstrably irreversible. The presence on the megakaryocyte membrane of internal standard melatonin solution does reduce the outward current even more sharply. CONCLUSIONS: There seems to be a positive correlation between cationic pump and megakaryocyte intimate processes of platelet production.

Publication Types:

- In Vitro
- Research Support, Non-U.S. Gov't

PMID: 12503031 [PubMed - indexed for MEDLINE]

Adv Exp Med Biol. 1999;460:373-6.

Cytochalasin B influence on megakaryocyte patch-clamp.

Di Bella L, Gualano L, Bruschi C, Minuscoli S, Tarozzi G.

Publication Types:

- In Vitro

PMID: 10810535 [PubMed - indexed for MEDLINE]

J Clin Oncol. 2002 May 15;20(10):2575-601.

Related Articles, Links

Full Text
J Clin Oncol

Comment in:

- J Clin Oncol. 2002 Oct 1;20(19):4127-8; author reply 4128-9.

Melatonin: from basic research to cancer treatment clinics.

Vijayalaxmi, Thomas CR Jr, Reiter RJ, Herman TS.

Departments of Radiation Oncology, The University of Texas Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 78229, USA.
vijay@uthscsa.edu

Melatonin, the chief secretory product of the pineal gland, is a direct free radical scavenger, an indirect antioxidant, as well as an important immunomodulatory agent. In both in vitro and in vivo investigations, melatonin protected healthy cells from radiation-induced and chemotherapeutic drug-induced toxicity. Furthermore, several clinical studies have demonstrated the potential of melatonin, either alone or in combination with traditional therapy, to yield a favorable efficacy to toxicity ratio in the treatment of human cancers. This study reviews the literature from laboratory investigations that document the antioxidant and oncostatic actions of melatonin and summarizes the evidence regarding the potential use of melatonin in cancer treatment. This study also provides rationale for the design of larger translational research-based clinical trials.

Publication Types:

- Review

PMID: 12011138 [PubMed - indexed for MEDLINE]

Bromocriptina - Indicazioni

Prevenzione o inibizione della lattazione 2,5 mg al giorno 1 (prevenzione) o per 2-3 giorni (inibizione); in seguito 2,5 mg 2 volte al giorno per 14 giorni.

Ipogonadismo, galattorrea, sterilità, all'inizio 1-1,25 mg al giorno prima del sonno notturno, da aumentare gradualmente; dose abituale 7,5 mg al giorno in dosi frazionate da aumentare, se necessario, fino a un massimo di 30 mg al giorno; dose abituale in caso di infertilità senza iperprolattinemia, 2,5 mg 2 volte al giorno.

Patologie cicliche benigne della mammella e disturbi mestruali ciclici (soprattutto dolore al seno), 1-1,25 mg prima di coricarsi, da aumentare in modo graduale; dose abituale 2,5 mg 2 volte al giorno.

Acromegalia, all'inizio 1-1,25 mg prima di coricarsi, da aumentare in modo graduale a 5 mg ogni 6h.

Prolattinoma, all'inizio 1-1,25 mg prima di coricarsi; da aumentare in modo graduale a 5 mg ogni 6h (in alcuni casi i pazienti possono richiedere fino a 30 mg al giorno).

Clin Oncol (R Coll Radiol). 2004 Dec;16(8):549-60. Related Articles, Links

Comment in:

- Clin Oncol (R Coll Radiol). 2005 Jun;17(4):294.

The contribution of cytotoxic chemotherapy to 5-year survival in adult malignancies.

Morgan G, **Ward R**, **Barton M**.

Department of Radiation Oncology, Northern Sydney Cancer Centre, Royal North Shore Hospital, Sydney, NSW, Australia. gmorgan1@bigpond.net.au

AIMS: The debate on the funding and availability of cytotoxic drugs raises questions about the contribution of curative or adjuvant cytotoxic chemotherapy to survival in adult cancer patients. MATERIALS AND METHODS: We undertook a literature search for randomised clinical trials reporting a 5-year survival benefit attributable solely to cytotoxic chemotherapy in adult malignancies. The total number of newly diagnosed cancer patients for 22 major adult malignancies was determined from cancer registry data in Australia and from the Surveillance Epidemiology and End Results data in the USA for 1998. For each malignancy, the absolute number to benefit was the product of (a) the total number of persons with that malignancy; (b) the proportion or subgroup(s) of that malignancy showing a benefit; and (c) the percentage increase in 5-year survival due solely to cytotoxic chemotherapy. The overall contribution was the sum total of the absolute numbers showing a 5-year survival benefit expressed as a percentage of the total number for the 22 malignancies. RESULTS: The overall contribution of curative and adjuvant cytotoxic chemotherapy to 5-year survival in adults was estimated to be 2.3% in Australia and 2.1% in the USA. CONCLUSION: As the 5-year relative survival rate for cancer in Australia is now over 60%, it is clear that cytotoxic chemotherapy only makes a minor contribution to cancer survival. To justify the continued funding and availability of drugs used in cytotoxic chemotherapy, a rigorous evaluation of the cost-effectiveness and impact on quality of life is urgently required.

Publication Types:

- Review

PMID: 15630849 [PubMed - indexed for MEDLINE]

BMJ. 2000 Apr 1;320(7239):895-8.

Comment in:

- BMJ. 2000 Apr 1;320(7239):884-5.
- BMJ. 2000 Dec 9;321(7274):1470; author reply 1471-2.
- BMJ. 2000 Dec 9;321(7274):1471-2.
- BMJ. 2000 Dec 9;321(7274):1471; author reply 1471-2.
- BMJ. 2000 Dec 9;321(7274):1471; author reply 1471-2.

How many deaths have been avoided through improvements in cancer survival?

Richards MA, Stockton D, Babb P, Coleman MP.

Department of Palliative Medicine, St Thomas's Hospital, London SE17 7EH, UK.

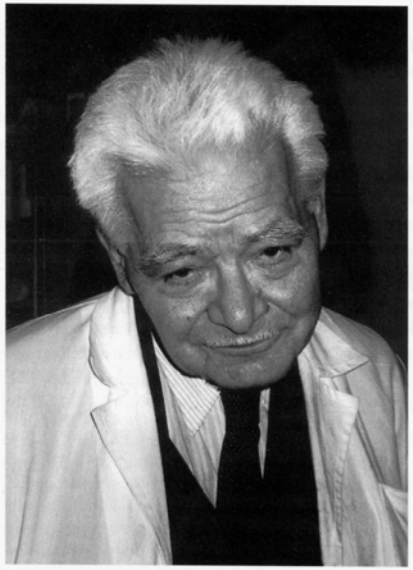
OBJECTIVE: To estimate how many deaths from cancer have been avoided in England and Wales because of recent improvements in survival. Design: Analysis of national statistics. SETTING: England and Wales. Subjects: 1.5 million adults with diagnosis of one of 47 different cancers during 1981-5 or 1986-90. Main outcome measures: Reduction in number of cancer deaths within five years of diagnosis among patients with cancer diagnosed during 1986-90 compared with patients with cancer diagnosed during 1981-5. RESULTS: 17 041 deaths were avoided within five years of diagnosis among patients with cancer diagnosed during 1986-90. This represents 3.3% of the cancer deaths that would have been expected if survival had been the same as for patients with cancer diagnosed during 1981-5. Two thirds of the avoided deaths arose from improvements in survival for just five cancers: female breast cancer (4822), cancers of the colon (2560), rectum (1090), and bladder (1157), and melanoma of the skin (1098). The largest proportionate reductions in excess deaths were for melanoma of the skin (23%) and cancers of the testis (17%) and bone (17%). About 12 000 (70%) of the avoided deaths arose among adults aged under 75 at death. Improvements in survival from cancers of lung, prostate, stomach, ovary, and brain were small: they accounted for 33% of all cancers but only 11% of avoided deaths. CONCLUSIONS: Small gains in survival from common cancers save more lives than larger gains for uncommon cancers. If recent rates of improvement in cancer survival continue, about 24 000 deaths within five years of diagnosis would be avoided in patents aged under 75 by the year 2010, representing about a quarter of the government's overall target of 100 000 fewer cancer deaths.

PMID: 10741993 [PubMed - indexed for MEDLINE]

Omaggio prof. Luigi Di Bella

Luigi Di Bella MD. PhD.

Luigi Di Bella was born on July 17, 1912 at Linguaglossa, a small Sicilian village near Catania (Italy).



So poor was his family that, after completing his secondary education, it was only by virtue of the several scholarships he had won that he could attend the faculty of Medicine at the University of Messina. He was noted and sought after as an intern by Prof. Pietro Tullio, Medicine Nobel prize candidate 1930 and 1932. At age nineteen, Luigi Di Bella associated his name to his master's in his first joint paper, and prior to graduating in 1936, he had already published nine works and won four national contests.

During the Autumn of 1936 he initiated teaching physiology and biochemistry at the University of Parma. In 1937 he was presented with a scholarship by the acclaimed scientist Guglielmo Marconi, then president of CNR (National Research Council). In 1938 he earned his second University degree, in Pharmacology, and the third one, in Chemistry.

With the rank of medical captain, he set off for Greece, where he was in charge of a Military Hospital. He was indefatigable in caring for the patients in his charge. So much so that he was eventually overwhelmed by

the strain and, in 1943, sick with malaria and a severe hepatitis, he had to be discharged. After a brief convalescence, Luigi Di Bella resumed teaching and researching at the University of Modena and had several scientific works published. In the period 1937 through 1948 his name appears on as many as thirty-five papers, a number of which were based on his studies of aneurine, retinoids and on his research on hypothalamus and pituitary gland functions. In 1948 he won the Human Physiology and Biochemistry professorships. Having to endure hindrance and rivalries in his research effort, he personally designed a private laboratory and went ahead with its construction, occasionally assisted by a few labourers. From 1951 onwards much research work was carried out in this "Private Laboratory of Physiology".

In 1969, after thirty years of research, Luigi Di Bella communicated to a national congress (SIBS) his first findings pointing to an innovative therapy

To cite this article: **Neuro Endocrinol Lett** 2007; **28**(3):219–220

Giuseppe Di Bella

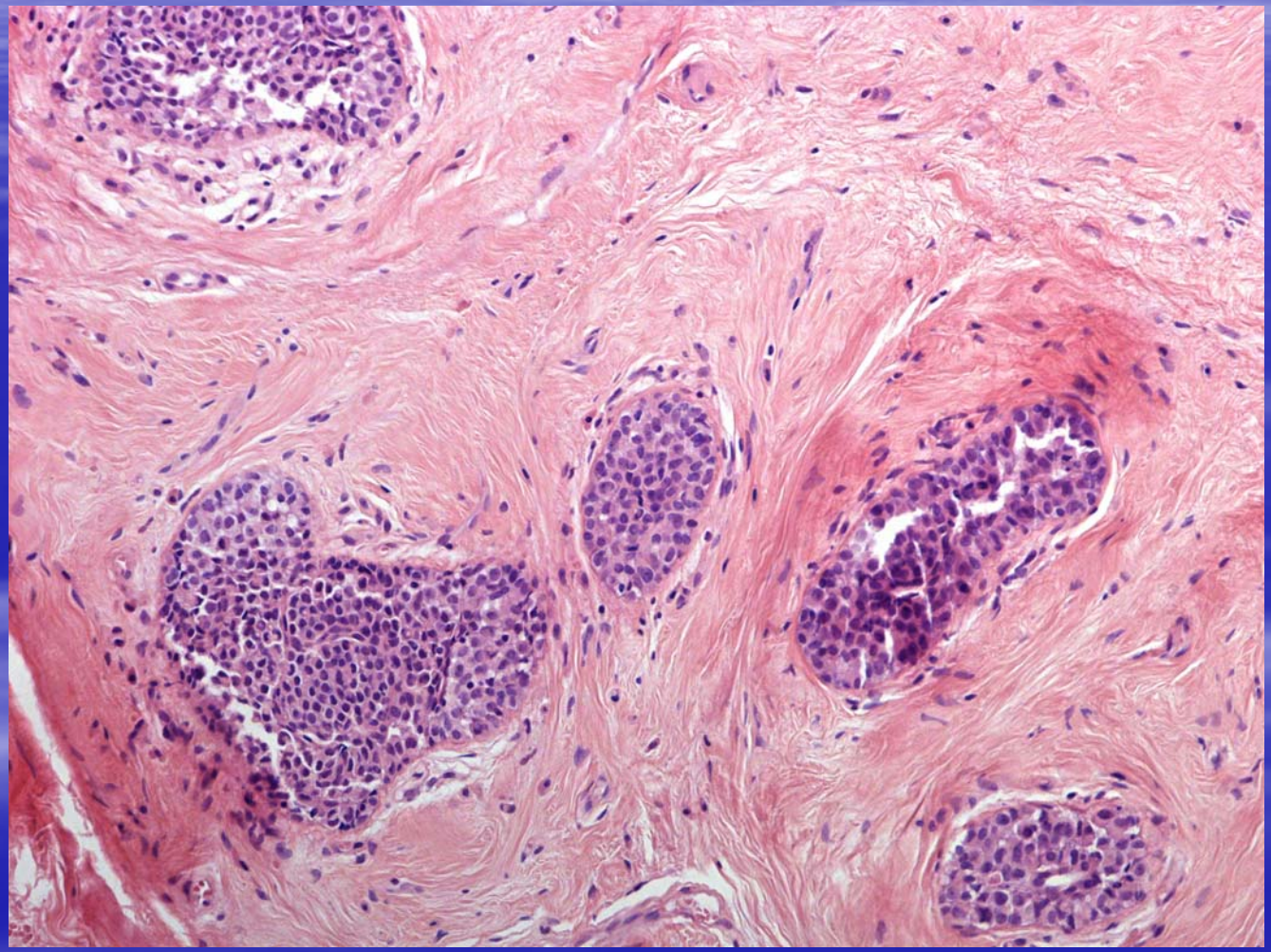
Target therapy:
Risposta alla terapia biologica di 18 carcinomi della testa e del collo

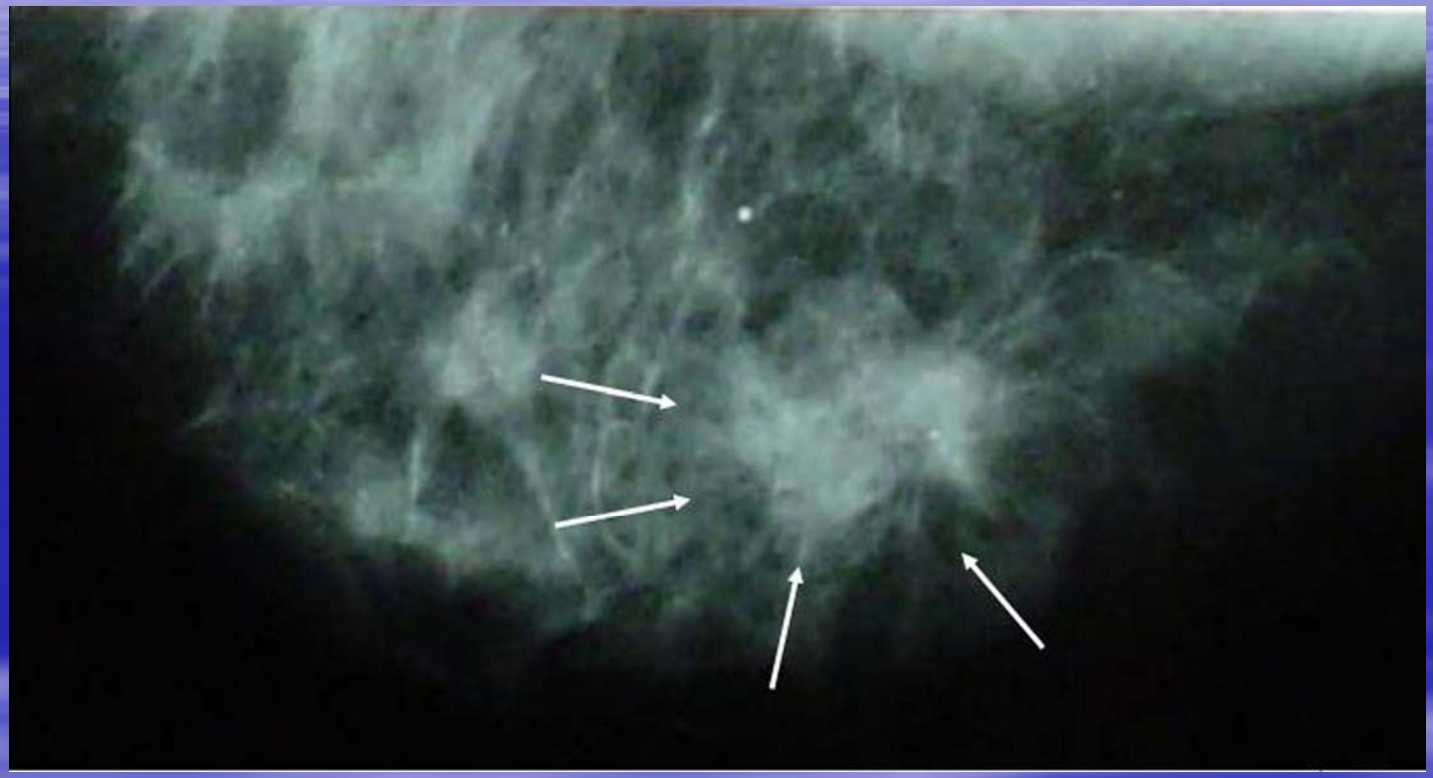
La mancata valorizzazione di molecole antitumorali differenzianti e antiproliferative a bassa tossicità ed elevato potenziale antiblastico come retinoidi, vitamine D3, E, C, Somatostatina, MLT, inibitori prolattinici, insieme all'elevato effetto mutageno, la grave tossicità, la depressione immunitaria chemioindotte, spiega i gravi limiti delle attuali oncoterapie. Esse consentono il 29% di sopravvivenza a 5 anni (M.A. Richards, e AA (BMJ 2000;320:895–898), non ottenuta dalla chemio, ma da chirurgia+radioterapia+chemio. Un'inaccettabile percentuale di mortalità da chemio è denunciata da un'agenzia della Reuters Healt [Wesport,CT 2001-05-17]: "Unexspected high mortality rated associated with chemotherapy regimen". Il dato è confermato dalla pubblicazione di Gerrard [Br.J. Cancer 1998 Jun 77(12) 281-5] **con l'11% di decessi, non causati dal tumore ma unicamente da chemioterapia.** La sopravvivenza ottenuta dall'oncoterapia si riduce ad un 29% a 5 anni (Richards,BMJ2000;320:895–898). Del 29% solo il 2,5% era dovuto alla chemio, come pubblicato da Morgan G. e AA "The contribution of cytotoxic chemotherapy to 5-year survival in adult malignancies" [Clin Oncol 2004 Dec.16(8):549-60]. Statistica basata su 14 anni di osservazione, 225000 pazienti, 22 varietà tumorali: **su cento ammalati la chemioterapia consente solo al 2,5% di raggiungere i 5 anni,** dopo i quali, Lopez nello studio clinico "Long–term results…Experience at the 20 th…" GacMed Mex [1998 mar. Apr,134(2):145-5] ha accertato che metà dei pazienti sopravvissuti a cinque anni, nel lungo termine, muore per tumore. Componenti della Terapia: ***Somatostatina, Bromocriptina, Betacarotene, Axeroftolo palmitato, Ac trans retinoico, Alfatocoferile acetato, Diidrotachisterolo, Melatonina adenosin glicina, ciclofosfamide, calcio, ac ascorbico, Glucosamina solfato, Galattosamina solfato.*** La terapia biologica recettoriale ha consentito in questi casi risposte obiettive parziali o complete, stabilità e qualità di vita, sopravvivenza, in assenza di tossicità, nettamente superiore alle mediane di sopravvivenza e ai dati della letteratura in queste patologie e stadi, attraverso un meccanismo d'azione recettoriale differenziante, citostatico, apoptotico, antiproliferativo, antimetastatico, antiangiogenetico, trofico, immunomodulante.

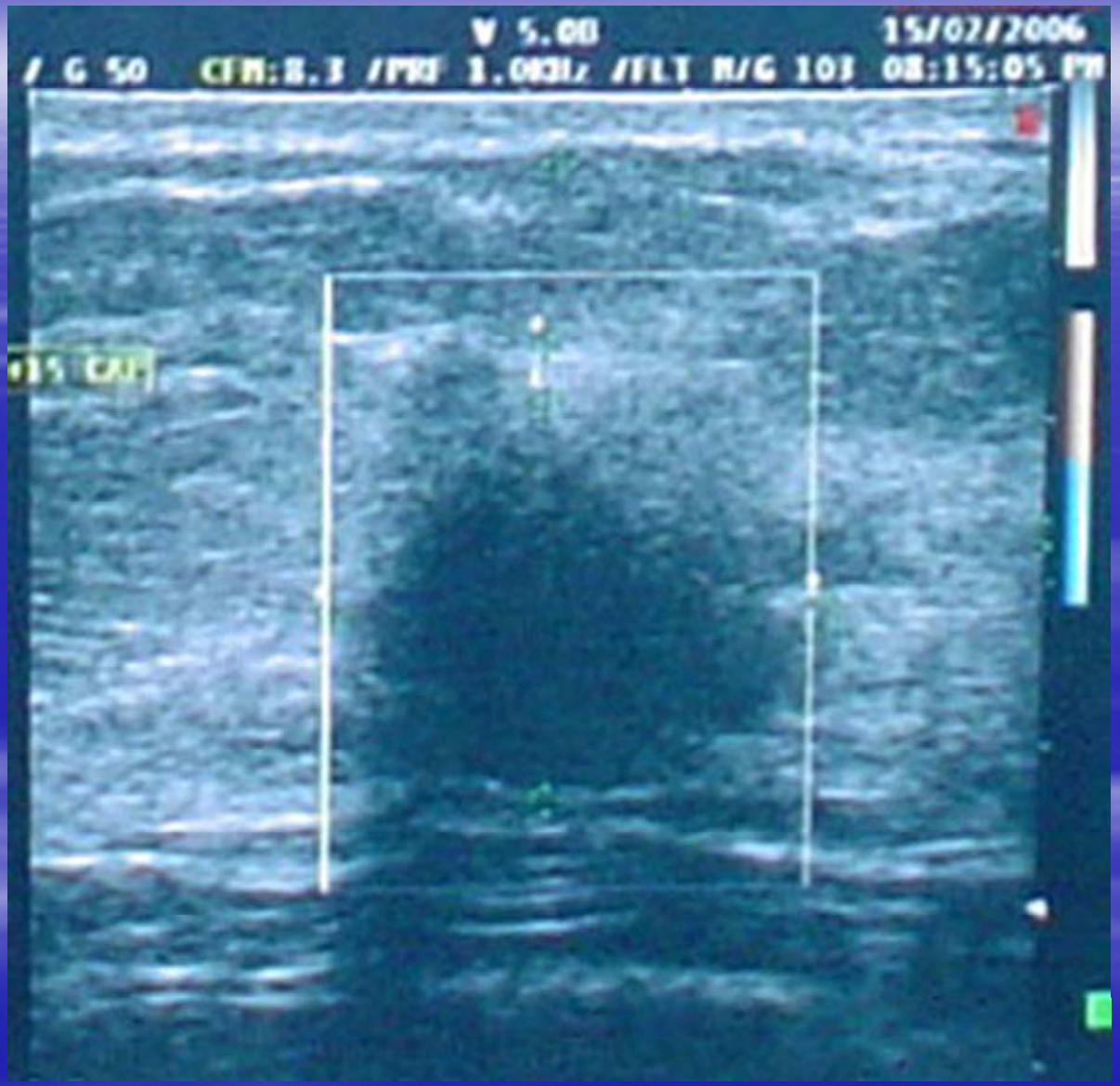
Complete objective response to biological therapy of plurifocal breast carcinoma

ABSTRACT

For a woman with breast carcinoma, Prof. L. Di Bella's biological therapy (MDB) for seven months, produced a 50% partial objective response, and was totally cured in 14 months, extended to the bilateral axillary adenopathies, without toxicity. MDB entails anti-proliferative molecules such as somatostatin, prolactin and estrogen inhibitors along with differentiating and apoptoptic molecules such as MLT, Retinoids, vitamins C, D3, E, calcium, and amino-sugars, combined with minimal doses of chemotherapy. The hemato-chemical exams showed no damage, but a progressive reduction of prolactin, estradiol, IGF1, and maintenance of low levels of GH. The objective result, without toxicity, of this case, proves the effectiveness of this therapy and conforms to the positive results already published on the use of MDB on Low Level LNH and pulmonary carcinomas in the 3rd and 4th stages. MDB, without the need for hospitalization or day hospital, without toxicity, and without even minimally reducing the patient's daily work routine, allowed the patient to avoid surgical trauma and the significant collateral effects of chemo- and radiotherapy. Precocious use of MDB as the first line therapy, on an organism that is not debilitated by the mutagenic toxic and immuno-depressive effects of chemo- and radiotherapy, greatly facilitated the result. We feel it is useful to highlight this case to stimulate interest and further study of the possibilities opened up in oncology by MDB biological and receptor therapy.



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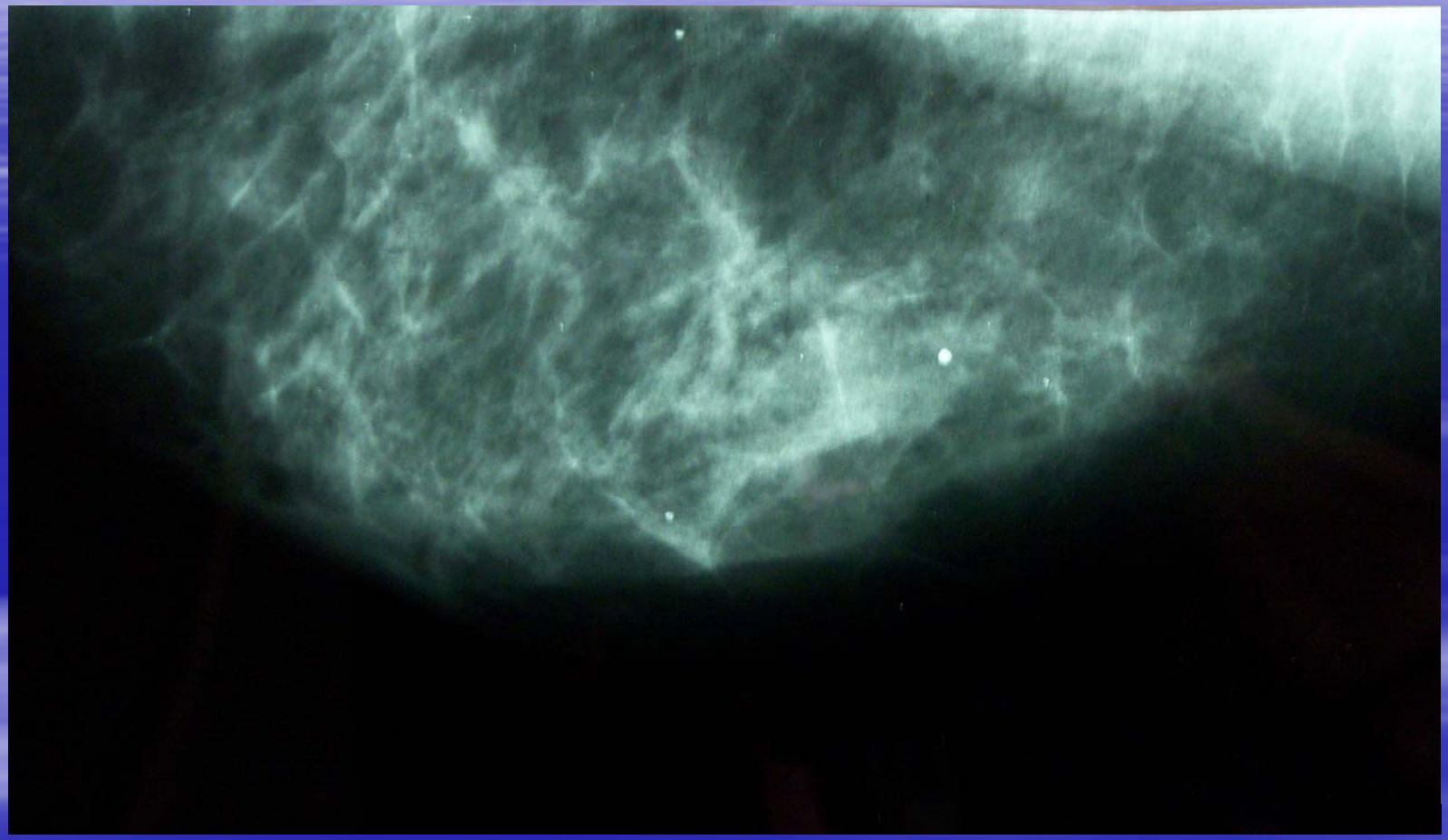

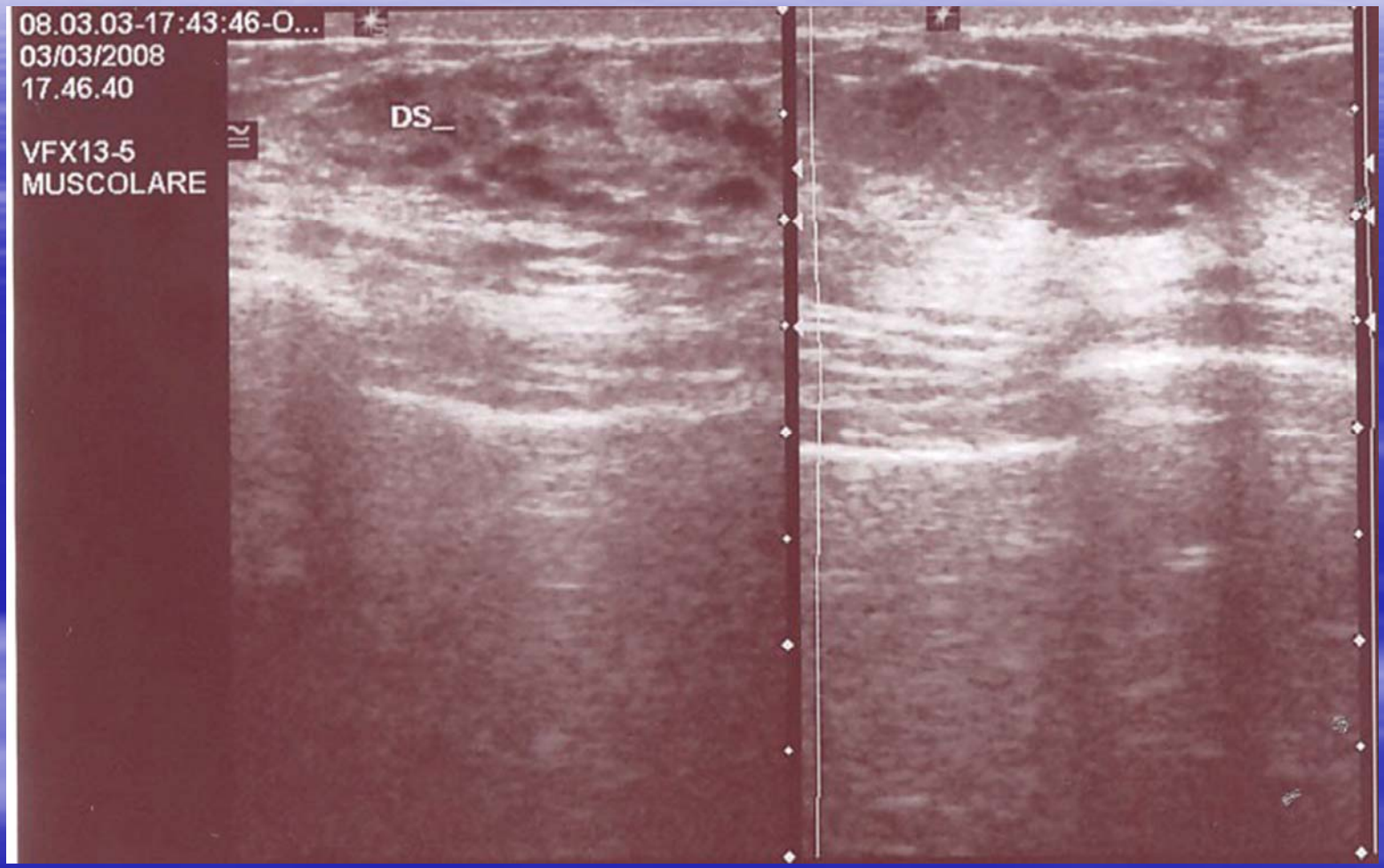
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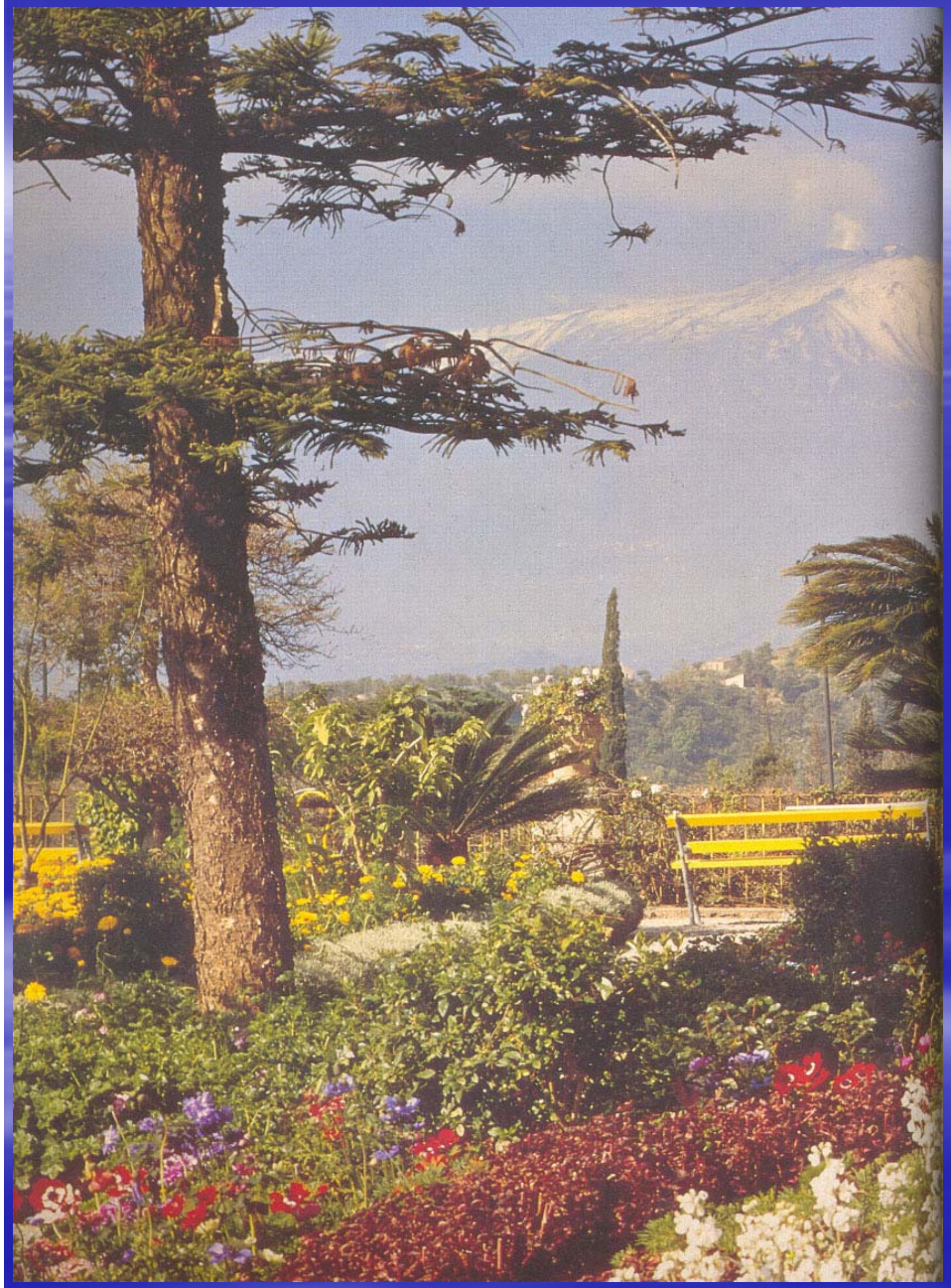

L’essenziale sta nell’attivare tutti gli inibitori dei noti fattori di crescita alle dosi e con tempestività e tempi opportuni.
Il protocollo MDB è nato in quest’atmosfera, quella della vita e non dell’intossicazione e morte delle cellule, metodo che asseconda o esalta le reazioni vitali, senza ricercare con precisione statistica le dosi più opportune per uccidere.
Il tumore è deviazione dalla vita normale, per cui occorre portare le reazioni deviate alla norma, attraverso l’esaltazione di tutti quei mezzi che la Fisiologia considera essenziali per la vita

Per maggiori informazioni

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