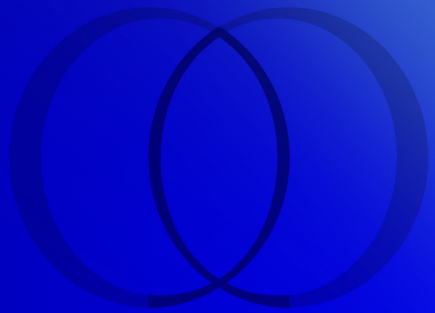


A-D Research Foundation

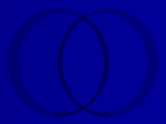
A-D Research Foundation is committed to:

- Developing a new understanding of the patho-mechanism of cancer
- Developing new, breakthrough therapies by utilizing this knowledge

Currently held views on cancer mechanism

Main Emphasis on Genetics:

- From a single cell that loses its differentiated state through sequential mutations
- Initiation-promotion-progression concept explains the steps in a sequential process
- Oncogenic theories suggests that defects in tumor suppressor genes cause malignancy



P. Grandics, The Cancer Stem Cell:Evidence for its Origin as an Injured Autoreactive T Cell. Mol. Cancer 2006, **5**:6.

The cancer stem cell concept

- Cancer may develop out of a single cell
- Just a small fraction of tumor cells have the ability of disease propagation
- Cancer stem cells could be mutated normal stem cells
- Cancer stem cells may develop from other cell types

Observations & Analysis

- Body mounts a low intensity immune response to cancer
- Immunosuppressive cytotoxic antineoplastic therapies may cause regression of a clinically established cancer
- Immunosuppression that can be lethal in a fungal infection may benefit cancer suppression
- Autoimmunity is also controlled by immunosuppression
- Cancer cells "attack self" comparably to autoreactive T cells
- Could there be a relationship between autoimmunity and cancer?
- Could the cancer stem cell arise from damaged autoreactive
- T cells?

Comparison of inflammatory cells and cancer cells

Inflammatory T cells:

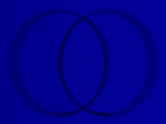
- Inflammatory cytokine secretion
- Attachment to neutrophils, macrophages, endothelium
- Cause platelet aggregation
- Secrete tissue factor
- Induce clotting
- Temporary wound stroma development

Cancer cells:

- All the same except that the wound stroma is permanent (tumor)

Infection, inflammation & cancer

- Microbial antigens are present in the patient's sera
- Pathogen eradicating therapy led to the regression of some cancers
- Hit-and-stay pathogens distort the immune response using the TLR signaling system
- Th2, Treg dominance established
- Th2 cytokines antagonize cellular immune response
- Tumor cells secrete Th2 polarizing cytokines that inhibit tumor specific cytotoxic T cells

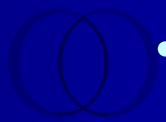


Infection, autoimmunity & cancer

- A number of pathogens are linked to autoimmunity & cancer
- Antinuclear antibodies (ANA) were found in the sera of 19% of patients
- Autoantibodies are observed against tissue-specific antigens, nucleoproteins, membrane receptors, proliferation-associated antigens, tissue-restricted antigens, etc.
- About 60% of cancers express anti-p53 autoAbs
- Infections may induce autoimmune serological features without overt autoimmune disease or organ involvement
- Cancer patients exhibit a higher percentage of autoreactive T cells
- Mechanism of autoimmunity via molecular mimicry

A new cancer stem cell concept

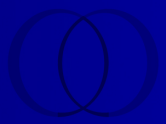
- Autoreactive T cells are normally eliminated by apoptosis
- T cells require IL-2, IL-4, IL-7, IL-9 and IL-15 for viability
- Tumor cell-secreted cytokines inhibit apoptosis
- Cytokines inhibit chemotherapy or radiation-induced apoptosis
- Cytokine withdrawal causes apoptotic death
- Persistent infections stimulate a cytokine response that enhances tumor cell viability
- Defective apoptosis leads to autoimmunity and cancer
- The cancer stem cell may be a “by-product” of cellular immunity



Similarity of CTLs and cancer cells

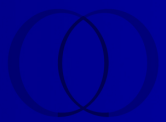
- Cytotoxic lymphocytes (CTL) express FasL
- Cancer cells also express FasL
- Cancer cells use the FasL mechanism to kill

  Fas sensitive, tumor infiltrating T cells
- Cancer cells behave like CTLs
- Cancer cells express CTLA-4 antigen



Further observations

- Common acute lymphoblastic leukemia antigen was detected on glioma and melanoma cell lines
- Myeloid antigen Leu-7, expressed on natural killer (NK) cells and T cell subsets, was detected on small cell lung carcinoma and a variety of other solid tumors
- Hodgkin's disease expressing Leu-7 may be related to NK cells or T cells rather than B cells
- Cancer stem cells embedded in an environment of normal host tissue may undergo a differentiation-like process (repair attempt)



Genomic damage vs malignancy

- Benign colonic adenomatous polyps and synchronous adenocarcinoma, exhibit comparable and very large numbers of genomic alterations (>10,000 events per cell)
- There is no fundamental genetic difference between benign and malignant tumors
- The genomic damage is characteristic of apoptosis as opposed to sequential mutation
- Genomic damage precedes malignant transformation

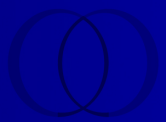
Characteristics of the cancer stem cell

Retains properties of cytotoxic T cells:

- Homes in to sites of inflammation
- Secrete inflammatory cytokines (in an unregulated fashion)
- Activates the coagulation system (tumor stroma formation)
- Stimulate new vasculature, endothelium
- Attachment to other inflammatory cells
- Present in the circulation

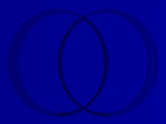
What is the true nature of cancer?

- Is cancer really a genetic disease?
- Cancer has memory
- Memory T cells play a role in overcoming infections
- Defective immune system fails to control peripheral immunity
- Defective apoptosis may produce cancer stem cell
- Evidence shows that gastric epithelial carcinoma originate from bone marrow derived cells
- Cancer is a disease of the immune system. It is NOT a genetic disease!



Therapeutic take home lessons

- Radiation, chemo & surgery are marginally effective
- They enhance a pre-existent hypercoagulable state
- Deletion of even the resting T cell compartment can occur
- Immune suppression encourages spread of infections
- Infections increase the inflammatory response
- Inflammation in turn enhances the viability of cancer cells
- Multi-drug resistance can develop during chemotherapy
- Disease recurrence, metastases & disease progression follows
- Patient expires



Cancer: A nutrient deficiency syndrome?

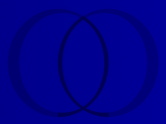
There is a proven correlation between nutrient deficiencies and cancer risk

- Immigrant population studies emphasize environmental factors
- Dietary interventions are protective
- Dietary interventions can also be curative

P. Grandics. J Carcinogenesis 2003 **2**:9

Critical nutrients affecting DNA integrity, immune function and cell proliferation

- Folate, vitamin B12 and other B vitamins
- Minerals: iron, zinc, selenium, potassium, magnesium
- Plant phenolics: flavonoids, phenolic lignans
- Iodine
- Essential lipids



The gastrointestinal link

- There is a correlation between impaired digestion and cancer
- The gut is a most important immune organ
- Resident bacterial flora participates in nutrient assimilation
- Prolonged stress down-regulates digestive system
- Adventitious agents overrun the gut in cancer
- Pancreatic digestive enzymes positively affect the course of cancer
- The excretory system must be cleansed in cancer patients

Overcoming tumor adaptation

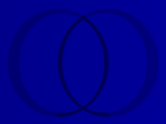
- Acquired drug resistance (MDR) is a common problem in cancer
- ATP-dependent drug efflux pump (P-170 GP or MDR-pump)
- Quinine inhibits MDR
- Quinine is anti-microbial and anti-inflammatory
- Used to be a body tonic,
- Hence the origin of Tonic Water

Cancer from a systemic perspective

- Human organism is a vast matrix of interconnected systems
- Coincident, multiple nutrient deficiencies identified in cancer
- Vast array of metabolic and regulatory pathways are affected
- General systemic effect leads to a systemic breakdown
- Single active agent therapies are unrealistic
- A SYSTEMS APPROACH is needed

Is cancer a single disease?

- Cancer stem cells identified
- Is there a common progenitor?
- Nutrition provides a unifying perspective
- Dietary (systemic) approach could reverse the disease
- This is indirect proof of a common mechanism



Essential ingredients of the anti-cancer dietary composition

- Cane molasses
- Apple cider vinegar
- Rose oil/Rose petal extract
- Folic acid
- Vitamin B12
- Iodine
- Quinine
- Sulfur

Completed individual case studies with Stage III-IV patients

- AML
- CLL
- Colon carcinoma
- Breast carcinoma
- Prostate carcinoma
- Lung (NSC) carcinoma
- Pancreatic carcinoma
- Cervical carcinoma

In all cases, clinically significant responses were obtained

Example case studies with Stage III-IV highly lethal cancers

- Acute myeloid leukemia
- Cholangiocarcinoma

AML case study

Objectives: The aim of this study was to determine the possible clinical benefit of molasses-based dietary compositions(designated as MSQ 13, MSQ 15, and MSQ 18) in a case of both primary and recurrent adult AML.
Design: The design was a single case study.
Settings/location: The setting was in the home.
Interventions: The regime of dietary compositions initially was administered as follows: MSQ-131tbsp t.i.d. for 1 mo, MSQ-15 2tbsp t.i.d. for 3 mo. After recurrence, MSQ-18 was taken at 2 tbsp t.i.d. for 3 mo.
Outcome measures: Clinical improvement and regression of AML were the outcome measures.
Conclusions: Treatment with the MSQ dietary compositions resulted in disease regression and the reversal of clinical manifestations over two episodes of AML. Therefore, further studies are warranted to evaluate the utility of this approach for the clinical management of AML.

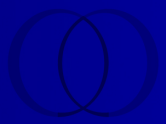


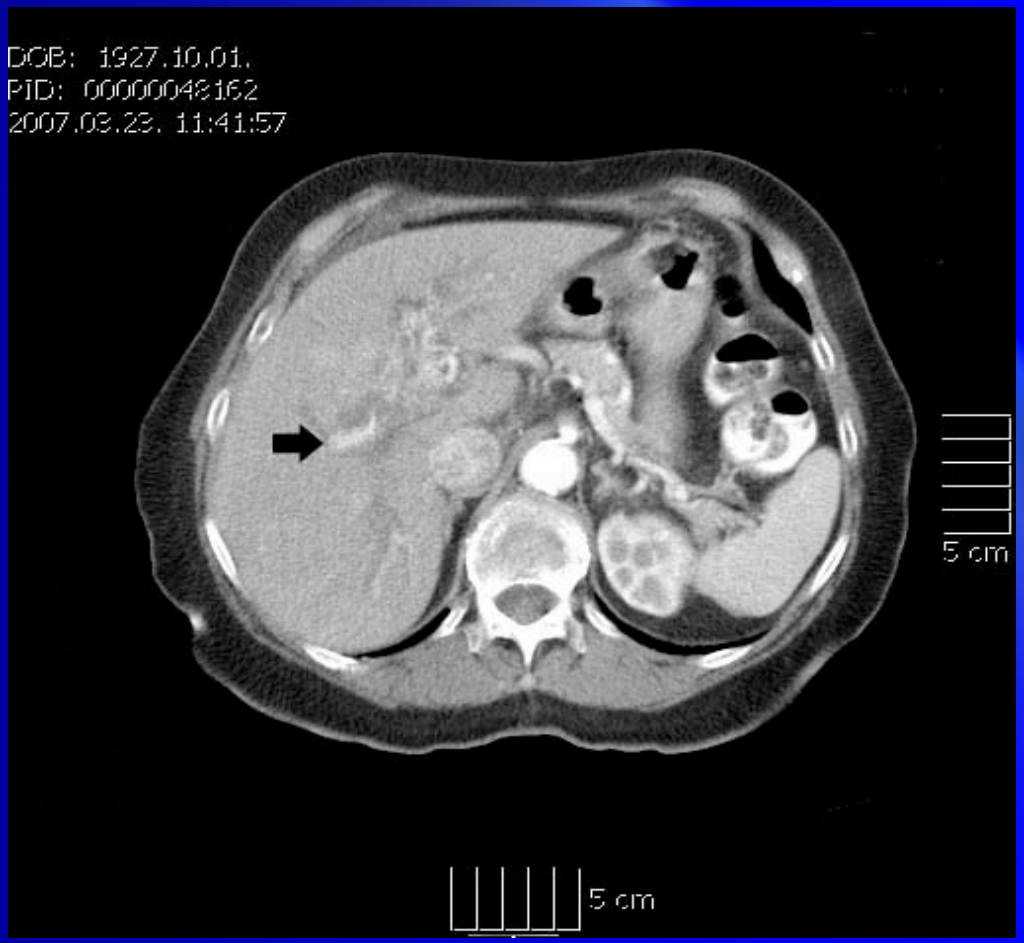
Table 1. Complete Blood Testing Data Over the Courseof MSQ Therapy

Date Unit	WBC G/l	RGC T/L	HGB g/l	HCT l/l	MCV fl	MCH pg	MCHC g/l	PLT G/l	We.1h. mm/h	We.2h. mm/h	Glucose mmol/l	Urea mmol/l	Creatinine umol/l
2002													
10.02	14.2	3.09	118.6	0.29	70.0	27.0	325.0	132.0	15	32	4.7	2.4	55.0
10.09	13.9	3.66	126.0	0.31	76.0	27.0	330.0	140.0	16	36	4.7	3.1	57.0
10.16	12.4	3.21	117.0	0.30	78.0	26.0	316.0	138.0	18	36	4.7	2.9	55.3
10.24	14.1	3.15	116.0	0.29	76.0	26.0	315.0	136.0	15	30	4.8	2.6	55.0
10.29	13.9	3.20	115.0	0.30	76.0	26.5	315.0	137.0	15	30	4.7	2.7	56.0
11.04	13.7	3.20	113.0	0.27	76. 0	26.0	315.0	137.0	19	38	4.7	2.4	54.0
11.12	11.1	3.99	128.0	0.33	78.0	28.0	331.0	141.0	21	62	4.9	3.3	59.0
11.19	12.1	4.40	129.0	0.32	79.0	28.5	322.0	139.0	16	32	3.9	2.8	57.5
11.27	14.5	2.90	119.0	0.27	78.0	24.5	305.6	129.0	18	37	2.8	2.4	53.5
12.16	18.9	2.00	92.0	0.64	59.0	21.1	287.0	119.0	27	56	1.1	1.9	43.9
12.30	19.5	1.80	91.0	0.14	59.0	20.0	286.5	119.0	26	52	1.9	1.6	43.6
2003													
01.03	19.9	1.77	91.5	0.13	58.7	19.9	286.0	119.0	28	56	1.2	1.6	43.3
01.06	20.0	1.75	94.4	0.13	58.6	19.9	286.0	119.0	29	58	1.2	1.6	43.2
01.10	19.8	1.80	90.0	0.13	58.8	19.9	286.0	115.0	32	64	1.8	1.6	43.4
01.13	19.0	2.00	90.0	0.15	60.0	20.0	285.0	113.0	34	68	2.3	1.4	40.9
01.15	18.0	2.40	98.0	0.17	64.2	21.5	290.0	126.0	25	50	2.6	1.5	45.0
01.17	18.5	2.20	92.7	0.16	62.9	21.0	228.3	128.0	29	58	2.5	1.5	43.0
01.29	18.9	2.10	91.0	0.16	61.5	21.8	289.6	129.0	31	62	2.4	1.4	45.0
01.22	18.0	2.15	90.6	0.19	62.0	21.7	290.0	129.0	34	68	2.4	1.4	44.0
01.24	17.6	2.17	90.5	0.19	62.3	21.9	290.0	129.0	30	60	2.5	1.4	45.5
02.17	19.5	1.80	91.9	0.14	59.0	19.9	286.5	119.2	26	52	1.9	1.6	43.6
02.19	18.8	2.00	92.9	0.15	60.0	21.0	287.6	119.5	25	50	2.0	1.9	44.0
02.21	19.1	2.00	92.8	0.16	59.9	19.9	284.7	119.8	22	44	1.9	1.5	43.2
02.24	13.5	3.20	115.0	0.30	76.0	26.0	314.0	137.0	16	32	4.7	2.7	56.0
02.26	12.9	3.70	117.0	0.30	78.0	26.0	318.0	138.0	18	36	4.6	2.7	55.5
02.28	12.3	3.80	120.0	0.31	79.0	27.0	320.0	138.0	18	36	4.7	2.9	56.0
03.03	11.6	3.66	126.0	0.31	76.0	27.0	330.0	142.0	16	32	4.7	3.1	57.0
03.05	11.5	3.90	128.0	0.30	77.1	27.2	325.5	141.2	19	38	3.9	3.5	56.5
03.07	11.3	4.10	127.3	0.29	77.3	27.2	324.5	146.1	21	36	3.6	5.6	56.6
03.10	11.3	4.00	127.8	0.30	78.0	27.2	325.8	146.9	18	36	3.8	3.6	56.0
03 .17	11.2	3.90	127.5	0.31	78.9	27.2	325.0	146.8	16	32	4.0	3.5	56.1
03.21	11.2	3.70	127.5	0.32	78.1	27.2	325.0	146.8	16	32	4.2	3.5	56.0
03.24	11.1	3.70	127.6	0.32	78.2	27.2	325.0	146.8	15	30	4.1	3.5	56.0
03.28	11 .2	3.69	127.5	0.32	78.2	27.2	325.0	146.8	15	30	4.0	3.5	56.0
03.31	11.1	3.70	127.6	0.32	78.2	27.2	325.0	146.8	15	30	4.0	3.5	56.0
04.21	11.1	3.75	127.6	0.32	78.2	27.2	326.0	146.8	14	28	4.0	3.5	56.0
2004													
10.22	20.6	1.65	89.1	0.10	56.9	19.0	281.6	119.0	19	36	4.40	1.57	42.96
10.29	18.3	2.00	92.8	0.14	61.0	20.0	284.2	120.1	18	34	4.40	1.62	43.10
11.02	18.0	2.40	96.0	0.16	63.4	21.3	286.2	123.0	18	34	4.50	1.70	43.90
11.05	17.8	2.50	99.9	0.17	65.1	22.3	289.0	125.5	17	34	4.60	1.75	44.00
11.09	17.0	2.70	101.2	0.20	67.0	24.0	292.5	127.1	21	39	4.40	1.83	44.20
11.12	16.9	2.85	106.0	0.23	67.9	24.3	296.0	128.3	22	40	4.80	1.86	43.00
11.15	16.8	3.07	108.5	0.25	68.0	24.7	298.2	129.1	24	42	4.60	1.90	43.30
11.17	16.7	3.12	110.0	0.26	69.0	24.9	299.9	130.0	26	44	4.40	1.89	43.45
11.19	16.0	3.20	110.4	0.27	70.0	25.0	300.4	130.2	24	42	4.80	1.90	45.50
11.22	15.6	3.40	112.8	0.28	74.5	26.2	306.0	131.0	24	42	4.70	2.10	46.20
11.24	15.5	3.45	113.0	0.28	75.0	26.3	307.0	132.2	24	42	4.70	2.15	46.25
11.26	15.5	3.50	113.2	0.29	75.5	26.3	307.5	132.9	24	42	4.60	2.20	47.10
11.29	14.0	3.90	116.0	0.31	79.3	27.0	311.0	135.3	22	40	4.70	2.36	49.60
12.16	13.2	4.00	120.0	0.32	81.0	27.5	320.0	137.0	20	38	4.80	2.40	52.90
2005 01.16	6.7	4.72	136.0	0.42	89.2	28.8	323.0	214.0	16	32	5.74	3.90	48.00

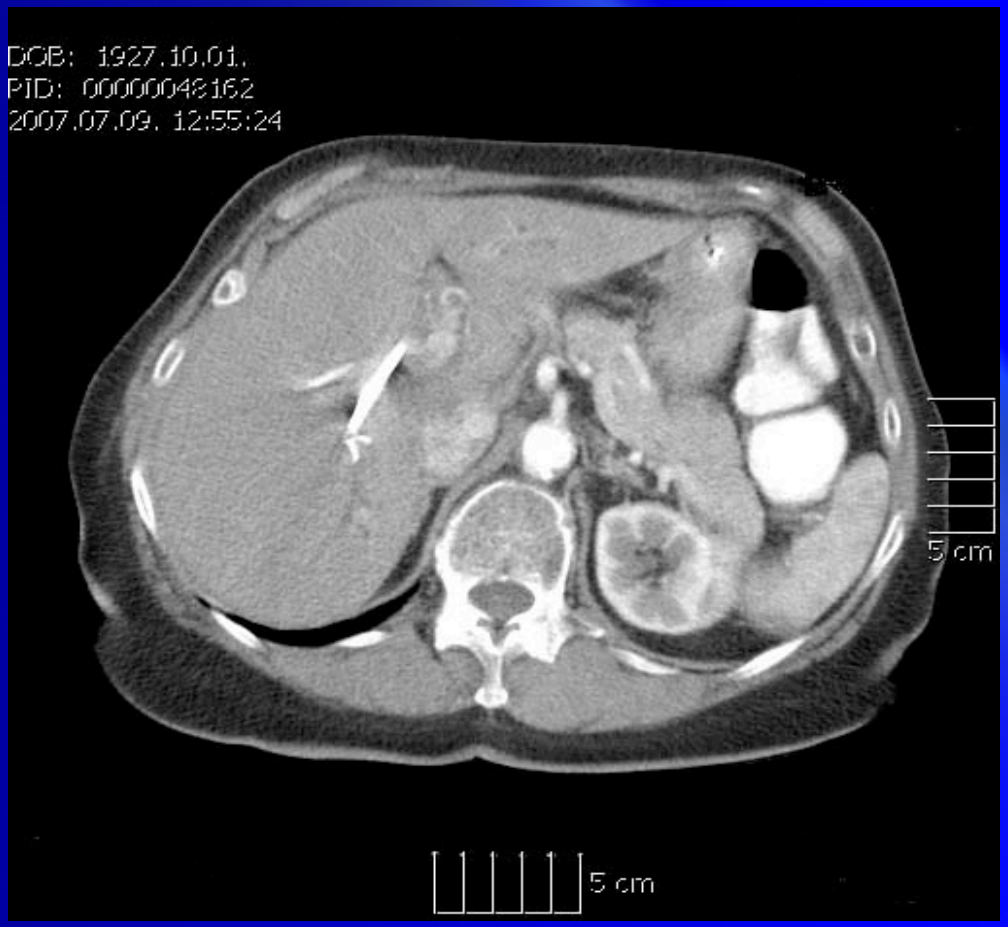
Tumor Regression and Improved Survival in a Case of Stage IV Cholangiocarcinoma (Klatskin Tumor) Achieved by a Novel Nutritional Therapy

Objectives: Cholangiocarcinoma is a rapidly lethal cancer of the biliary system. The aim of this study was to determine the possible clinical benefit of the molasses-based MSQ 15D, 15E, and 15F dietary supplements in a case of Stage IV cholangiocarcinoma.
Design: Single case study.
Settings/Location: Home.
Interventions: The regime of dietary supplements was administered as follows: all MSQ compositions, 2tbsp TID.
Outcome measures: Clinical improvement and regression of the tumor.
Conclusions: Treatment with the MSQ 15 formulae resulted in tumor regression and clinical improvement. Therefore, this approach may provide a novel therapeutic modality for cholangiocarcinoma.

Tumor identified by CT scan

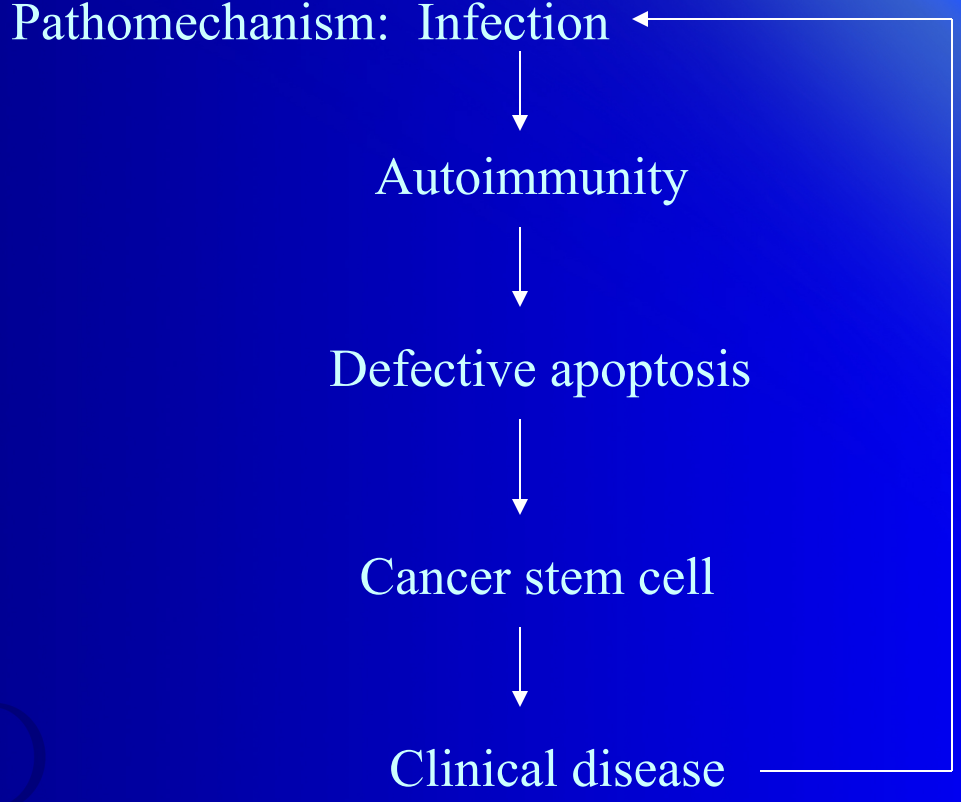


Tumor regression demonstrated by CT scan



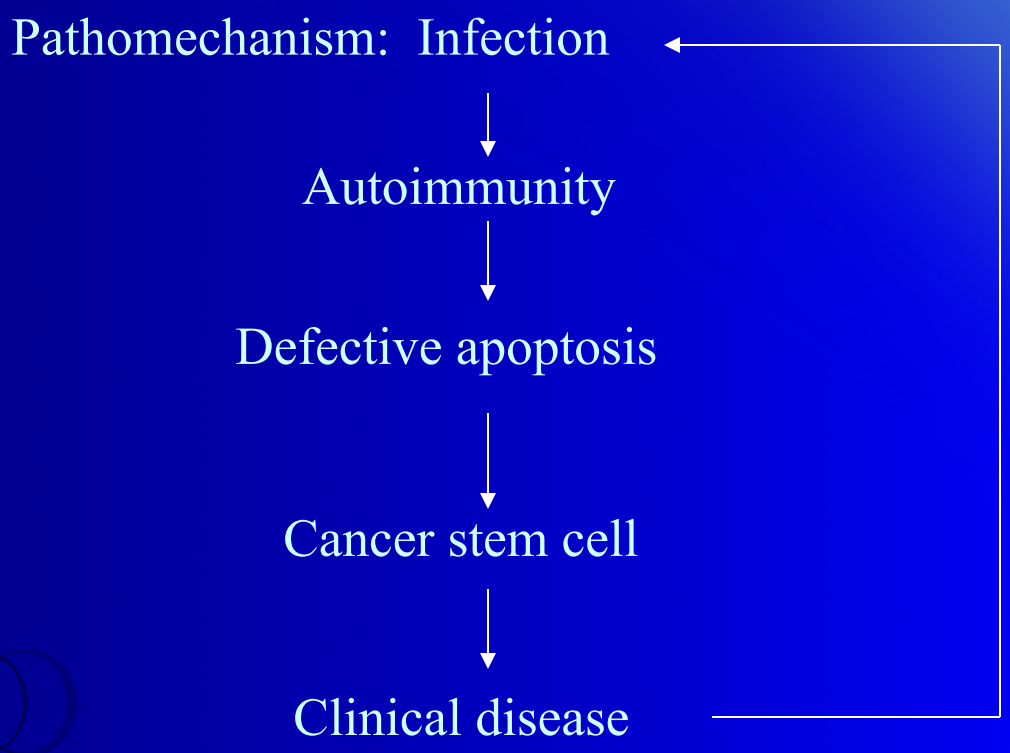
Conclusions I.

Cancer has a common initiation point: cancer stem cells



Conclusions II.

Immunosuppressive therapies reinforce this negative feedback loop



Conclusions III.

- Therapies should support the immune system
- Systemic pathogen identification & eradication is essential
- Innate repair mechanisms should be supported
- Manage any thrombotic event

Conclusions IV.

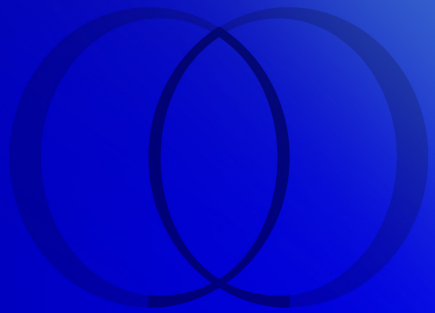
Critical issues for cancer therapy:

- Reduce inflammatory processes
- Restore immune functions
- Support neuro-endocrine functions
- Restore digestive functions
- Emphasize the role of life-style factors

(excessive stress, poor hygiene, inadequate diet, alcoholism, smoking, drugs, etc.)

Conclusions V.

- The "Un-Holy Trinity" of cancer:
  a. Immune system deficiencies
  b. Neuroendocrine deficiencies
  c. Metabolic/Dietary deficiencies
- A SYSTEMS APPROACH is essential for effective therapy
- Current thinking must be expanded to allow a SYSTEMS APPROACH



A-D Research Foundation