Proteolytic Enzymes:
Nature's Answer to Inflammation

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7 SIGNS of a SOUND Gut

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7 SIGNS OF A SOUND GUT
Saturday, April 12 • Austin, TX

Milton Bastidas, DC, CIHP

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  - Lead Researcher on Leaky Gut Study, Inflammation (Protease) Study, Glyphosate Study, Detox (Protease) Study
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Learning Objectives

- Overview of proteolytic enzymes and their systemic benefits
- Discuss cellular mechanism of inflammation
- Discuss the role of inflammation in pain and autoimmunity
- Learn the effect of proteolytic enzymes on pain and autoimmunity
- Overview of cancer and its pathophysiology
- Review normal cell cycle
- Identify signaling factors that keeps cell cycle in check
- Briefly discuss the hallmarks of cancer
- Discuss tumor microenvironment and biomarkers that support cancer cell survival
- Review proteolytic enzymes' potential role in combatting cancer and its scientific basis
- Case studies: Osteoarthritis of knee, Ulcerative Colitis, and Prostate Cancer

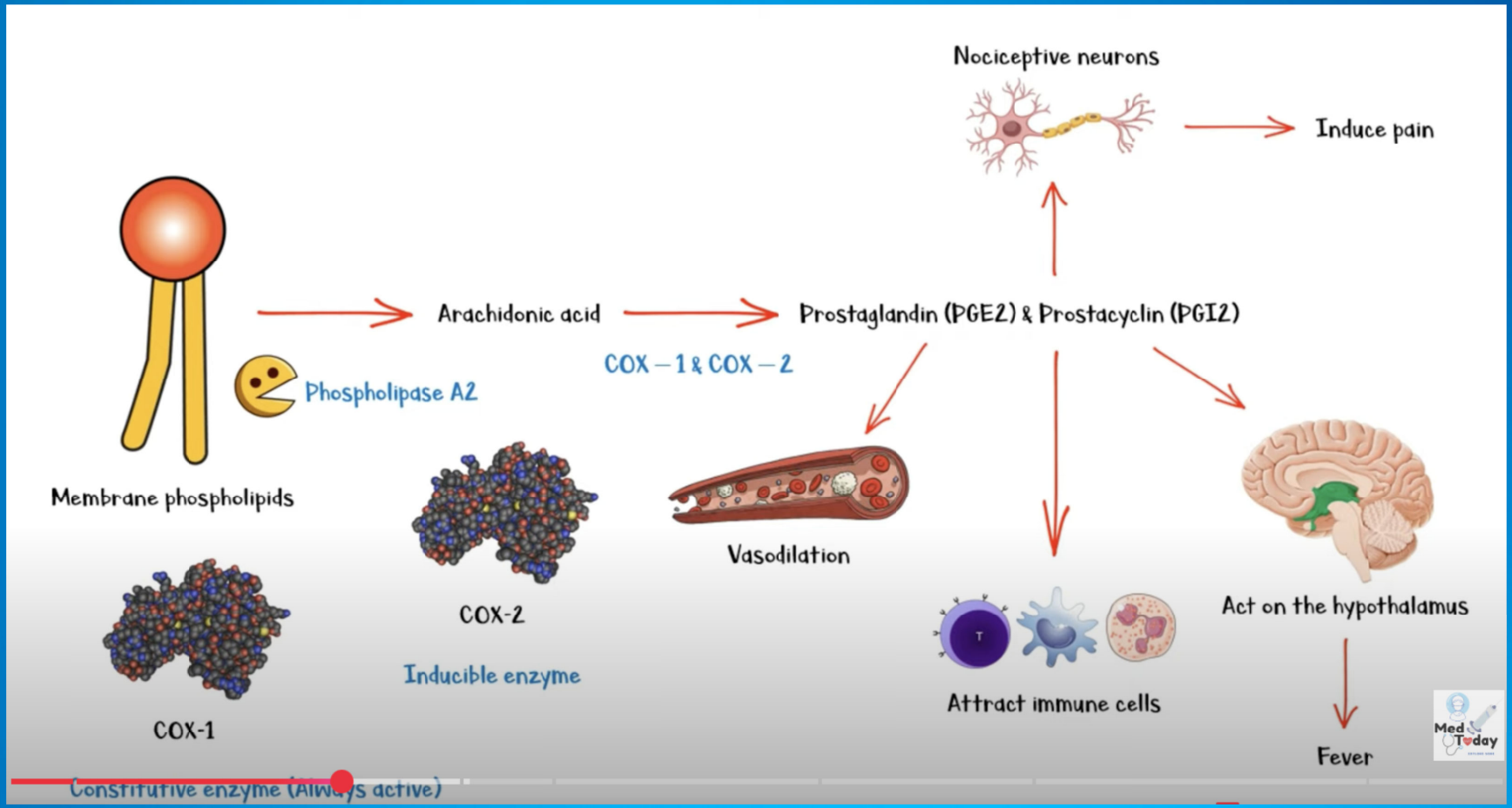
Proteolytic Enzymes: Health Benefits

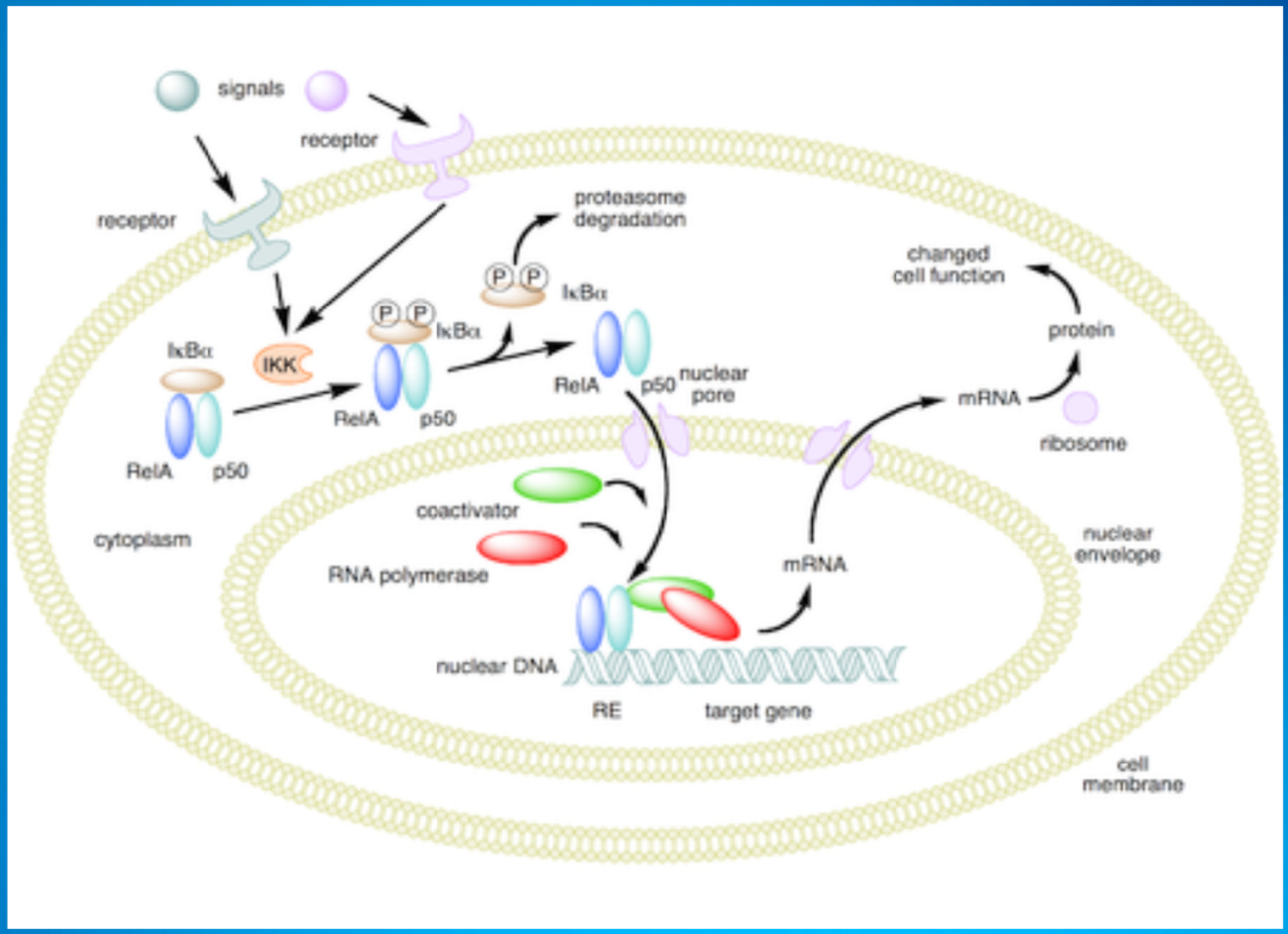
- They accelerate the volume and fluidity of blood flow
- Enzymes such as bromelain modulate arachidonate pathway
- Reduce acute phase reactants like CRP and Fibrinogen
- Enzymes also break down and remove necrotic debris in wounds
- Systemic enzyme therapy has been shown to overcome the “cytokine storm”
- They act as a "biological vacuum cleaners“ eliminating impurities, foreign proteins, immune complexes and harmful microorganisms from the blood stream and tissues
- Enzymes break down immune complexes which block the immune cells
- Enzymes activate alpha-2 macroglobulin, the “cytokine catcher” which usually exists in blood in an inactive form
- Enzymes aid in destruction of cancer cells

What is Pain?

- Pain is a distressing feeling often caused by intense or damaging stimuli.
- The International Association for the Study of Pain defines pain as "an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage.”
- Noxious stimuli sets off physiological mechanisms that employ metabolic enzymes to increase inflammation and pain to protect and repair damage tissue.

Pain Mechanism





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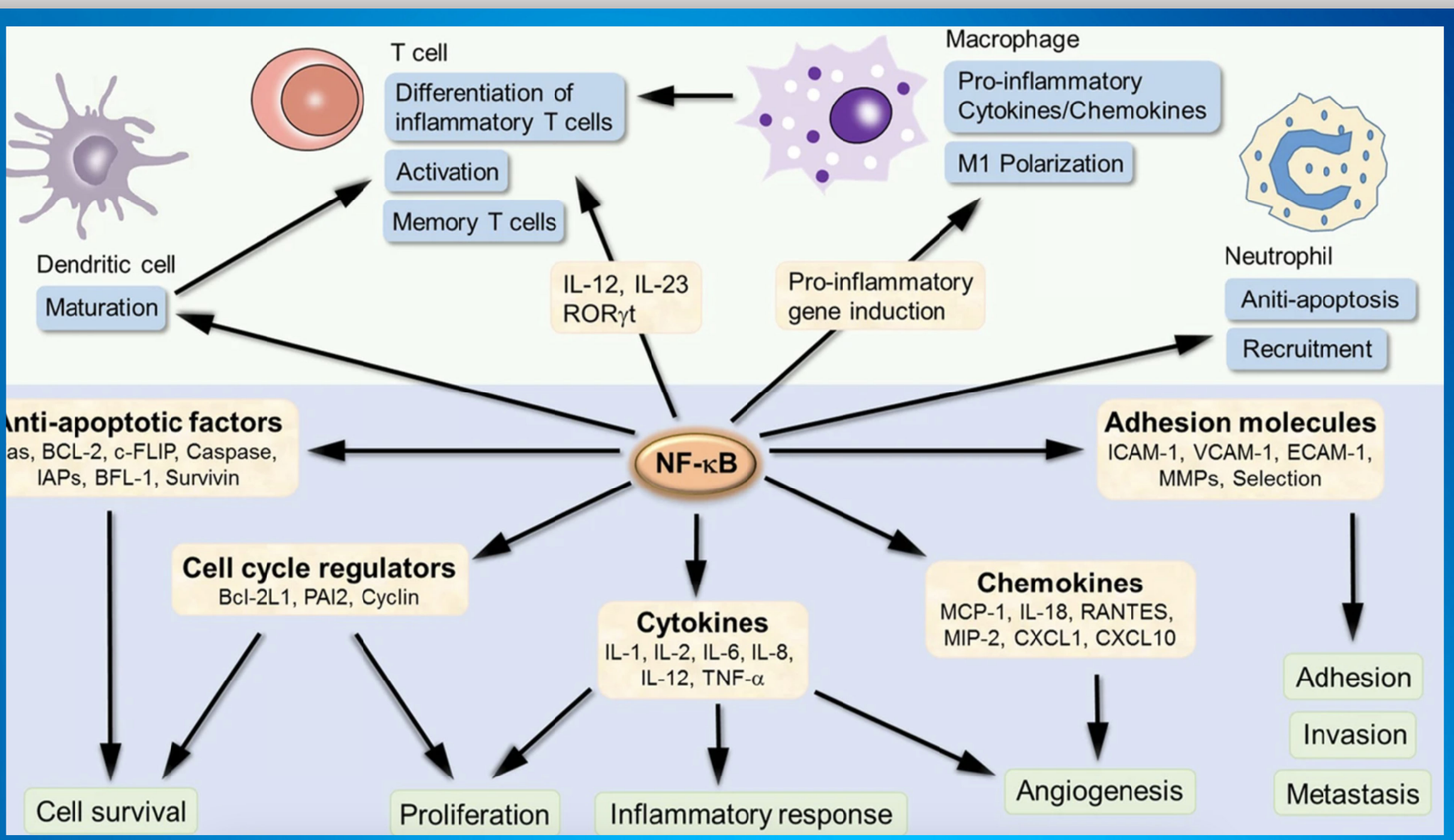
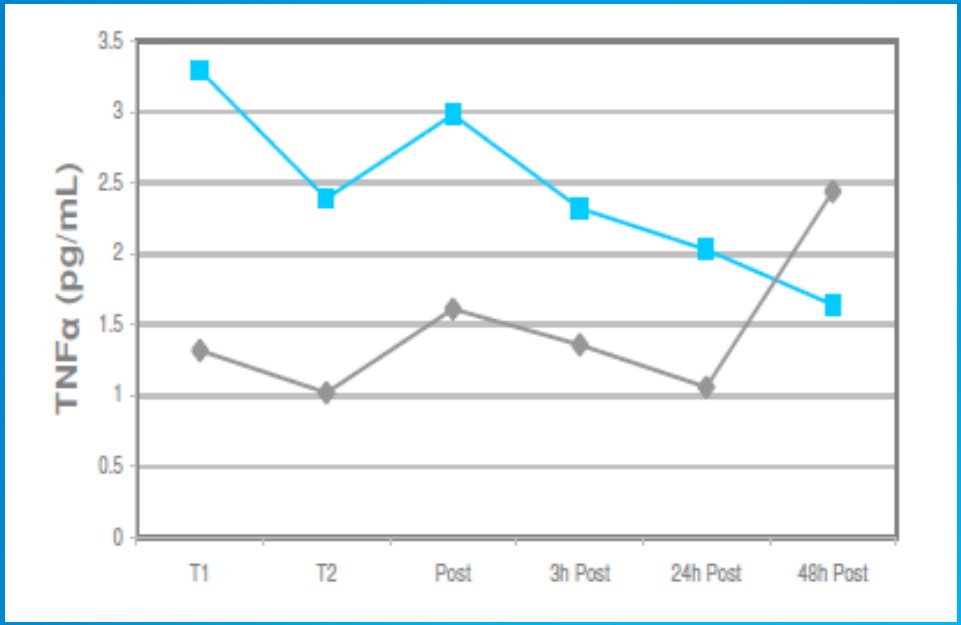


Tumor necrosis factor alpha (TNFα)

- TNFα is a cytokine that plays an important role in the inflammatory response, stimulating the secretion of IL1 and IL6
- The secretion of TNFα needs to occur in any type of inflammatory or disease process, however its persistent secretion and long-term effects on the body could be harmful
- For health and recovery, a controlled synthesis and secretion of TNFα is desired

Tumor necrosis factor alpha (TNFa)

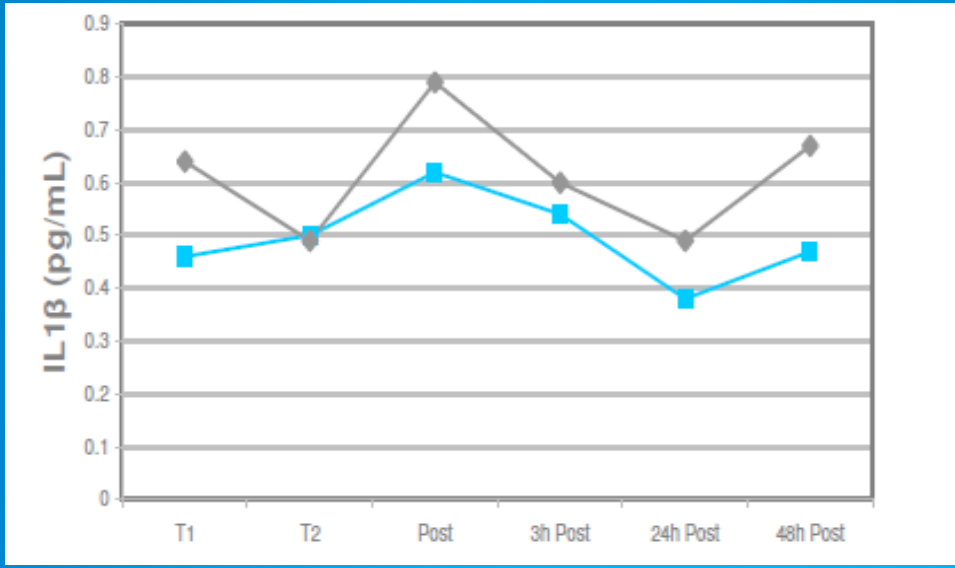


The above figure shows how TEC's proteases allowed the synthesis and secretion of TNFα to occur immediately post-exercise, followed by a controlled and steady reduction after 3, 24, and 48 hours.

Interleukin 1 beta (IL1β)

- Interleukin 1 beta (IL1β) in high concentrations within the blood circulation induces fever, triggers the inflammatory response of the liver including a blood pro-coagulation effect, and promotes catabolism
- The levels of IL1β were relatively lower in the protease group than the placebo group

Interleukin 1 beta (IL1β)

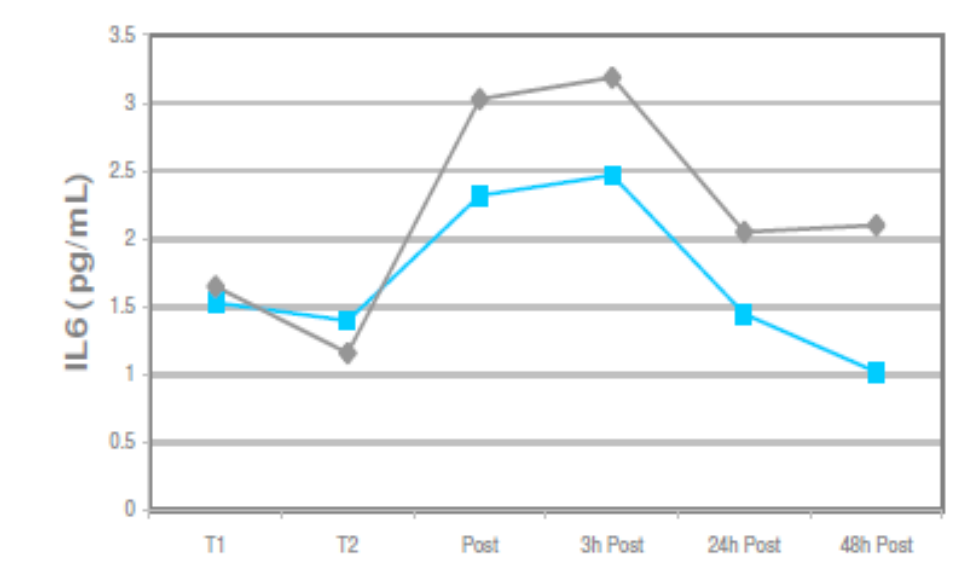


The rise in IL1β immediately post-exercise for the protease group **(24%)** was less than half that seen in the placebo group **(62%)** and demonstratives effective control of inflammation.

Interleukin 6 (IL6)

- A pro-inflammatory cytokine promoting fever and high levels of acute phase liver proteins
- In the placebo group, the increase in IL6 post-exercise was double that of the protease group

Interleukin 6 (IL6)

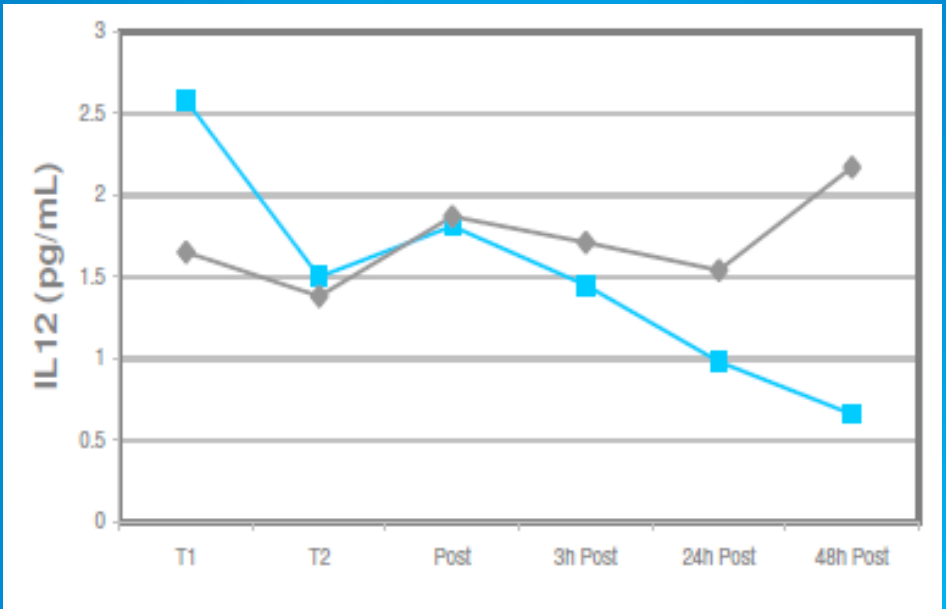


Also the protease group had overall lower serum concentrations of IL6 than the placebo group.

Interleukin 12 (IL12)

- Another pro-inflammatory cytokine
- Studies have shown that decreases in IL12 help control some autoimmune disorders, suggesting Transformation's protease as a good candidate in the management of certain degenerative disorders
- This further demonstrates the beneficial effects Transformation's protease blend can provide in the modulation of inflammation

Interleukin 12 (IL12)

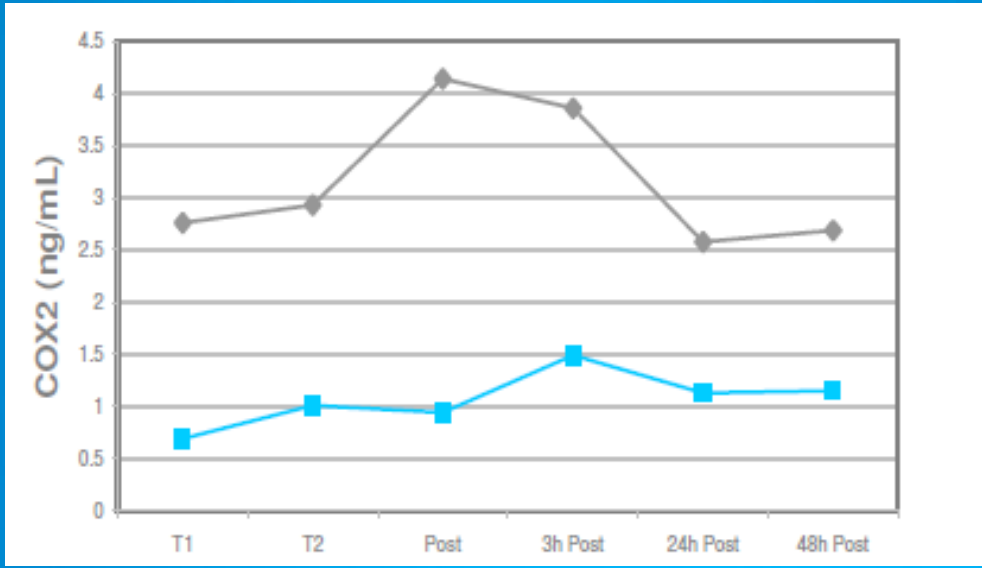


Looking at the study results post-exercise to 48 hours post-exercise, the levels of IL12 dropped **63%** in the protease group compared to a **16%** increase in the placebo group.

Cyclooxygenase 2 (COX-2)

- An enzyme that is involved in pain and inflammation
- The greater its activity, the greater the pain and inflammation, and a decrease in COX2 activity results in less pain
- Several pharmaceutical drugs are used to help control its activity, however those drugs are not without serious side effects
- This study revealed that COX2 levels in the protease group were significantly lower than in the placebo group

Cyclooxygenase 2 (COX-2)



Note also that these levels appear more controlled in the protease group post-exercise, whereas the placebo group showed a **41%** increase in COX2.

Conclusions

- Relative to the inflammatory cytokines the study results show that Transformation's protease blend has considerable potential for use in controlling inflammatory conditions in the body
- The data also showed a beneficial decrease in COX2 activity, which shows these proteases can be used to manage pain without negative side effects

The Role of Protease on Pain

Experimental evidence suggests that bromelain's action as an anti-inflammatory is mediated via the following factors:

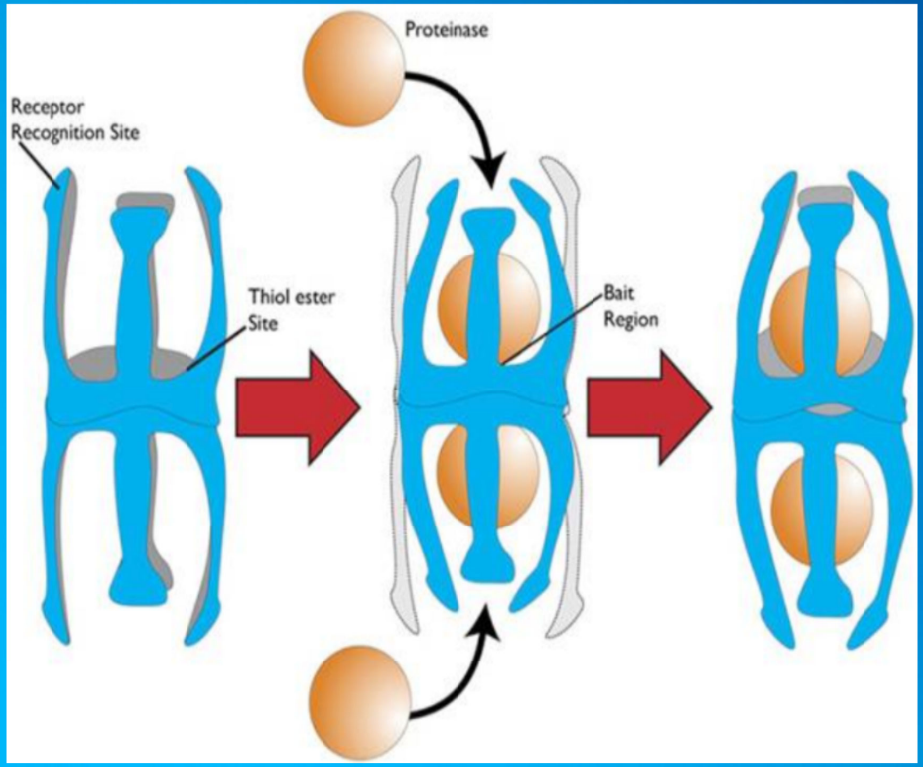
- By increasing serum fibrinolytic activity, reducing plasma fibrinogen levels and decreasing bradykinin levels (which results in reduced vascular permeability) and hence reducing oedema and pain
- By mediating prostaglandin levels (by decreasing levels of PGE2 and thromboxane A2)
- Through modulation of certain immune cell surface adhesion molecules, which play a role in the pathogenesis of arthritis

Enzymes activate alpha-2 macroglobulin, the “cytokine catcher” which usually exists in blood in an inactive form

This in turn promotes faster clearance of cytokine TNF-a.

Thus, stimulus for expression of the adhesion molecules is reduced.

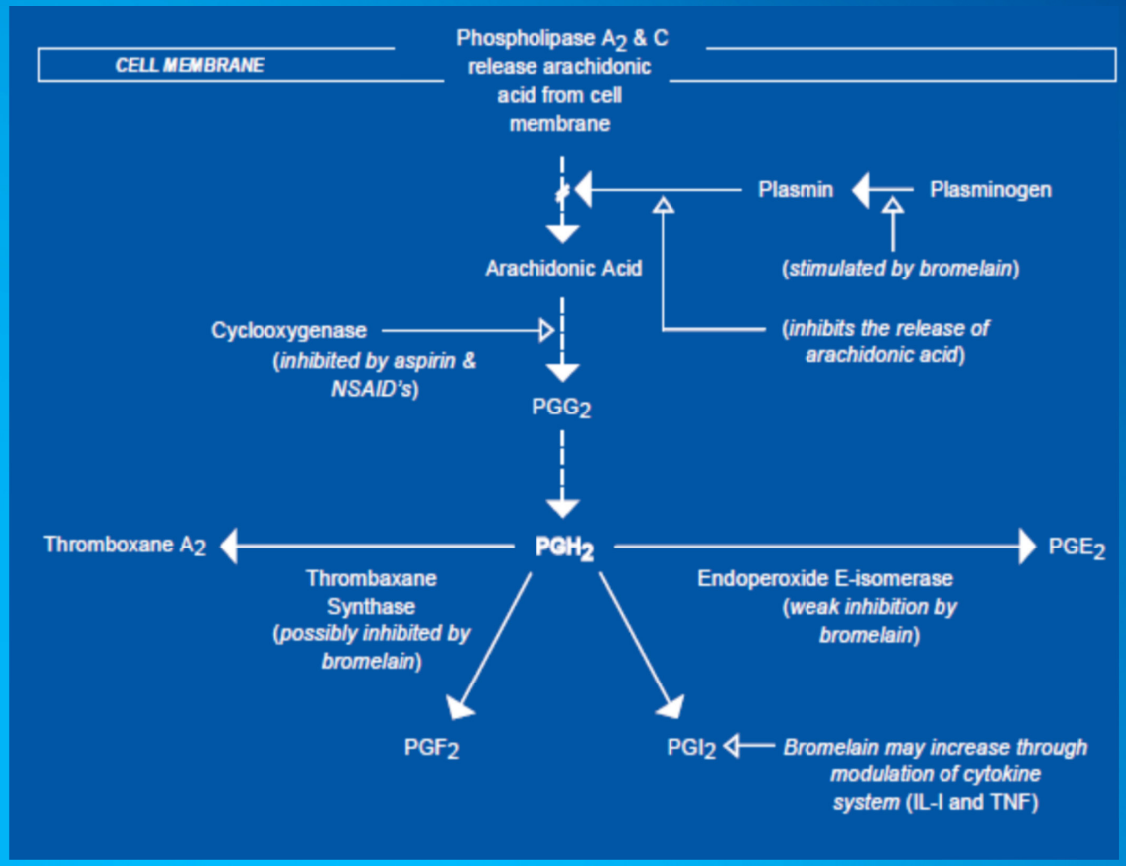
This assists in minimizing the heightened inflammatory process.



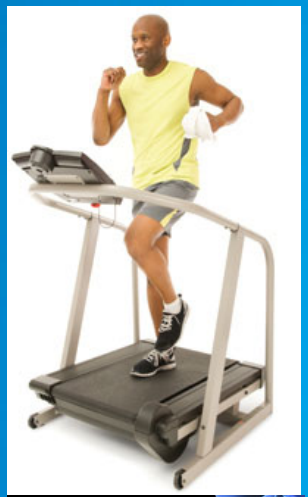
Enzymes such as bromelain modulate arachidonate pathway

Thromboxane production is decreased with no effect on cyclooxygenase.

This leads to a decrease in edema and inflammation and re-establishment of balance between the 2 types of prostaglandins.



Why a new clinical trial?



The Baylor Study shows results after exercise-induced (acute) inflammation

We wanted to show how Protease would affect “silent” inflammation

In my practice I see……

Tests:

CRP

Homocysteine

Fibrinogen

SED rate

The Trial: Protocol

Participants were asked to continue current diet and exercise with no change, the only modification was the addition of Protease/placebo

Group I: 1 cap Protease 2 x day (total = 6)

Group II: 2 caps Protease 3 x day (total = 5)

Group III: 3 caps Protease 4 x day (total = 3)

Group IV: placebo (total = 4)

Trial Results: Group 3

Overall average (3 pts) showed

- 75% reduction in CRP
- 8% increase in Homocysteine
- 26% reduction in Fibrinogen
- 7% reduction in Sed Rate

This group outperformed the rest in terms of positive results and significant decreases especially in CRP and Fibrinogen

Trial Results: Group 3

	CRP	Homocysteine	Fibrinogen	Sed Rate
JB1	20.9	8.4	403	16
JB2	12.2	8.9	314	17
JB3	7.5	8.8	311	11
AJ1	12.3	6.9	439	1
AJ2	0.5	8.4	254	6
AJ3	0.8	9.2	297	6
DB1	2.5	13.2	342	10
DB2	0.2	10.6	191	4
DB3	0.3	12.9	261	8

Reduce acute phase reactants like CRP and Fibrinogen

Fibrinogen - Acute phase reactant which increases sharply in states of inflammation and presence of IL6, key factor in blood viscosity, and promotes formation of blood clots inside coronary arteries

C Reactive Protein - An acute phase reactant which increases sharply in response to inflammation, binds to phosphocholine expressed on the surface of dead or dying cells (and some types of bacteria) in order to activate the complement system, and is synthesized by the liver in response to cytokines such as IL1b, IL6, IL12, and TNF alpha released by macrophages and fat cells

Conclusion

Of the 4 markers observed in all 4 groups there was ***a significant decrease in CRP and Fibrinogen*** in the high dosed group compared to the other 3 groups

This finding is consistent with the study performed at Baylor University where Protease proved its strength against inflammatory cytokines such as IL1b, IL6, TNFa, and IL12

Enzymes also break down and remove necrotic debris in wounds

- Papain acts as a debris-removing agent, with no harmful effect on sound tissues because of the enzyme's specificity, acting only on the tissues, which lack the α1antitripsine plasmatic antiprotease that inhibits proteolysis in healthy tissues.
- Topical bromelain separates eschar at the interface with living tissue. It is hypothesized that bromelain activates collagenase in living tissue which then attacks the denatured collagen in the eschar. This produces a demarcation between living and dead tissue. By using bromelain, grafting can occur as soon as 24 hours after the accident. Utilizing bromelain cream in the treatment of burns usually results in minimal or no scar tissue formation.

When we return...

Autoimmunity

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Autoimmunity

- Autoimmune diseases affect 5-9% of the world's population.
- It is now known that genetics play a relatively small part in the pathophysiology of autoimmune disorders in general, and that environmental factors have a greater role.
- The most common of these environmental factors are toxic chemicals, food/diet, and infections.
- Toxic chemicals can directly damage self-tissue and cause the release of autoantigens, or can bind to human tissue antigens and form neoantigens, which can provoke autoimmune response leading to autoimmunity.
- The food we eat every day commonly has colorants, preservatives, or packaging-related chemical contamination.
- The food itself may be antigenic for susceptible individuals.
- The most common mechanism for food-related autoimmunity is molecular mimicry, in which the food's molecular structure bears a similarity with the structure of one or more self-tissues. The solution is to detect the trigger, remove it from the environment or diet, then repair the damage to the individual's body and health.

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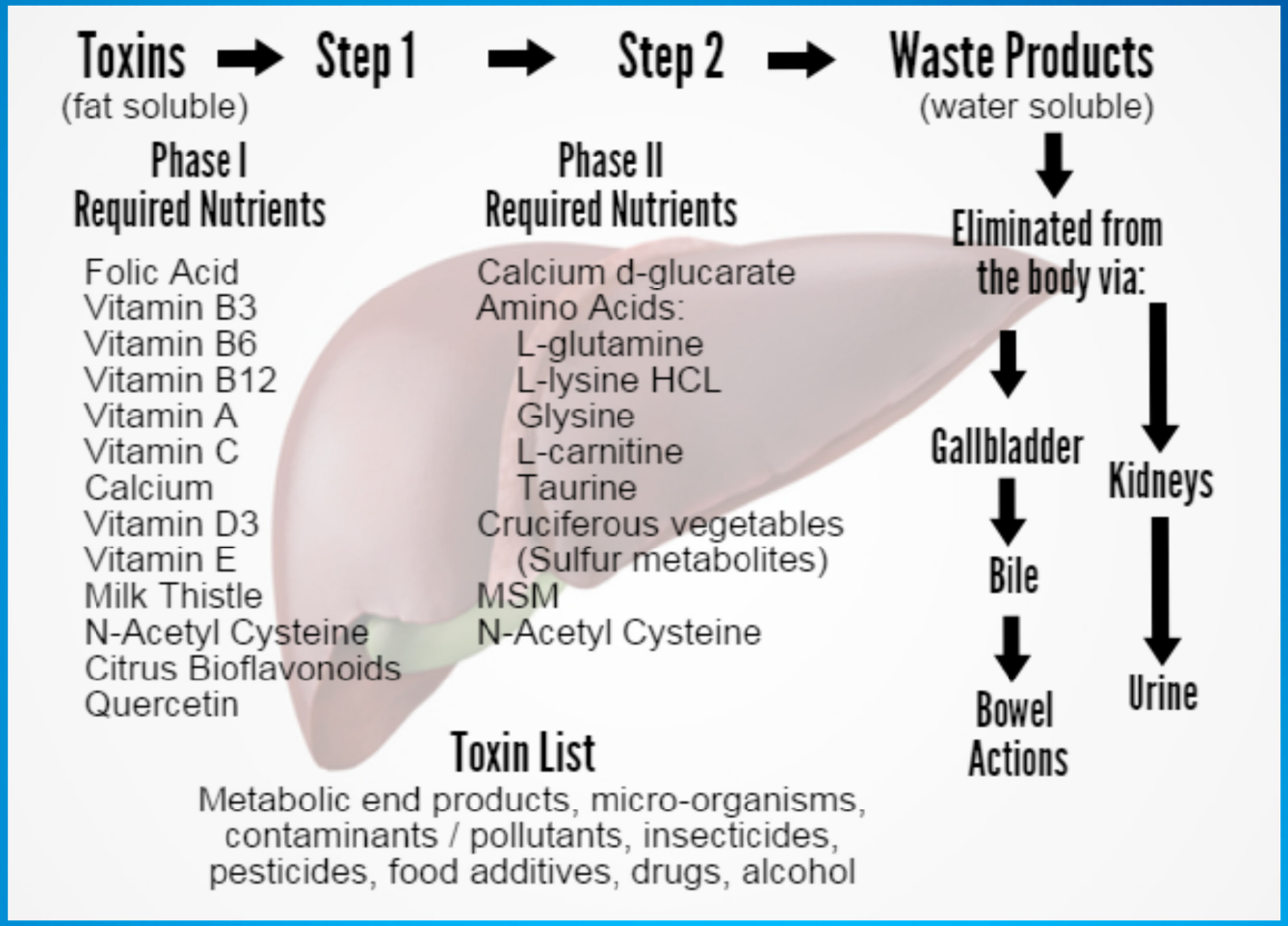
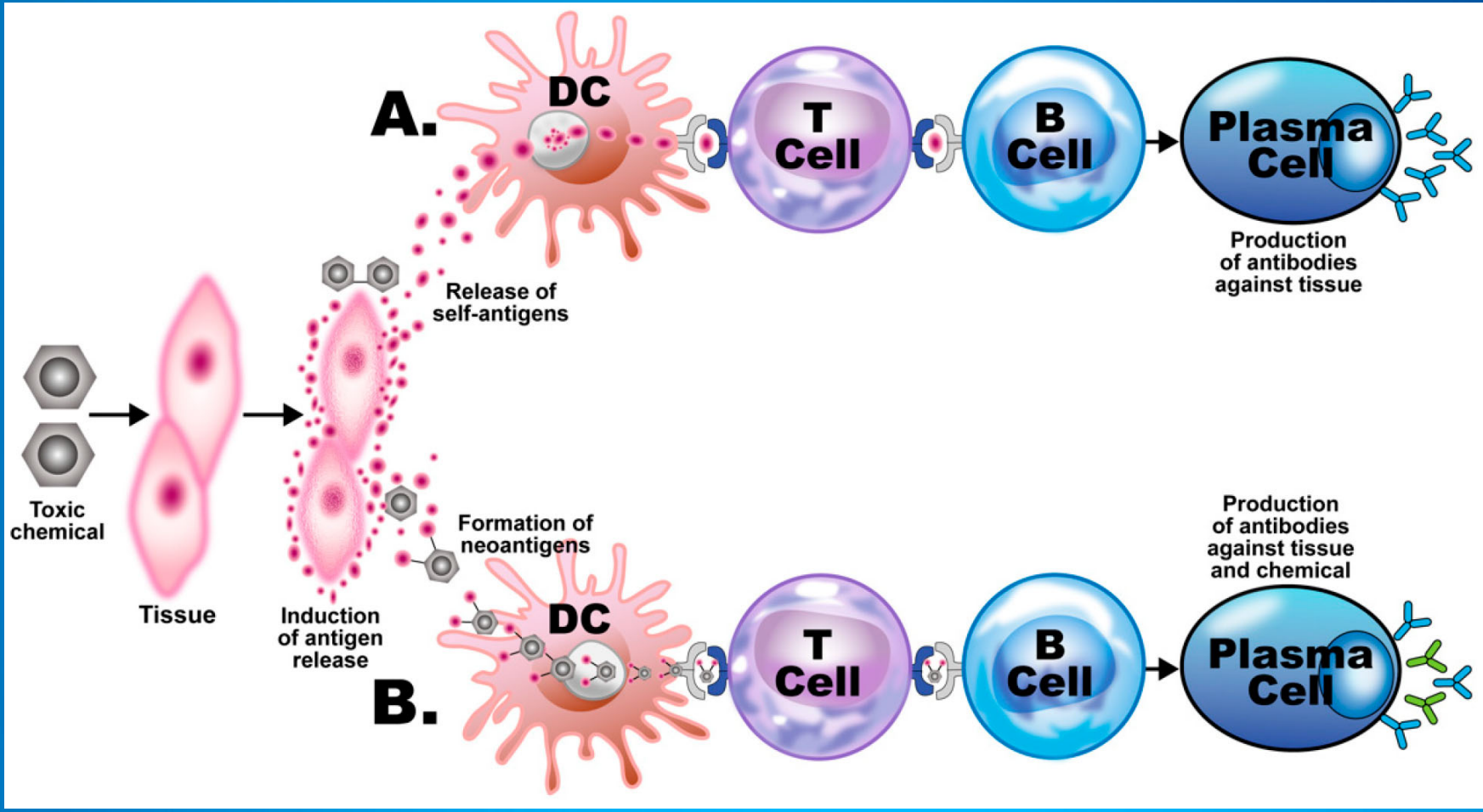
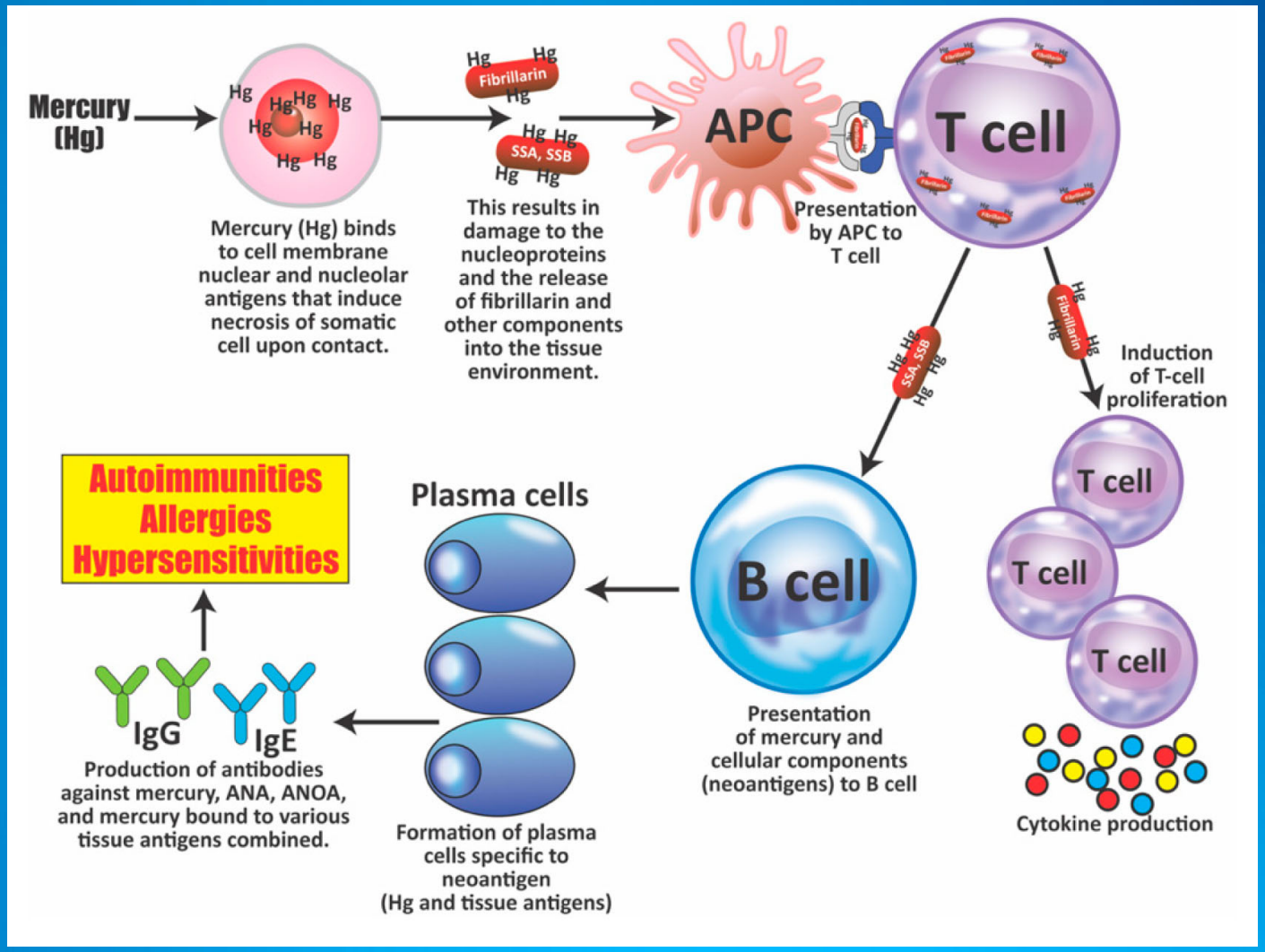
Liver Phases





Vojdani A, Vojdani E. The role of exposomes in the pathophysiology of autoimmune diseases I: toxic chemicals and food. *Pathophysiology*. 2021 Dec 18;28(4):513-543.



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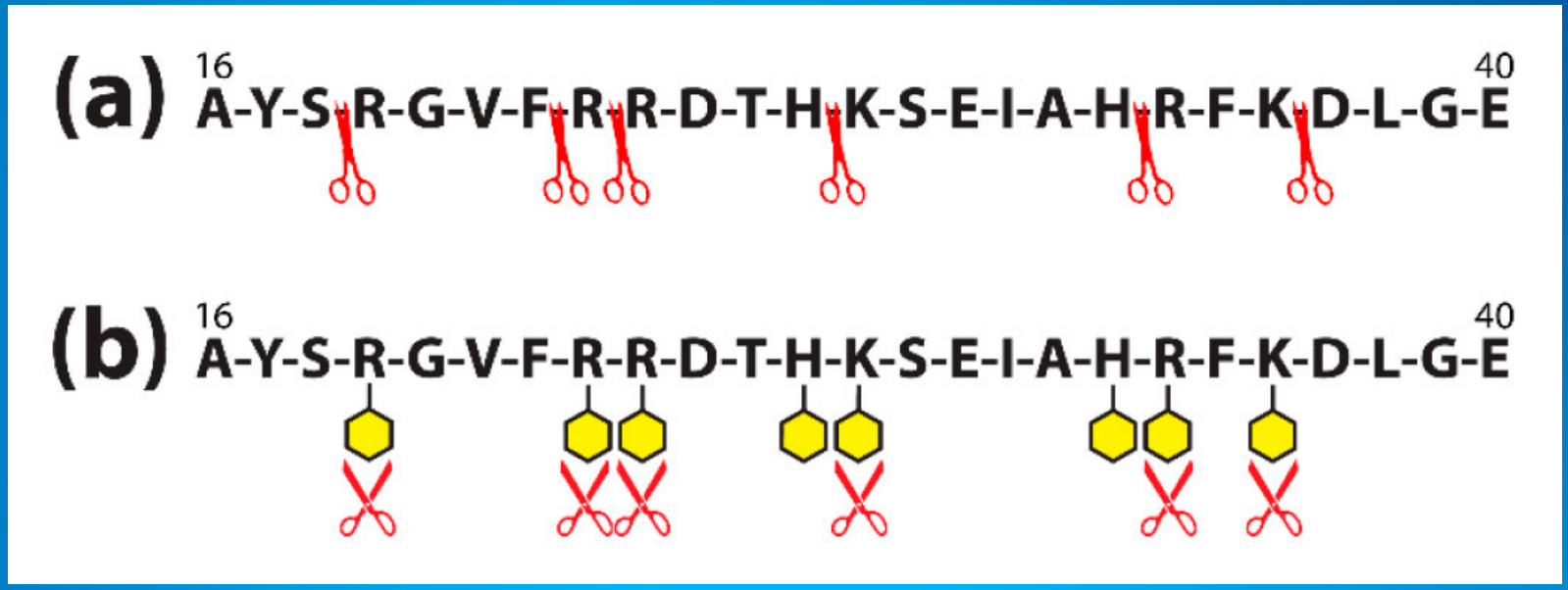

Amino acid sequence of albumin peptide before (a) and after (b) food colorant binds to different amino acids contained in the chain. (a) Trypsin (symbolized by red scissors) is shown cleaving the amino acid chain of a 16–40 sequence of albumin; (b) colorants (symbolized by yellow hexagons) bind to the major amino acids arginine (R), histidine (H), and lysine (K) present in the albumin sequence, making it difficult for the trypsin to cleave the sequence, and decreasing digestive effectivity.

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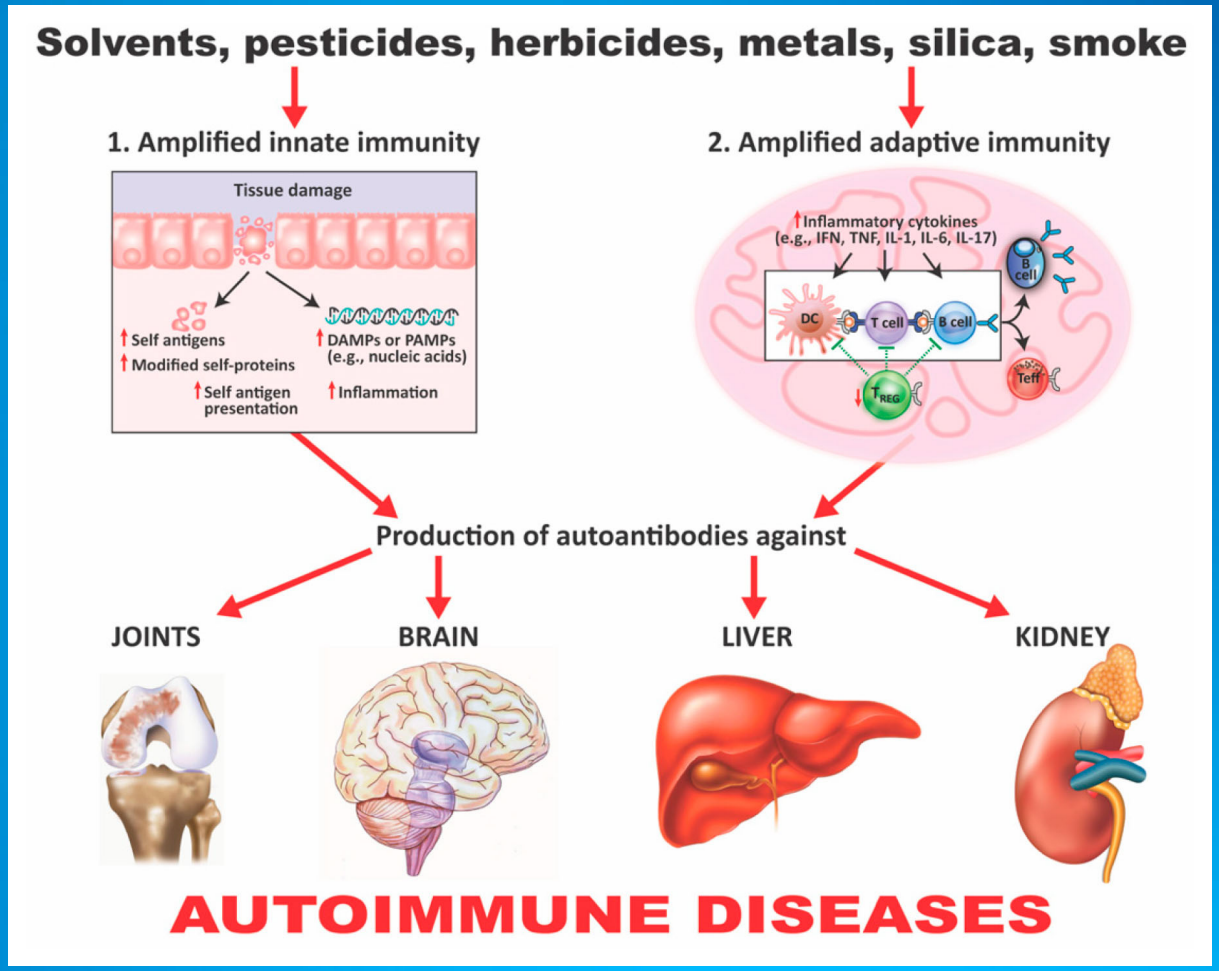

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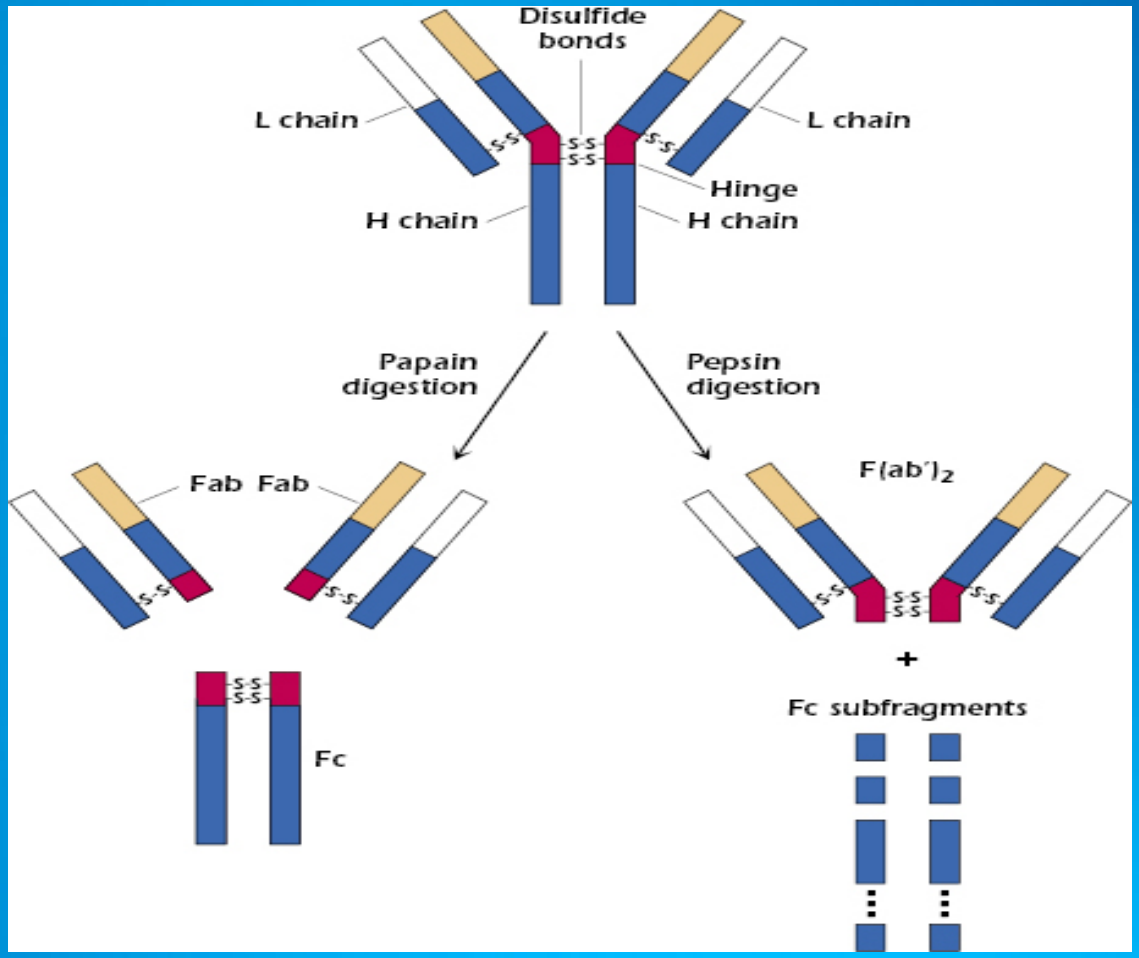
Autoimmunity

- Myasthenia gravis (MG) is a well-defined organ-specific autoimmune disease characterized by the functional loss of acetylcholine receptors (AChR) at the neuromuscular junction which is mediated by autoantibodies directed against the AchR.
- Treatment of MG mainly involves the use of acetylcholinesterase inhibitors, immunosuppressive drugs, thymectomy, plasmapheresis, and the i.v. administration of human immunoglobulins.
- Although such treatment results in significant improvement of disease, it is not free of potential side effects.

Autoimmunity

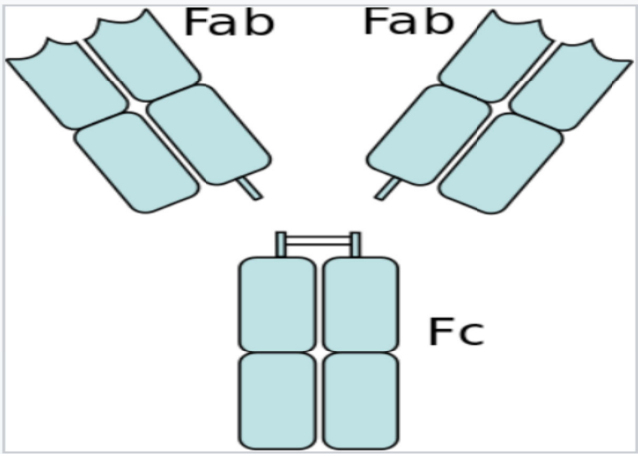
- In the present study we show that papain, administered intraperitoneally into rats previously treated with an anti-Main Immunogenic Region- Monoclonal Ab, can cleave anti-AChR antibodies in vivo and prevent MG symptoms, with no adverse side effects.
- Thus, these results suggest a potential therapeutic use for a proteolytic enzyme in MG.

Papain digestion of IgG



Enzymes break down immune complexes which block the immune cells

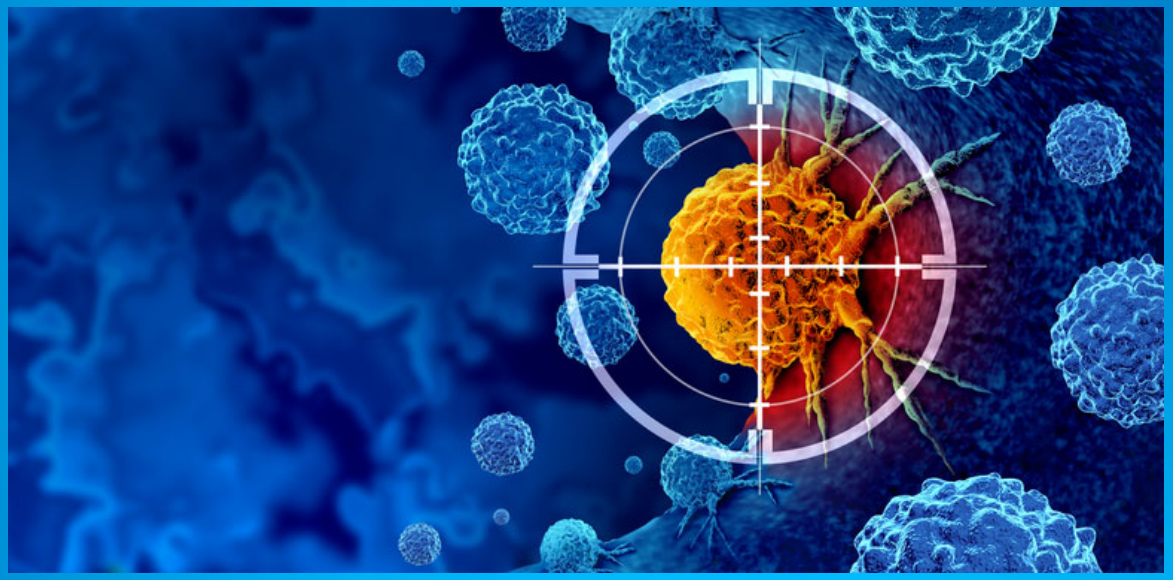
- They dissolve immune complex by removing Fc part of immunoglobulin and eliminate immune complexes from circulation.
- In the early phase, there may be worsening of the situation due to release of immune complexes fixed to tissues into the blood (Herxheimer reaction).



An antibody has Fab (fragment, antigen-binding) and Fc (fragment, crystallizable) regions. Fc receptors bind to the Fc region.

Proteolytic Enzymes

One of Nature's Answers to Cancer



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American Cancer Society

2024—First Year the US Expects More than 2M New Cases of Cancer

- This trend is largely affected by the aging and growth of the population and by a rise in diagnoses of 6 of the 10 most common cancers—breast, prostate, endometrial, pancreatic, kidney, and melanoma
- The other 4 top 10 cancers are lung, colon/rectum, bladder, and non-Hodgkin lymphoma

Cancer patients are getting younger

- Cancer risk increases with age, and people most likely to be diagnosed with cancer are adults aged 65 and older but this trend is beginning to change
- Especially notable is the rise in colorectal cancer diagnoses among people younger than 50.
- Cervical cancer is increasing in incidence in an even younger population—women ages 30 to 44

Burden of 30 cancers among men: Global statistics in 2022 and projections for 2050 using population-based estimates

- Incident cancer cases are projected to reach 19 million globally by 2050, an 84.3% increase from the 2022 estimate
- The number of cancer deaths is projected to reach 10.5 million by 2050, a 93.2% increase from the 2022 estimate
- Lung cancer is projected to remain the leading cancer type for both cases and deaths by 2050, with both cases and deaths increasing by greater than 87% compared with the 2022 estimate

The *Lancet* Commission on prostate cancer: planning for the surge in cases; Lancet 2024; 403: 1683–722

- We project that the number of new cases of prostate cancer annually will rise from 1.4 million in 2020 to 2.9 million by 2040
- The projected rise in prostate cancer cases cannot be prevented by lifestyle changes or public health interventions
- Correspondingly, we estimated that prostate cancer deaths will rise by 85%, from 375,000 in 2020 to close to 700,000 by 2040

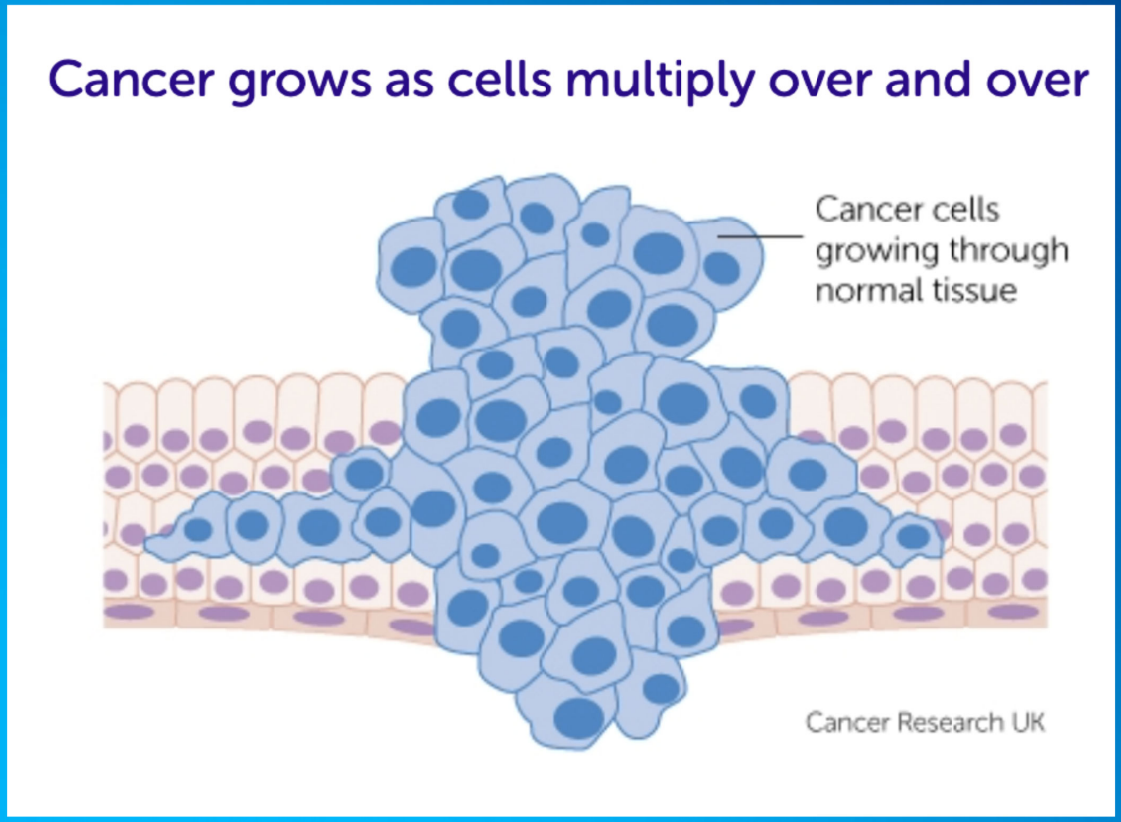
Proteolytic Enzymes

One of Nature's Answers to Cancer

Learning Objectives

- Review normal cell cycle
- Identify signaling factors that keep the cell cycle in check
- Briefly discuss the hallmarks of cancer
- Discuss tumor microenvironment and biomarkers that supports cancer cell survival
- Review proteolytic enzymes, their potential role in combating cancer, and their scientific basis
- Case Study

- Cancer occurs when abnormal cells divide in an uncontrolled way. Cancer starts when gene changes make one cell, or a few cells begin to grow and multiply too much. This may cause a growth called a tumor – called a primary tumor.
- Some cancers may eventually spread into other parts of the body – this is called a secondary tumor or a metastasis.
- There are more than 200 different types of cancer. Cancer and its treatments can affect body systems such as the blood and lymph circulation, the immune systems, and hormones.



Normal Cell Cycle

M: mitotic phase is a multistep process during which the duplicated chromosomes are aligned, separated, and move into two new, identical daughter cells.

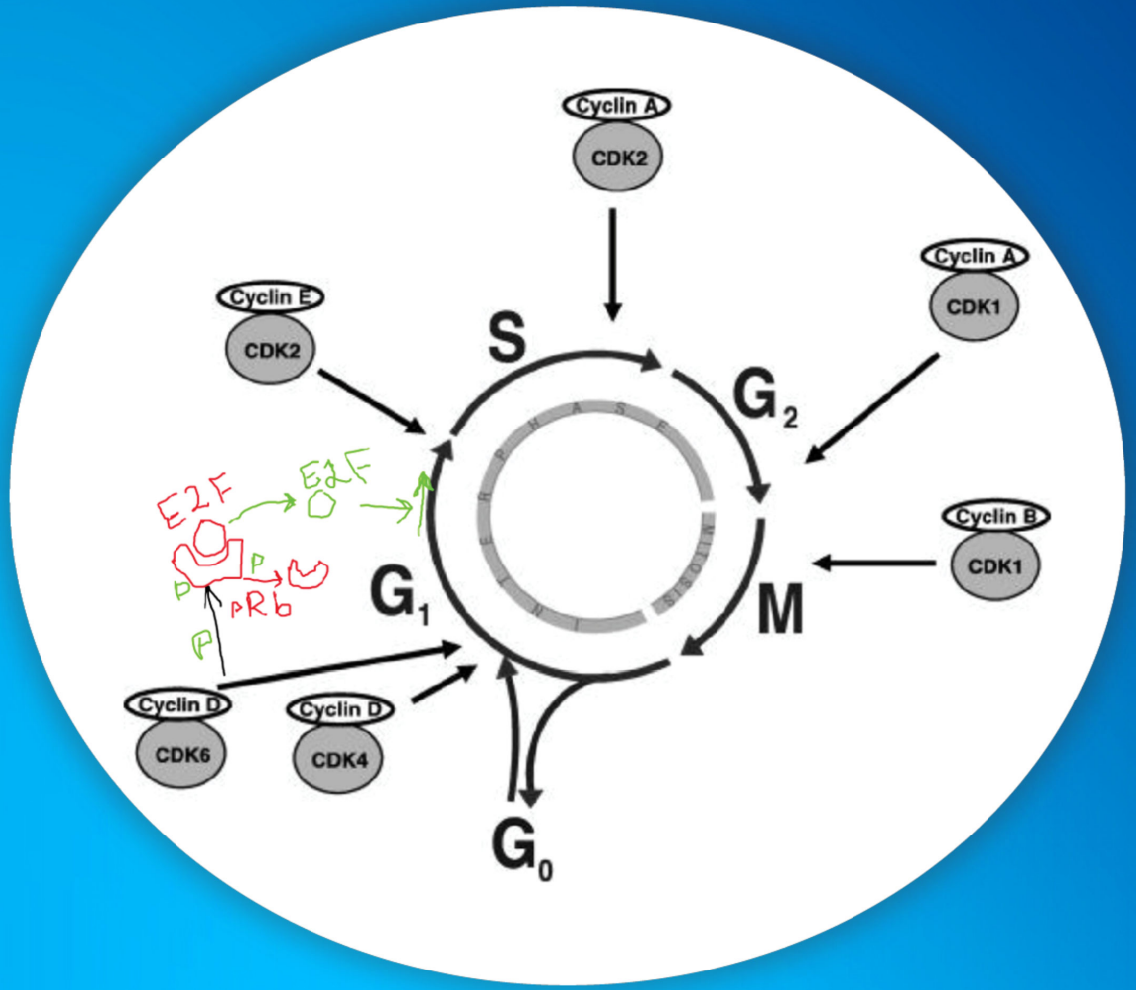
G0: Quiescent stage. Cells that never or rarely divide, such as mature cardiac muscle and nerve cells, remain in G_0 permanently.

G1: The cell is accumulating the building blocks of chromosomal DNA and the associated proteins as well as accumulating sufficient energy reserves to complete the task of replicating each chromosome in the nucleus.

S: DNA replication can proceed through the mechanisms that result in the formation of identical pairs of DNA molecules—sister chromatids. The centrosome is also duplicated during the S phase.

G2: The cell replenishes its energy stores and synthesizes proteins necessary for chromosome manipulation and movement. Some cell organelles are duplicated, and the cytoskeleton is dismantled to provide resources for the mitotic phase. There may be additional cell growth during G2.

- The transition from one cell cycle phase to another occurs in an orderly fashion and is regulated by different cellular proteins.
- Key regulatory proteins are the cyclin-dependent kinases (CDK), a family of serine/threonine protein kinases that are activated at specific points of the cell cycle during G1 (CDK4, CDK6 and CDK2), S (CDK2), G2, and M (CDK1).
- When activated, CDK induce downstream processes by phosphorylating selected proteins. Different cyclins are required at different phases of the cell cycle. The three D type cyclins (cyclin D1, cyclin D2, cyclin D3) bind to CDK4 and to CDK6 and CDK-cyclin D complexes are essential for entry in G1. Another G1 cyclin is cyclin E which associates with CDK2 to regulate progression from G1 into S phase. Cyclin A binds with CDK2 and this complex is required during S phase. In late G2 and early M, cyclin A complexes with CDK1 to promote entry into M. Mitosis is further regulated by cyclin B in complex with CDK1.



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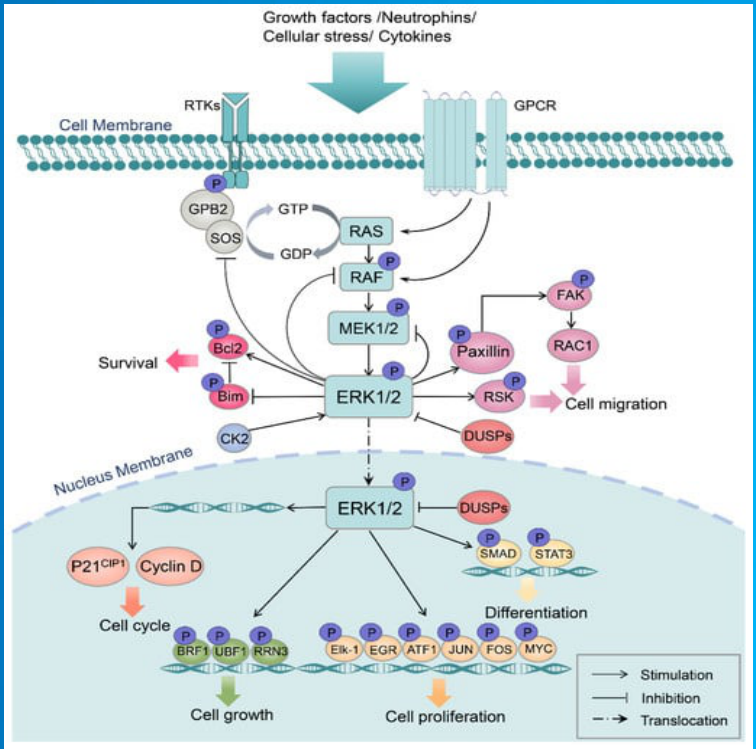
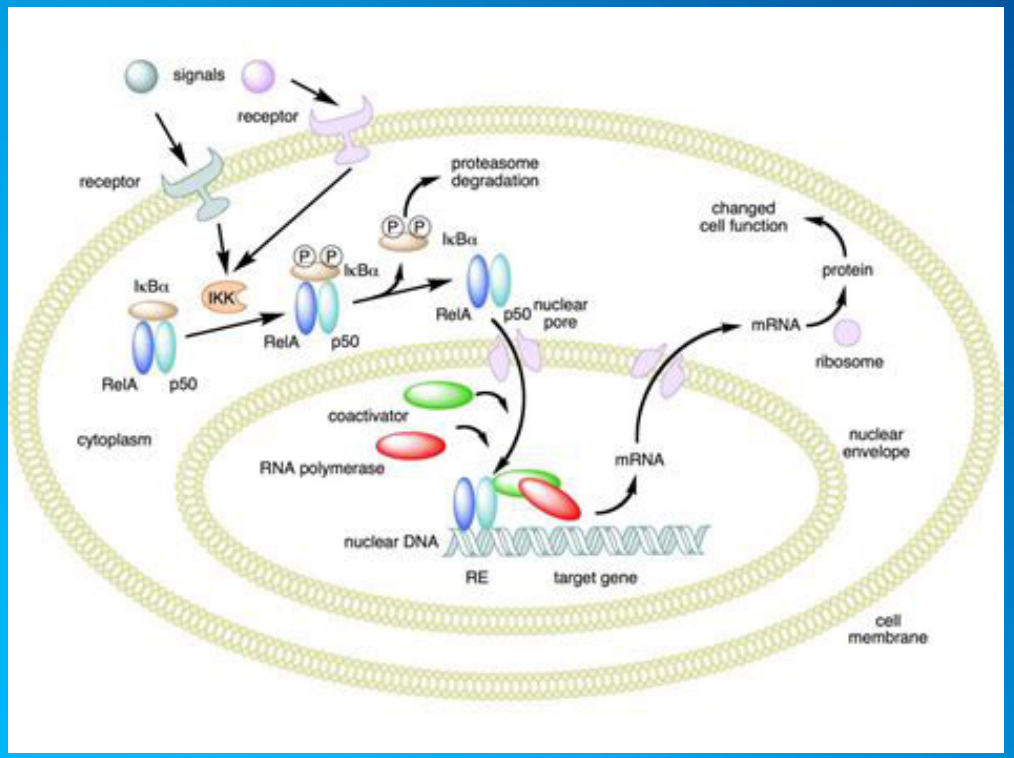
Kinases add phosphates; Phosphatases take off phosphates





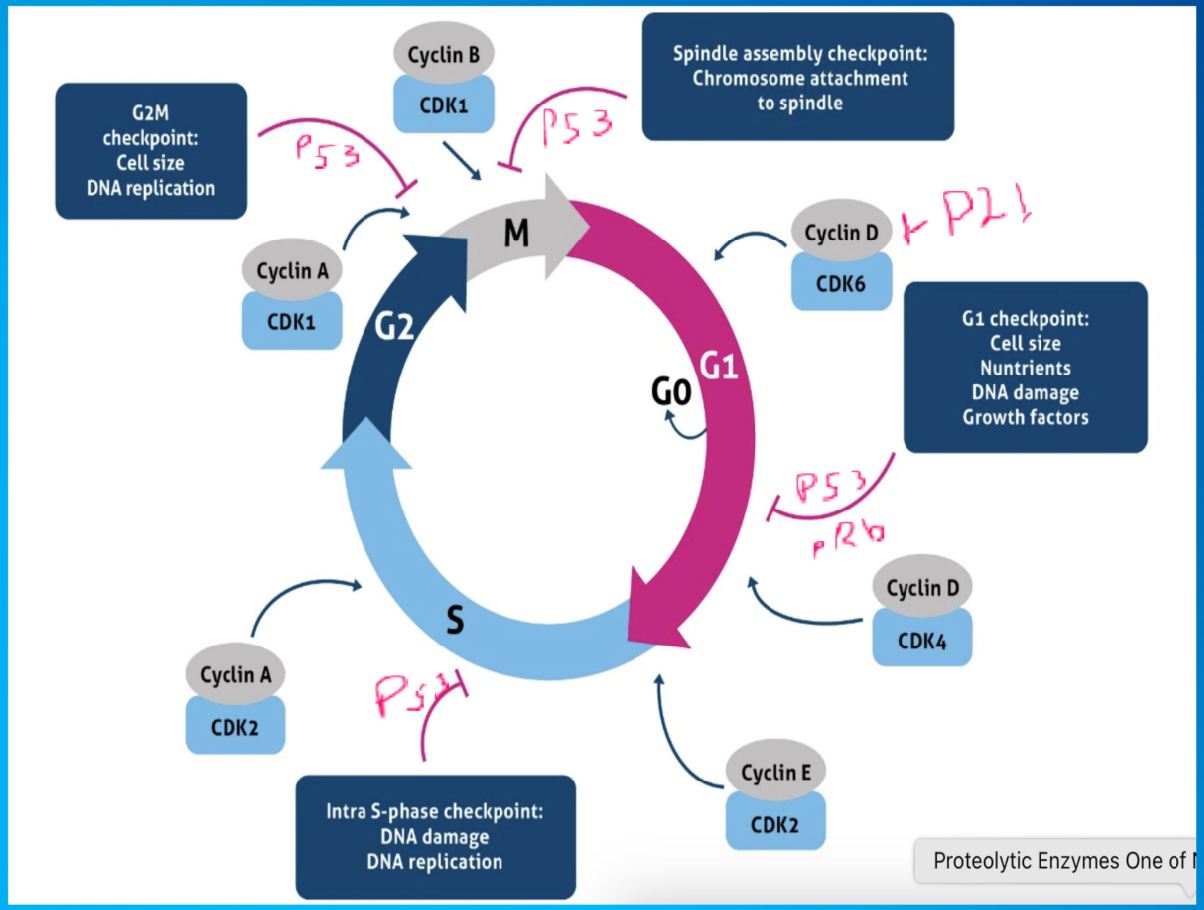
ERK: Extracellular signal-regulated kinase
MAPK: Mitogen-activated protein kinase
MEK: Ras/Raf/MAPK

Checkpoints: Regulated by Tumor Suppressors p53 and pRb

The cell cycle is based on three main checkpoints:

- Phase G1 – DNA integrity and cell size
- Phase G2 – DNA damage and chromosome duplication
- Phase M – Attachment of kinetochore and a spindle fiber

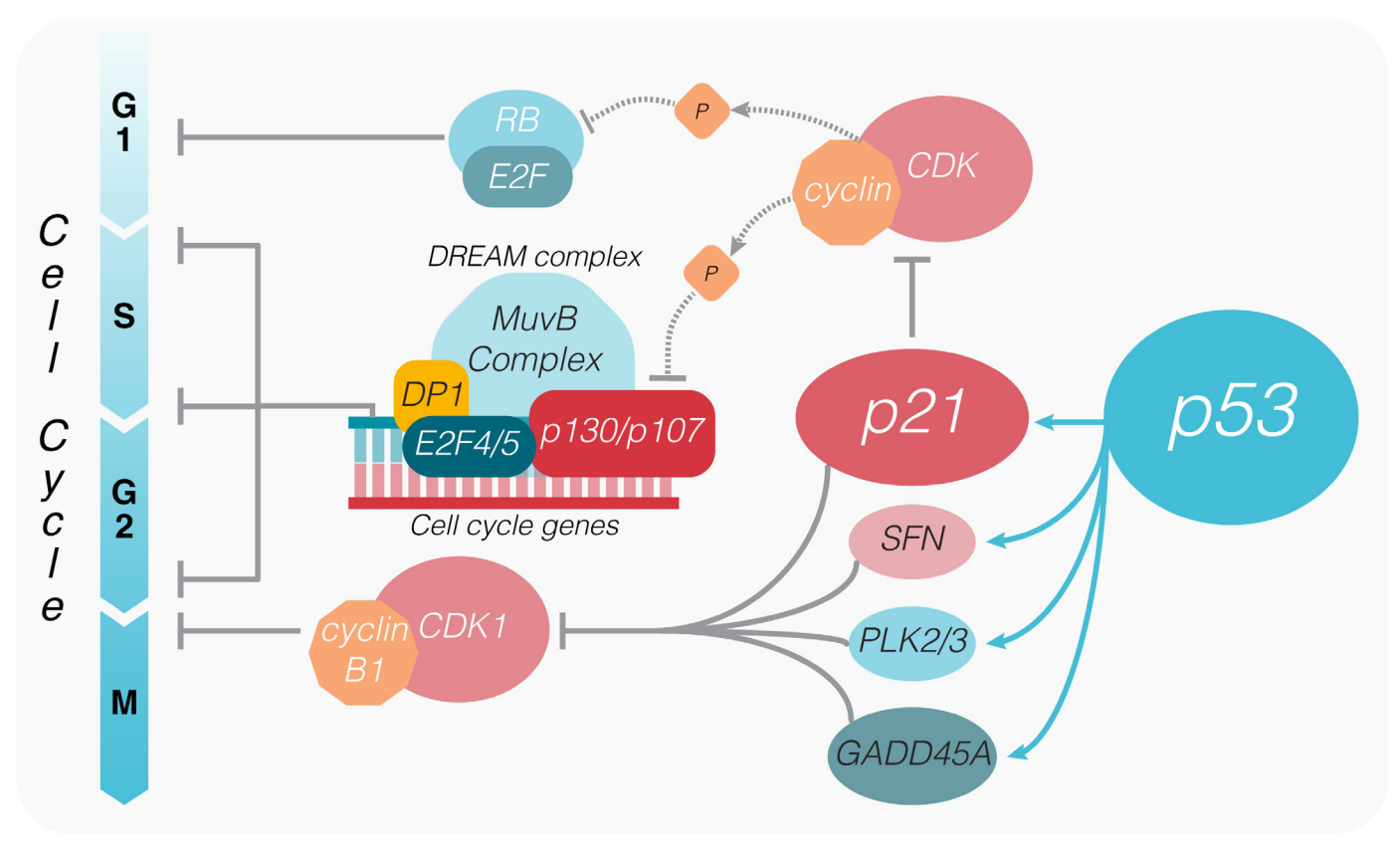
The key role of checkpoint proteins is to detect DNA damage and send a signal to delay cell cycle advance until the damaged chromosomes are repaired.



Cell Cycle Checkpoints and Signaling Factors

- P53- p53 has been shown to play a role of cell cycle arrest, senescence, DNA repair, and apoptosis
- pRb- Rb protein (pRb) is a master regulator of biological pathways influencing virtually every aspect of intrinsic cell fate including cell growth, cell-cycle checkpoints, differentiation, senescence, self-renewal, replication, genomic stability and apoptosis
- P21- Cyclin-dependent kinase (CDK) inhibitor p21 (also known as p21(WAF1/Cip1)) is one of these factors that promote cell cycle arrest in response to a variety of stimuli. P21 can be induced by both p53-dependent and p53-independent mechanisms. Some other important functions attributed to p21 include transcriptional regulation, modulation or inhibition of apoptosis. In addition, p21 can play a role in DNA repair by interacting with proliferating cell nuclear antigen
- BAX- When Bax protein is activated, its function is to bind and induce Mitochondrial Outer Membrane permeabilization. Such permeabilization results in mitochondrial swelling and rupture with subsequent leakage of intermembrane space proteins, specifically Cytochrome c and endonuclease G
- Bcl-2 - anti-apoptotic member that inhibits the activation and activities of Bax (pro-apoptotic)
- Caspases- Cytochrome c binds and activates cytosolic caspases, which are known to be the effector proteases of cell death

Tumor Suppressors



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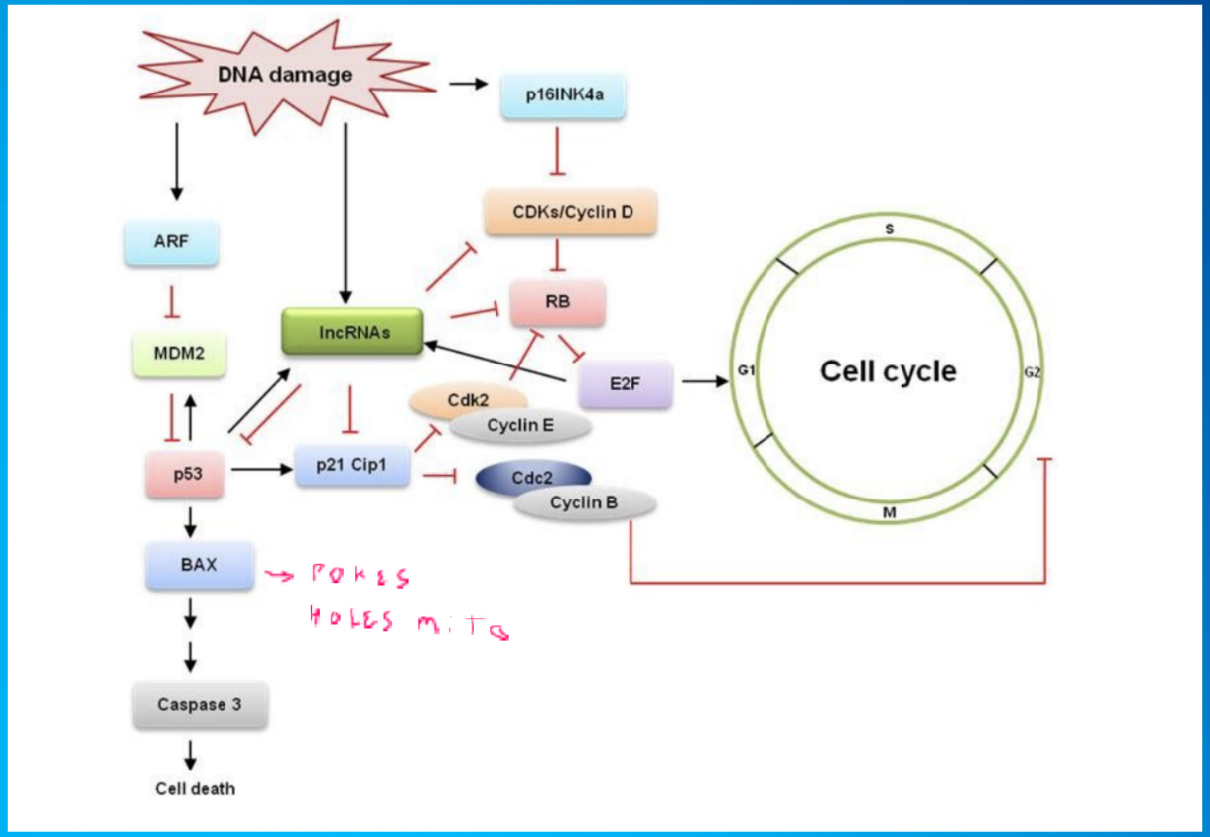
Tumor Suppressor Pathways

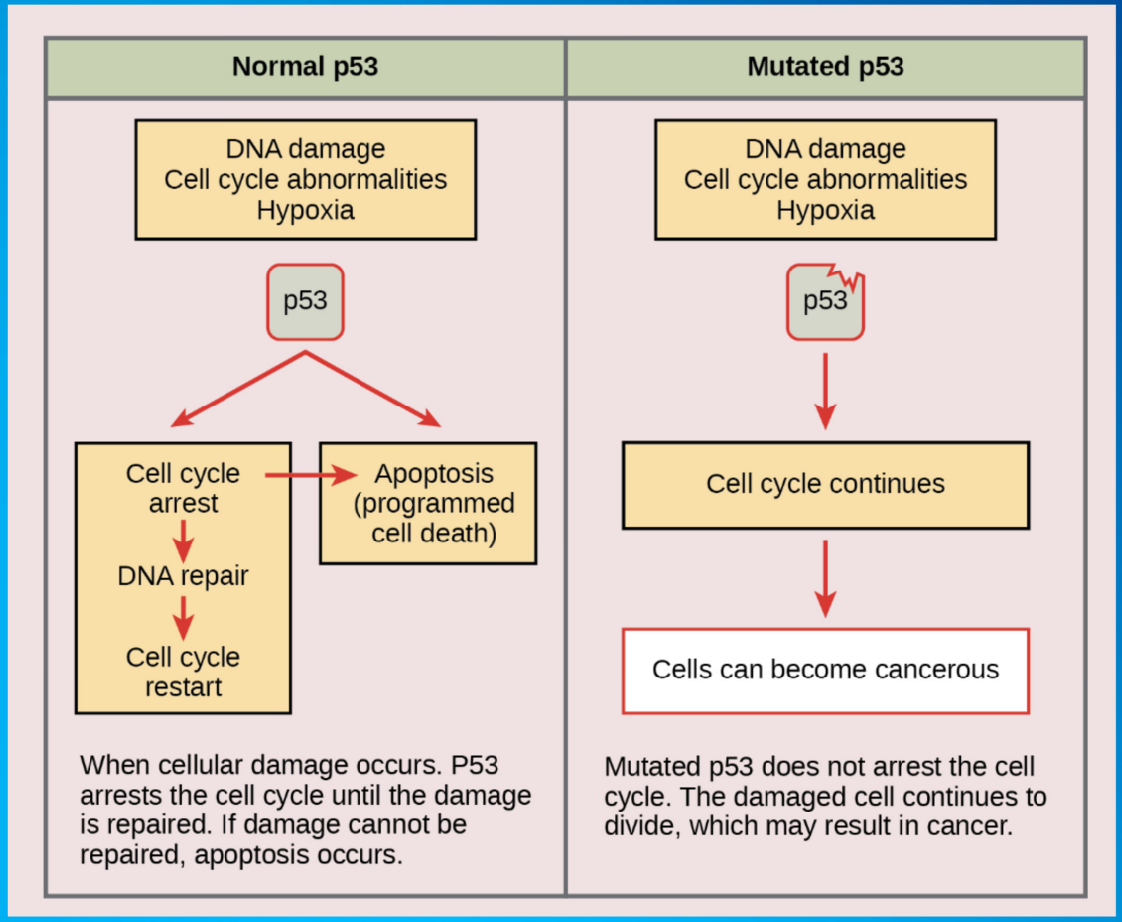
DNA damage by way of UV rays, hypoxia, certain viruses, oxidative stress, smoking, etc. turns on the tumor suppressor pathways p53 and retinoblastoma (RB) which control the DNA damage response. p16INK4a and p14ARF controls the activity of RB and p53. RB promotes cell cycle arrest in G1 and regulates entry into S phase by inhibiting the E2Fs. p53 mediates several effects, including causing G1 and G2 arrest and promoting apoptosis. Loss of p53 function also promotes genomic instability.
The *p53* gene is the most mutated gene in human cancer and regulation of p21 in response to DNA damage is lost when p53 is inactivated



Tumor Suppressor p53

The role of normal p53 is to monitor DNA and the supply of oxygen (hypoxia is a condition of reduced oxygen supply). If damage is detected, p53 triggers repair mechanisms. If repairs are unsuccessful, p53 signals apoptosis. A cell with an abnormal p53 protein cannot repair damaged DNA and thus cannot signal apoptosis. Cells with abnormal p53 can become cancerous.

(credit: modification of work by Thierry Soussi)



Example of potential p53 inhibitors

- **SARS-CoV-2 spike S2 subunit inhibits p53 activation of p21(WAF1), TRAIL Death Receptor DR5 and MDM2 proteins in cancer cells**

  "In summary, we identified the SARS-CoV-2 spike S2 subunit as a factor that interrupts p53 binding to MDM2 in cancer cells and demonstrated the suppressive effect of SARS-CoV-2 spike S2 on p53 signaling in cancer cells. As *loss of p53 function is a known driver of cancer development* and confers chemo-resistance, our study provides insight into cellular mechanisms by which SARS-CoV-2 spike S2 may be involved in reducing barriers to tumorigenesis"

- **S2 subunit of SARS-nCoV-2 interacts with tumor suppressor protein p53 and BRCA: an in-silico study**

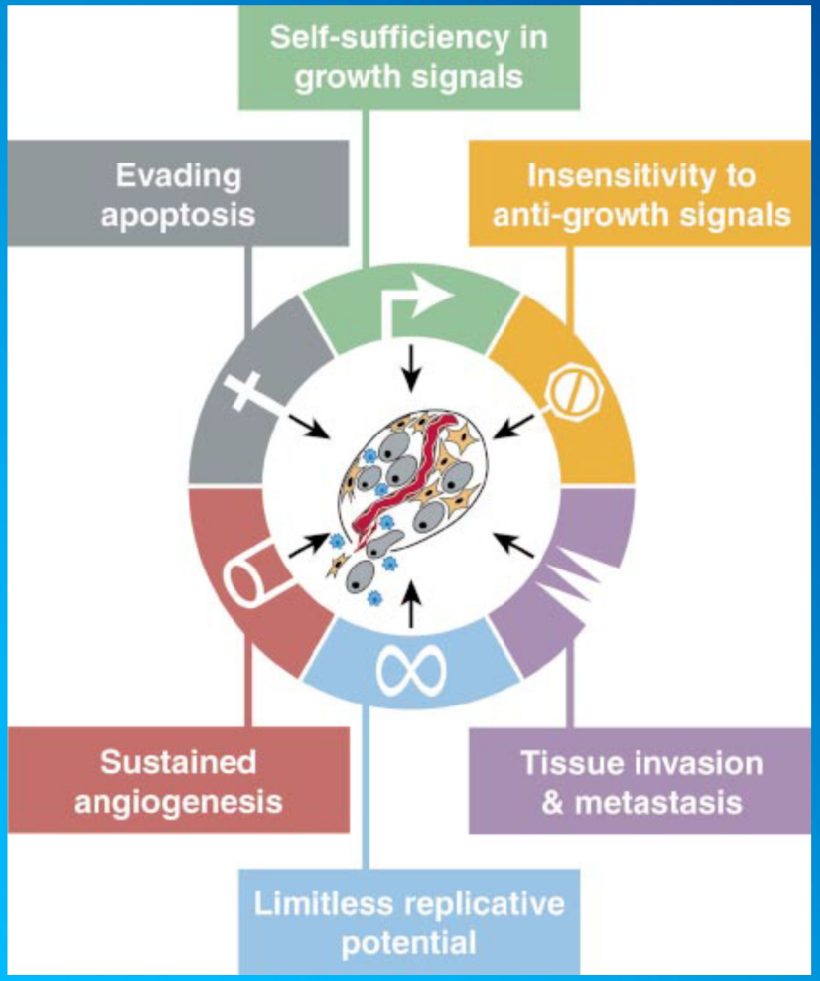
An in-silico modeling study that concluded the S2 segment of the SARS-CoV-2 Spike protein could be anticipated to inhibit the p53 and BRCA1/2 tumor surveillance systems. In-silico is a computer simulation to study biological events and data

Hallmarks of Cancer

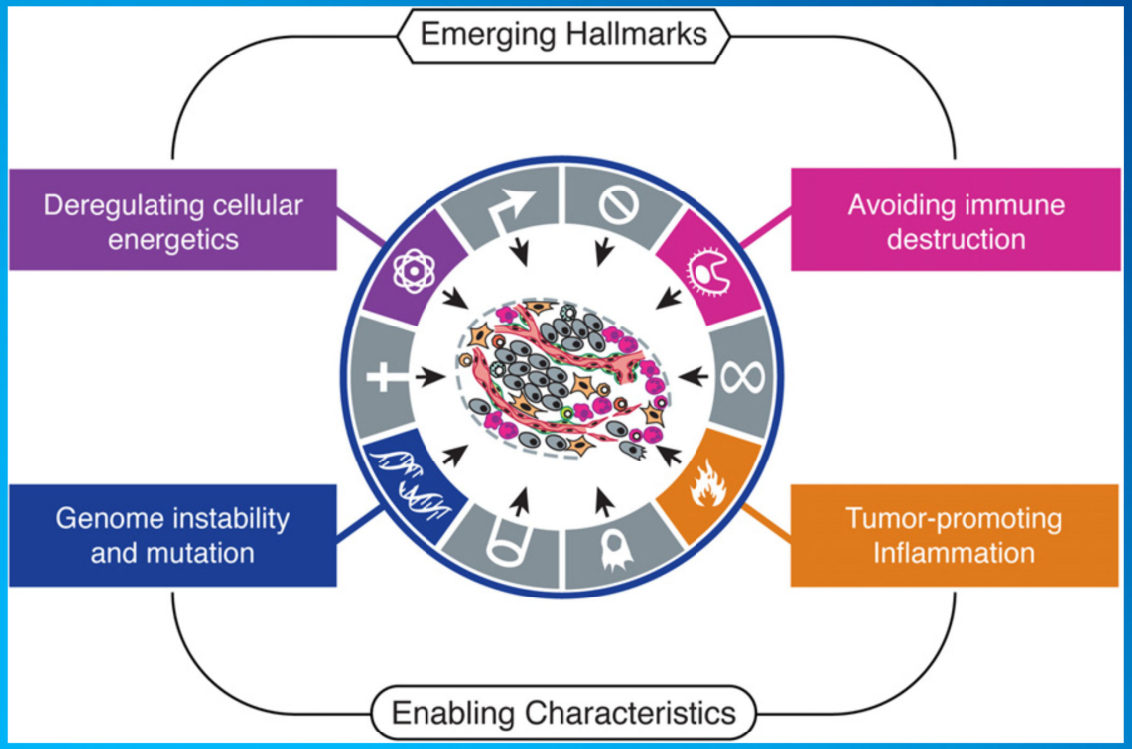
Research has revealed cancer to be a disease involving dynamic changes in the genome. The foundation has been set in the discovery of mutations that produce oncogenes with dominant gain of function and tumor suppressor genes with recessive loss of function; both classes of cancer genes have been identified through their alteration in human and animal cancer cells and by their elicitation of cancer phenotypes in experimental models (Bishop and Weinberg, 1996).

The vast catalog of cancer cell genotypes is a manifestation of six essential alterations in cell physiology that collectively dictate malignant growth: self-sufficiency in growth signals, insensitivity to growth-inhibitory (antigrowth) signals, evasion of programmed cell death (apoptosis), limitless replicative potential, sustained angiogenesis, and tissue invasion and metastasis.

Douglas Hanahan and Robert A. Weinberg 2000



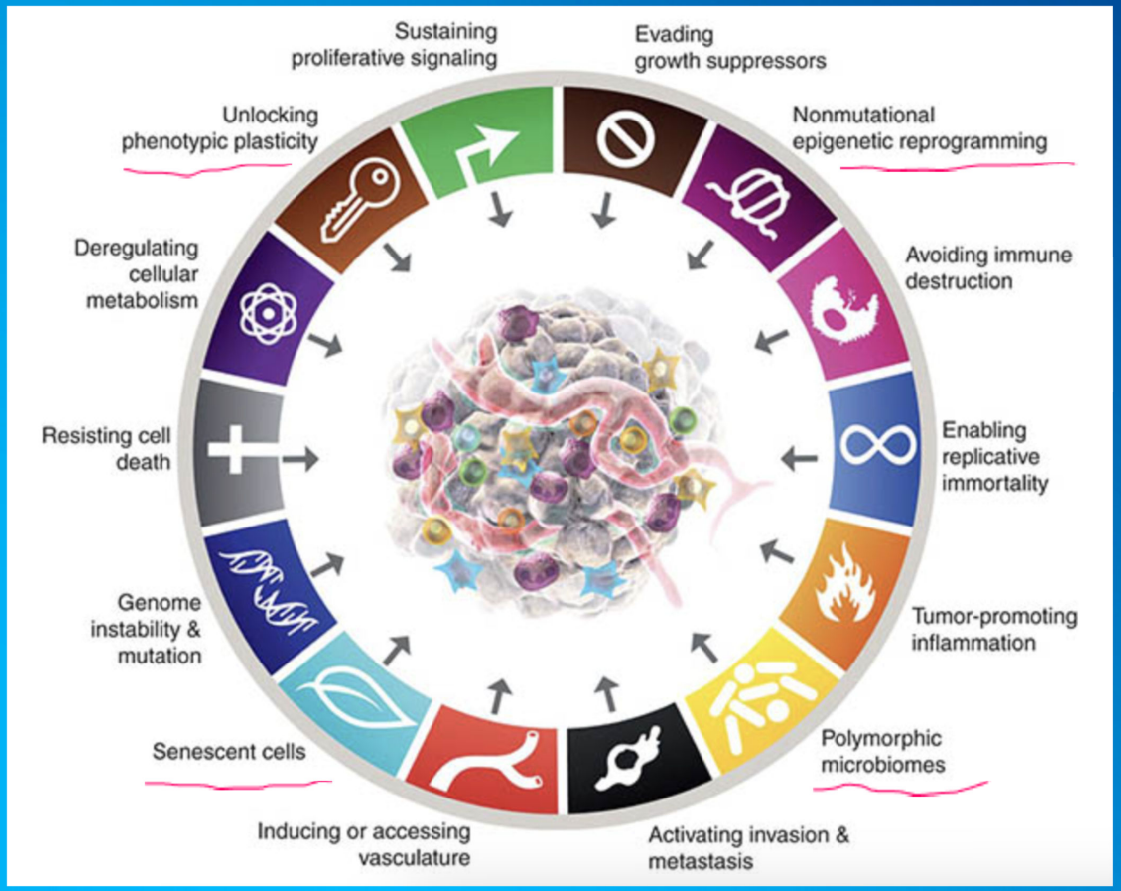
An increasing body of research suggests that two additional hallmarks of cancer are involved in the pathogenesis of some and perhaps all cancers. One involves the capability to modify, or reprogram, cellular metabolism to most effectively support neoplastic proliferation. The second allows cancer cells to evade immunological destruction, by T and B lymphocytes, macrophages, and natural killer cells. Because neither capability is yet generalized and fully validated, they are labeled as emerging hallmarks. Additionally, two consequential characteristics of neoplasia facilitate acquisition of both core and emerging hallmarks. Genomic instability and thus mutability endow cancer cells with genetic alterations that drive tumor progression. Inflammation by innate immune cells designed to fight infections and heal wounds can instead result in their inadvertent support of multiple hallmark capabilities, thereby manifesting the now widely appreciated tumor-promoting consequences of inflammatory responses.



Hallmarks of Cancer

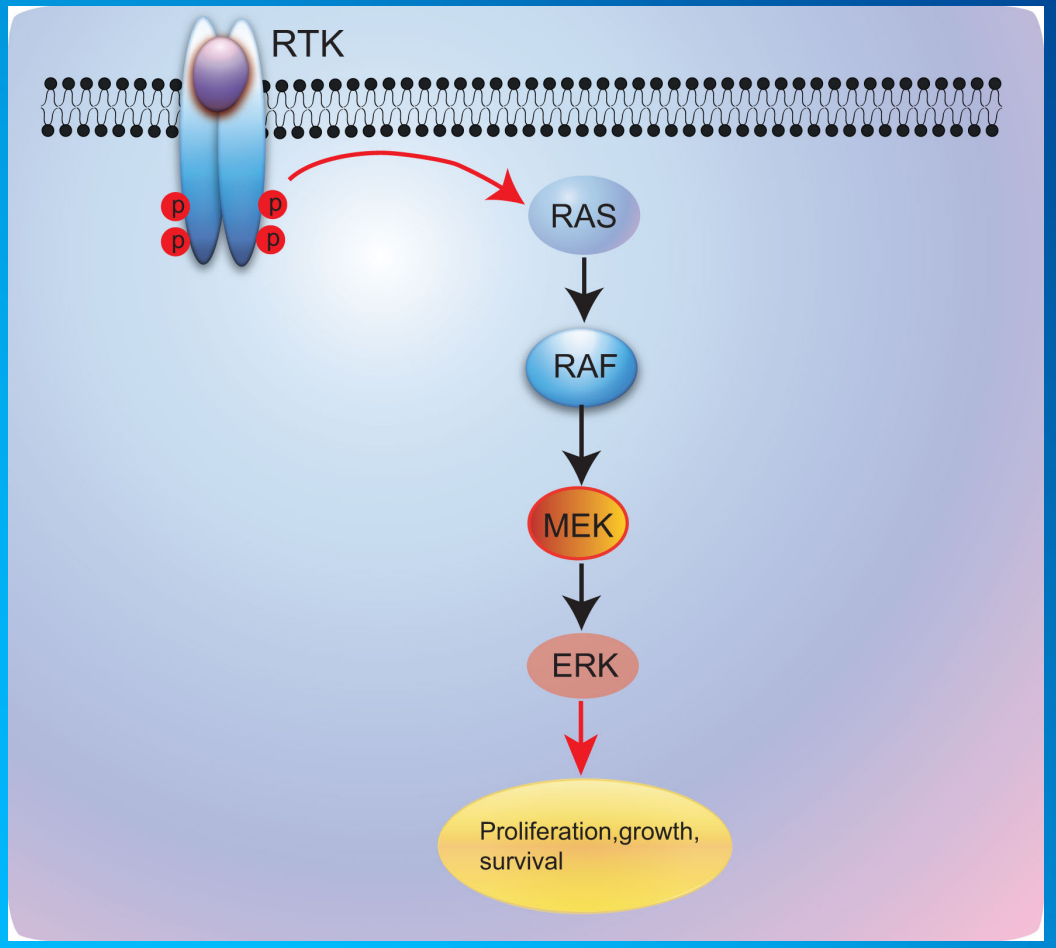
This revision incorporates additional proposed emerging hallmarks and enabling characteristics involving unlocking phenotypic plasticity, non-mutational epigenetic reprogramming, polymorphic microbiomes, and senescent cells.

The Hallmarks of Cancer: New Dimensions. Hanahan 2022



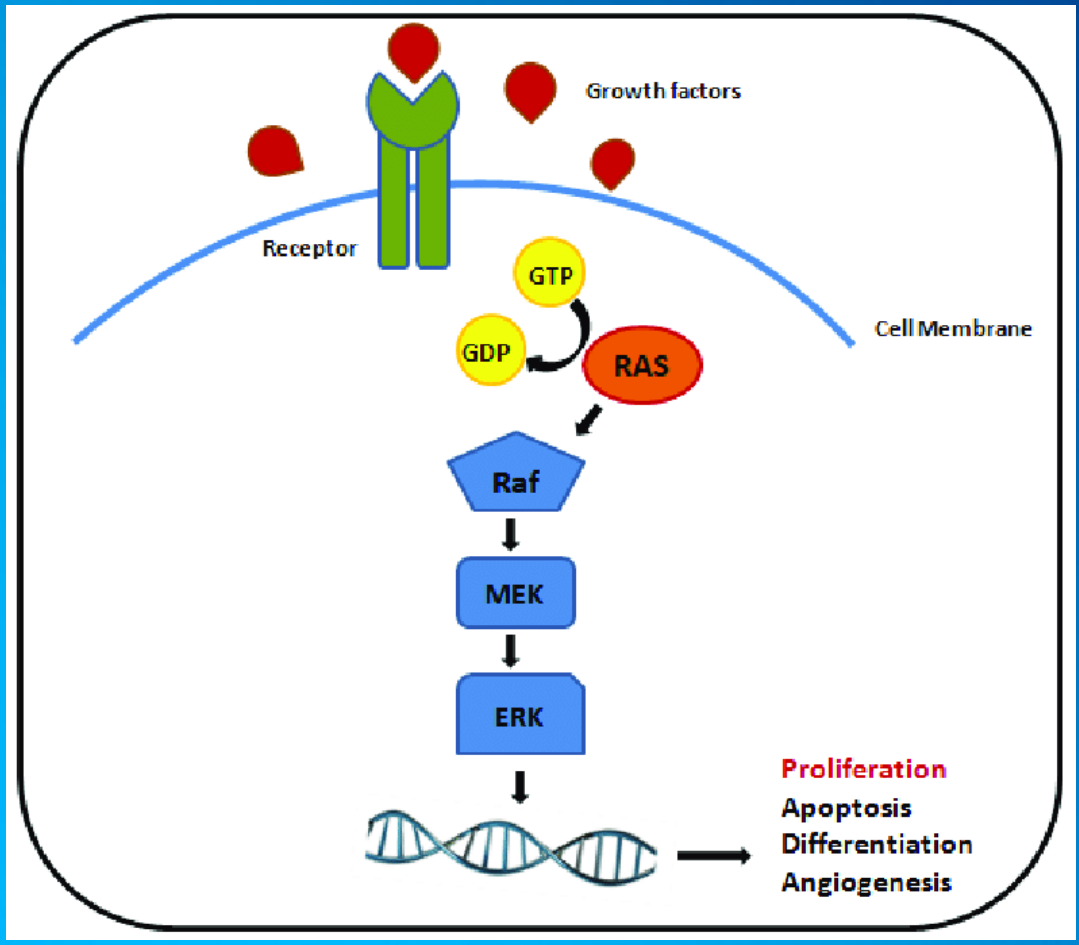
Ras-Raf-Mek-Erk signaling pathway

- Unlimited cell proliferation, dedifferentiation and a lack of apoptosis are important biological characteristics of tumors
- The activation of the ERK/MAPK signaling pathway promotes proliferation and has an anti-apoptotic effect
- Hypoxia-induced VEGF can inhibit the apoptosis of serum-starved cells by activating the ERK/MAPK signaling pathway
- Inhibiting the expression of this pathway can inhibit the proliferation of and lack of apoptosis in tumor cells and promote their differentiation.
- ERK1/2 signaling pathway is involved in cell survival following intestinal injury, and inhibition of this pathway can promote the apoptosis of intestinal injury cells
- Blocking the ERK/MAPK signaling pathway inhibited the proliferation of a diffuse large B cell lymphoma cell line and promoted cell apoptosis
- Inhibiting the expression of the ERK/MAPK signaling pathway to inhibit tumor cell proliferation may involve inhibition of the cell cycle



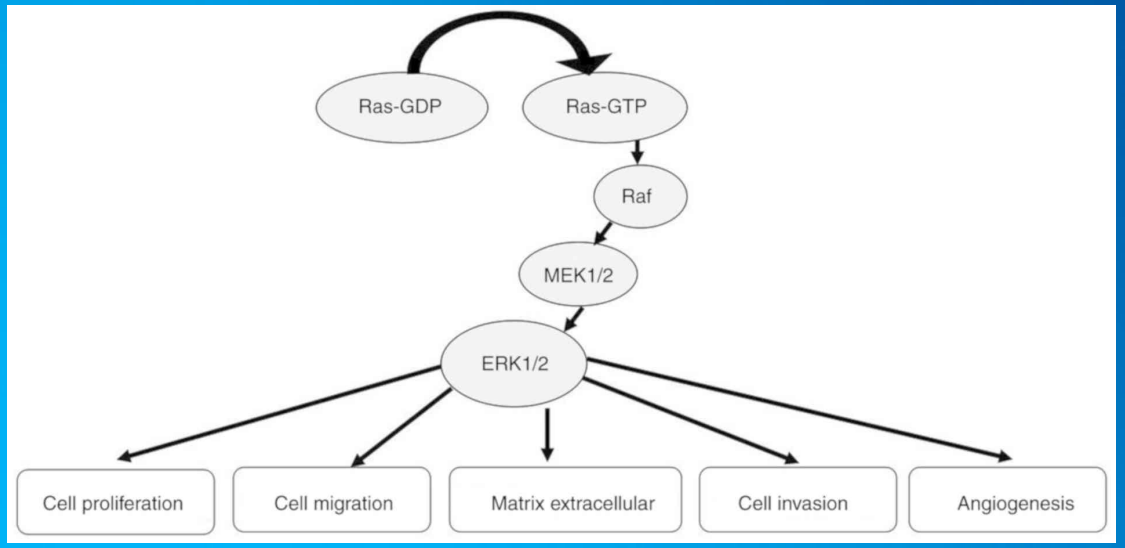
Ras-Raf-Mek-Erk signaling pathway

- The use of MEK1/2 inhibitors to inhibit ERK1/2 activity in colon cancer cells could prevent the cells from entering the S phase from the G1 phase and inhibit the growth of adherent cells
- Inhibition of the ERK/MAPK signaling pathway can reduce cell dedifferentiation and the anti-apoptosis effect
- ERK/MAPK signaling pathway promotes proliferation and inhibits apoptosis by influencing the activity of downstream cell cycle regulatory proteins, apoptosis-related proteins and other effector molecules, such as G1/S specific cyclin D1
- Gonadotropin-releasing hormone induces activation of the MAPK signaling pathway in normal and carcinoma cells of the human ovary and placenta
- SPACRC-like protein 1 (SPARCL1) is overexpressed in ovarian cancer; by inhibiting activation of the MEK/ERK signaling pathway, SPARCL1 is downregulated through the MEK/ERK pathway and inhibits the proliferation and migration of ovarian cancer cells



Raf-Mek-Erk signaling pathway

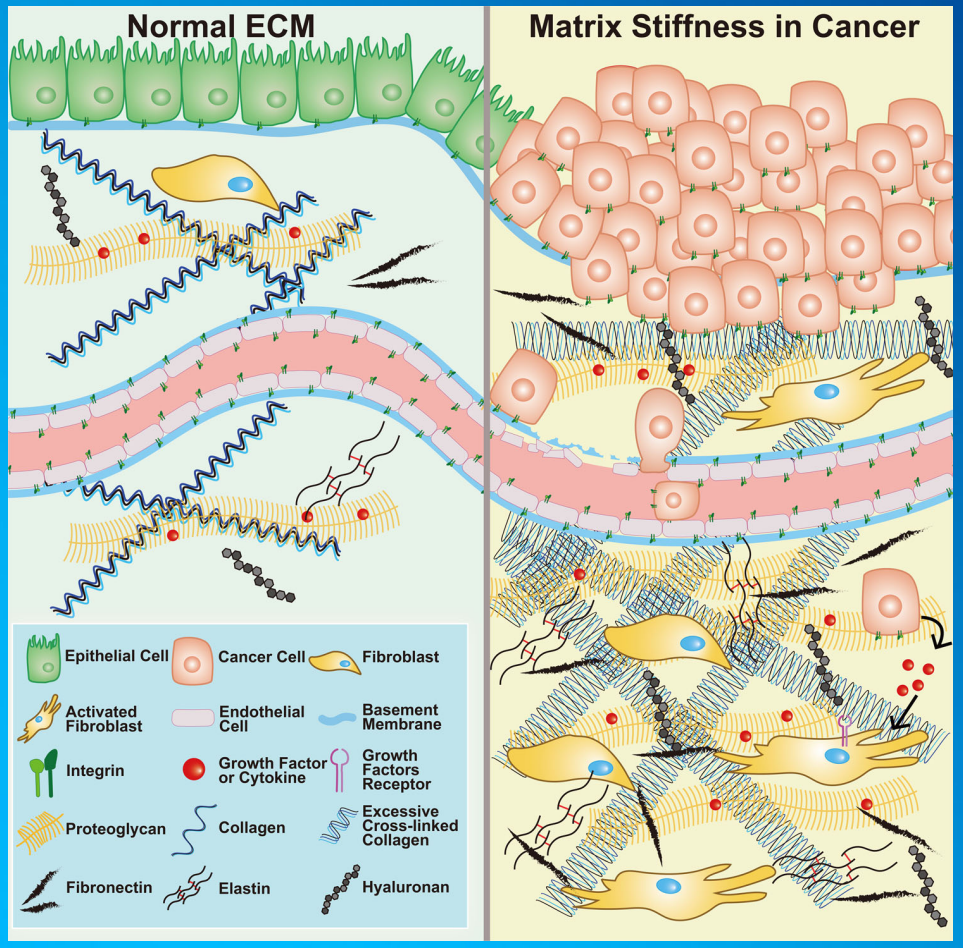
- Activation of ERK/MAPK signaling pathways activates other extracellular signaling pathways. Extracellular signals such as vascular endothelial growth factor (VEGF), platelet-derived growth factor and EGF can be activated by receptor tyrosine kinase autologous phosphorylation of the ERK/MAPK signaling pathway. Activated ERK may enter the nucleus and bind to transcription factors that induce gene expression in response to extracellular stimuli, and regulate cell proliferation, differentiation, apoptosis and transcription
- The ERK/MAPK signaling pathway is not only involved in regulating cellular biological functions, such as cell proliferation, cell differentiation, cell cycle regulation, cell apoptosis and tissue formation, but is also related to tumor formation. Elevated ERK expression has been detected in various human tumors, such as ovarian, colon, breast and lung cancer.
- The expression of MAPK phosphatase-1 (MKP-1) in normal ovarian surface epithelium and benign cystadenomas is increased compared to invasive carcinomas and low malignancy potential tumors and borderline tumors. Abnormal expression of MKP-1 and ERKs may play a role in the development of ovarian cancer.
- Continuous activation of the ERK/MAPK signaling pathway can promote the transformation of normal cells into tumor cells, while inhibition of the ERK/MAPK signaling pathway can restore tumor cells to a non-transformed state *in vitro* and can inhibit tumor growth *in vivo*
- Therefore, increased activation of the ERK/MAPK signaling pathway may be closely related to the occurrence and development of tumors



Extracellular Matrix

- Fibroblasts are regulated by many signals, including cytokines, chemicals, and environmental signals. TNF-α and interleukin (IL)-1 can induce the production of MMP-1, -3, and -9 by fibroblasts, leading to the degradation of collagen in the ECM

- Furthermore, ECM degradation contributes to the release of growth factors and cytokines. During tumorigenesis, MMP-2 and MMP-9 are upregulated in human colorectal cancer, and growth factors released from ECM cleaved by MMPs would promote tumor progression. For example, the VEGF is released when heparan sulfate is degraded, and such process promotes angiogenesis in colorectal carcinoma



Overexpressed molecules in the tumor microenvironment (ECM)

- MMPs: can release cytokines and fibroblast growth factors and vascular endothelial growth factors as well as degrade the ECM
- Transforming Growth Factor beta
- Cancer Associated Fibroblast (CAF)
- COX2 enzyme upregulation
- Interleukin 1beta upregulation
- Interleukin 6 upregulation
- CD44 adhesion molecule overexpression involved in metastasis

Proteolytic Enzymes

One of Nature's Answers to Cancer

Potential to impact:

- Cell cycle checkpoints
- Inhibit phosphorylation in cellular pathways that lead to proliferation
- Inhibit phosphorylation of Nf Kappa beta blocking COX2 stimulation
- Increase apoptotic signals
- Decrease anti-apoptotic signals
- Decrease proinflammatory cytokines
- Inhibit cell adhesion molecules that helps tumor metastasis
- Increase autophagy

PROTEASE

Transformation's most therapeutic systemic proteolytic formula

This proprietary blend of highly active, GI stable proteolytic enzymes has been combined to promote circulation, a strong healthy immune system, reduced inflammation, and timely detoxification.

Product Highlights

- Endo/exo peptidases break the inner/terminal bonds of amino acid chains for more efficient hydrolysis of proteins
- Protease blend (including bromelain plant enzymes) for reducing inflammation
- More than 400,000 HUT for the highest proteolytic activity available (600,000 PU = 51,000 HUT)
- 18 SAPU units from Protease 3.0
- Approx. 2,400 FU breaks down fibrin and clots and promotes healthy blood flow
- Calcium improves tolerance on an empty stomach

SUPPLEMENT FACTS

Serving Size 1 Capsule

Amount Per Serving		% Daily Value
Tzyme™ Protease Blend (peptidases, bromelain) (355,020 HUT + 19 SAPU) (600,000 PU)	492 mg	†

† Daily Value not established

Other Ingredients: Vegetable Capsule (Hypromellose, Water), Calcium Citrate

Clinical Applications

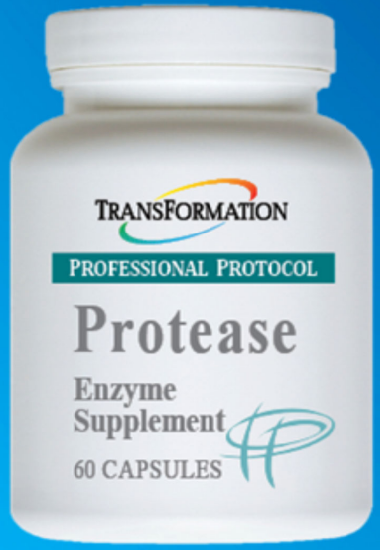
- Cancer of any kind
- Arthritis
- CVD / heart disease
- Chronic Fatigue Syndrome / Fibromyalgia
- Bacterial / Viral / Fungal Infections
- Hepatitis
- Kidney Disorders / Renal Insufficiency
- Eczema / Psoriasis
- Asthma / Emphysema
- All hormone imbalances
- Auto-immune disorders
- Autism
- Diabetes
- Muscle strains, soreness, injuries, and surgeries

For Your Information

- First choice when patient has been diagnosed with a condition (this is the "therapeutic" strength blend)
- It is better to take small doses of protease frequently throughout the day rather than large doses once or twice a day (protease has a half-life of approximately 3-4 hours; the goal is to keep the protease activity constant in the blood stream for therapeutic benefits)
- Compares with Nattokinase and Serra-peptidase
- May be given to children if condition warrants; may be given to pets
- Caution with patients on prescription blood thinning drugs (give protease formulas 3-4 hours away from Rx dose)
- May cause discomfort for individuals with stomach ulcers as protease will debride necrotic tissue and promote healing
- Discontinue taking Protease 24-48 hours prior to surgery and resume 24 hours post-surgery

Dosage

- Maintenance dose: 1 capsule 3 x day (rise, midday, rest) on an empty stomach
- General therapy dose: 2 capsules 3 x day between meals (approximately 1 hour before or 2 hours after meals)
- Therapeutic dose: 2-3 capsules 4-5 x day, or every 3 hours (goal is to keep high levels of activity in the blood stream at all times; "between meals" becomes difficult, so 30-60 minutes before or after meals is acceptable)
- **MAY BE TAKEN WITH FOOD IF UNABLE TO TOLERATE BETWEEN MEALS**
- Sometimes it is suggested 1 capsule may be taken with meals to enhance the digestion of proteins (diabetes, heartburn, acid reflux, gout, autism, high protein diet)
- For those who have difficulty swallowing pills, the capsules may be pulled apart and mixed in a small amount of tepid water or liquid and consumed immediately
- Topical application: open capsule and make a paste with a small amount of water, then apply to insect bite, fungal rash, mouth sores, inflamed gums, etc



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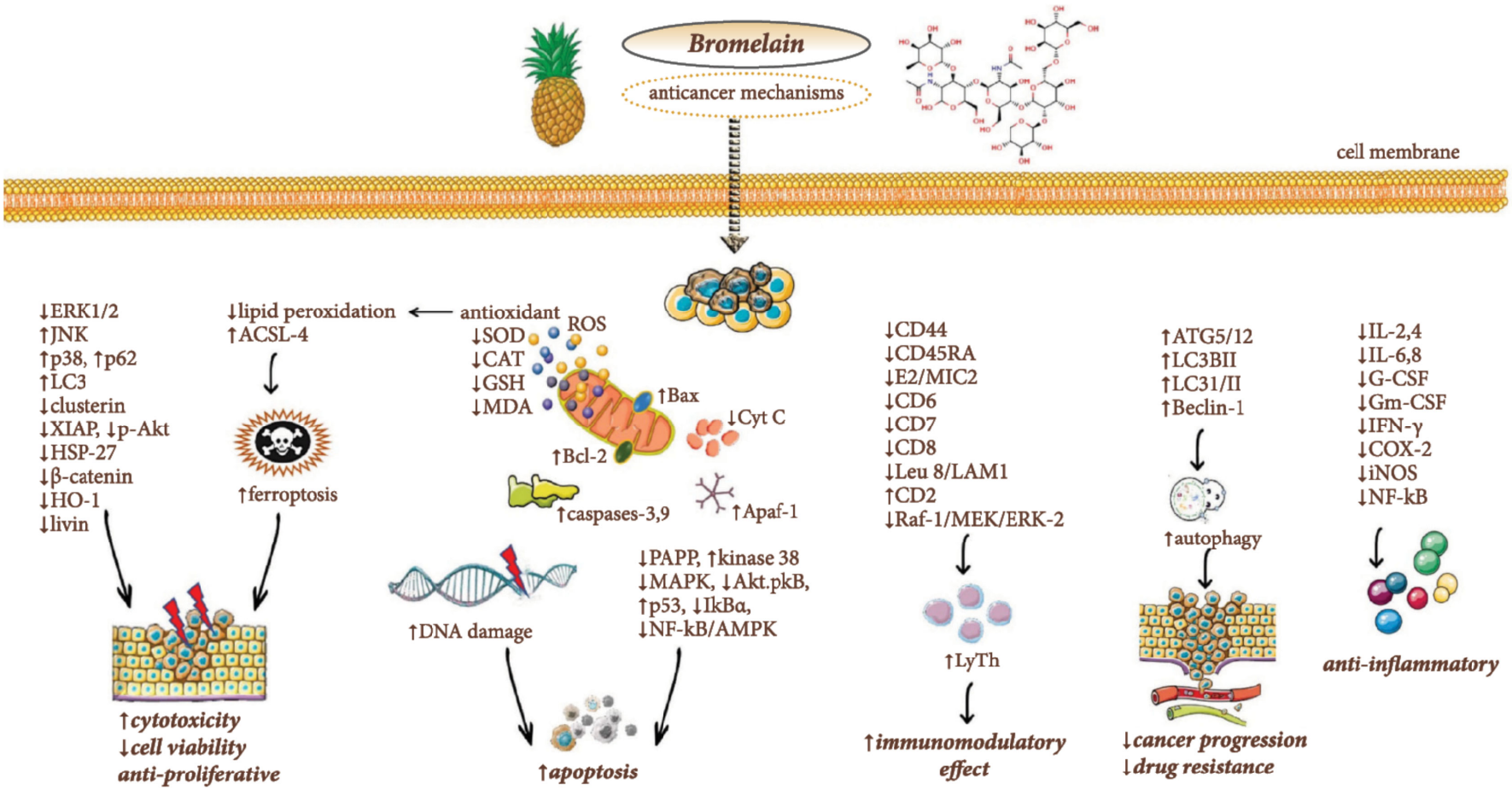
7 SIGNS OF A SOUND GUT

Saturday, April 12 • Austin, TX

ANTICANCER MOLECULAR MECHANISMS OF BROMELAIN



Bromelain

- An enzyme from pineapple
- A mixture of different thiol endopeptidases and other components like phosphatase, glucosidase, peroxidase, cellulase, escharase, and several protease inhibitors
- In vitro and in vivo studies demonstrate that bromelain exhibits various fibrinolytic, antiedematous, antithrombotic, and anti-inflammatory activities
- Considerably absorbable in the body without losing its proteolytic activity and without producing any major side effects

Antitumor activity of Bromelain in the literature

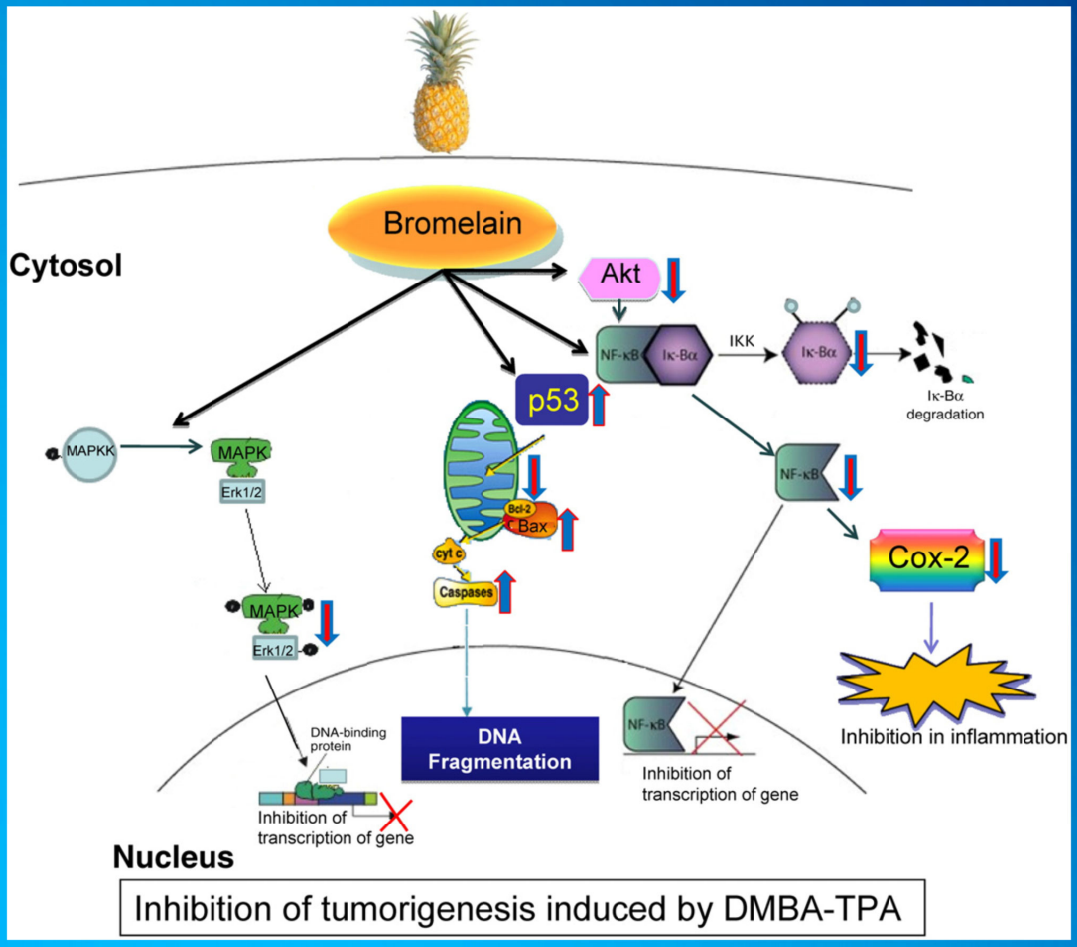
- Bromelain inhibits COX-2 expression by blocking the activation of MAPK regulated Nfkappa beta against skin tumor initiation triggering mitochondrial death pathway
- Bromelain, from Pineapple Stems, Proteolytically Blocks Activation of Extracellular Regulated Kinase-2 in T Cells
- Pineapple Bromelain induces Autophagy, facilitating apoptotic response in mammary carcinoma cells
- Regulation of p53, nuclear factor κB and cyclooxygenase-2 expression by bromelain through targeting mitogen-activated protein kinase pathway in mouse skin

Antitumor activity of Bromelain in the literature

- Bromelain treatment resulted in upregulation of p53 and Bax and subsequent activation of caspase 3 and caspase 9 with concomitant decrease in antiapoptotic protein Bcl-2 in mouse skin.
- Since persistent induction of cyclooxygenase-2 (Cox-2) is frequently implicated in tumorigenesis and is regulated by nuclear factor-kappa B (NF-κB), we also investigated the effect of bromelain on Cox-2 and NF-κB expression
- Results showed that bromelain application significantly inhibited Cox-2 and inactivated NF-κB by blocking phosphorylation and subsequent degradation of IκBα

Protease effects on cell signaling

In the present study, antitumorigenic activity of bromelain was recorded in DMBA-TPA-promoted 2-stage mouse skin model. Results showed that bromelain application delayed the onset of tumorigenesis and reduced the cumulative number of tumors, tumor volume and the average number of tumors/mouse. Bromelain treatment resulted in upregulation of p53 and Bax and subsequent activation of caspase 3 and caspase 9 with concomitant decrease in antiapoptotic protein Bcl-2 in mouse skin. Since persistent induction of cyclooxygenase-2 (Cox-2) is frequently implicated in tumorigenesis and is regulated by NF-κB, we also investigated the effect of bromelain on Cox-2 and NF-κB expression. Results showed that bromelain application significantly inhibited Cox-2 and inactivated NF-κB by blocking phosphorylation and subsequent degradation of IκBα. In addition, bromelain treatment attenuated phosphorylation of extracellular signal regulated protein kinase (ERK1/2), mitogen-activated protein kinase (MAPK) and Akt. Taken together, we conclude that bromelain induces apoptosis-related proteins along with inhibition of NF-κB-driven Cox-2 expression by blocking the MAPK and Akt/protein kinase B signaling in DMBA–TPA-induced mouse skin tumors, which may account for its anti-tumorigenic effects.



Proteolytic Enzyme | Health Benefits

- Systemic enzyme therapy has been shown to overcome the “cytokine storm” or “immunosuppression” seen in infections and cancer to salvage the host’s immune system
- Enzymes aid in destruction of cancer cells by activating death signals
- Enzymes activate alpha-2 macroglobulin, the “cytokine catcher” which usually exists in blood in an inactive form. Upon activation, this macroglobulin has high affinity for the TGF beta cytokine present in high levels in cancer
- Enzymes selectively reduce expression of CD44 adhesion molecules which encodes for metastasis
- Reduces proinflammatory cytokines such as IL6, IL1 beta, IL12, TNF alpha, NF kappa beta, and the COX2 enzyme upregulated in the tumor microenvironment

CASE STUDY Prostate Adenocarcinoma

- We have a 71yr. old male with a diagnosis of Prostate Adenocarcinoma confirmed by biopsy, MRI, Lymphadenopathy, and elevated PSA
- Pt's. family history includes Prostate cancer for his father and brother. Dad died of a heart weakened by radiation received for prostate cancer in the early 90's
- Pt. denies any allergies to drugs, foods, or environmental triggers and has unremarkable past medical history. Pt. states he feels well and has no symptoms. He is willing to make lifestyle changes and comply with our recommended protocol for his condition identified as a tumor
- His immediate concerns are the tumor on his prostate and elevated PSA
- The goal of our protocol is to reduce the prostate tumor significantly, bring PSA levels to normal <4ng/mL, eliminate the large pelvic lymph nodes, and reduce the Detrusor muscle hypertrophy observed in the bladder upon MRI.

CASE STUDY Prostate Adenocarcinoma

BIOPSY REPORT 12/14/22:

- Site A: No. of cores:1; Dimensions: 13 mm (left lateral base)
- Diagnosis Summary: PROSTATIC ADENOCARCINOMA; Gleason Score 7(4+3); 1 of 1 core involved; Tumor measures 7 mm in length; Microscopic Description: 90% of Gleason pattern 4.
- Site B: No. of cores: 3; Dimensions: 10,6,4 mm (left lateral mid)
- Diagnosis Summary: PROSTATIC ADENOCARCINOMA; Gleason Score 8(4+4); 3 of 3 cores involved; Tumor measures 13 mm in length; Microscopic Description: 100% of Gleason pattern 4.
- Site C: No. of cores: 2; Dimensions: 20,11mm (left lateral apex)
- Diagnosis Summary: Benign soft tissue. No prostatic glands present.
- Site D: No. of cores: 1; Dimensions: 14 mm (right lateral base)
- Diagnosis Summary: PROSTATIC ADENOCARCINOMA; Gleason Score 8(4+4); 1 of 1 core involved; Tumor measures 13 mm in length; Microscopic Description: 100% of Gleason pattern 4.
- Site E: No. of cores: 1; Dimensions: 13 mm (right lateral mid)
- Diagnosis Summary: PROSTATIC ADENOCARCINOMA; Gleason Score 8(4+4);1 of 1 core involved; Tumor measures 13 mm in length; Microscopic Description: 100% of Gleason pattern 4.
- Site F: No. of cores: 2; Dimensions: 10,8 mm (right lateral apex)
- Diagnosis Summary: PROSTATIC ADENOCARCINOMA; Gleason Score 8(4+4); 2 of 2 cores involved; Tumor measures 12 mm in length; Microscopic Description: 100% of Gleason pattern 4.
- Case Comments: Large cribriform glands present. This case has been reviewed in an Intradepartmental conference and all participating pathologists agree with the above diagnoses.

CASE STUDY Prostate Adenocarcinoma

PSA and HS CRP 10/07/22:

- PSA: 336 ng/mL
- Hs CRP: >10mg/L
- MRI REPORT 11/08/22: MRI Prostate with and without contrast on high field 3.0 Tesla showed:
- Prostate volume: 51 .69 cc
- Prostate dimensions: 5.2 x 5.2 x 3.9 cm
- Transition Zone: Central gland hypertrophy and large tumor measuring 15x29x30mm (APxMLxCC) at the posterior apex and mid prostate gland. The lesion extends posteriorly and inferiorly from the prostate capsule and is in close proximity to the anterior low rectum.
- Peripheral Zone: In the right mid posterior peripheral zone there is a markedly hypointense ADC signal measuring 14x8x12mm and increase permeability.
- Seminal Vesicles: the seminal vesicles are normal and symmetrical bilaterally.
- Extracapsular extension: the bilateral neurovascular bundles are not well defined and underlying invasion is within the differential.
- Bladder: there is detrusor muscle hypertrophy.
- Lymph Nodes: Mildly enlarged oval-shaped lymph node in the right pelvic sidewall measuring 9x7mm with a few other smaller lymph nodes also identified at this location.
- Other: heterogenous hypointense lesion measuring 11x10mm at the right pubic symphysis.

CASE STUDY Prostate Adenocarcinoma

- 12/7/22: Initial consultation, the patient had already been diagnosed by his Oncologist and provided lab testing and biopsy as shown above. The patient had begun taking a set of supplements when he learned of his diagnosis to start fighting his war against cancer. He was allowed to stay on several of them as I didn't see any contraindications with my protocol, and I didn't want to affect his belief in what he had started. After consent and consultation, the patient was recommended a treatment protocol of Protease IFC 2 caps between meals 3 times a day, Protease powder 1 teaspoon between meals 3 times a day (15 grams), L-Drain 1 dropper full in 8oz glass 3 times a day, Probiotic 42.5 1 cap in the morning and 1 cap at night along with a diet which excluded GMO's, gluten, dairy, and any artificial processing. Pt. initially had no adverse effects or discomfort in taking 15 grams of Protease Powder.
- 1/4/23: I recommended continuing the rest of the supplements at the same dose and only increasing the dose of the Protease Powder to 10 grams 3 times a day (30 grams) on an empty stomach until the end of the study on May 17th, 2023, which ran for a total of 23 weeks.

CASE STUDY Prostate Adenocarcinoma

- 2/3/23: by the direction of his Oncologist the patient began Testosterone blockers with one shot of Lupron depot
- 2/16/23: started Zytiga with Prednisone
- 3/3/23: he began Orgivyx for blocking Testosterone plus Prednisone plus Zytiga and was told that with these blockers he should see PSA go down within 4 to 6 months (July to September)
- 5/15/23: PSA was already 0.6 ng/mL (2 to 4 months earlier than expected by Oncologist) which could be due to the mega dose of proteolytic enzymes the patient had been taking since December.

CASE STUDY Prostate Adenocarcinoma

Follow up MRI and blood tests are as follows:

- MRI FINDINGS 5/15/23:Prostate volume: 15.54 cc down from 51.69 cc on previous MRI.
- Prostate dimensions: 3.4 x 3.0 x 3.0 cm down from 5.2 x 5.2 x 3.9 cm on previous MRI.
- PSA: 0.6 ng/ml. previously 336 on the 11 /8/2022 examination.
- Transition Zone: The transitional zone is low in T2 signal intensity. The central zone demonstrates low ADC signal symmetrically. If additional biopsy is indicated, the right central zone demonstrates focal moderate hypointense ADC and mild hyperintensity DWI, without increased permeability and measures greater than 1.5 cm in size (PI-RADS 3). This demonstrates no increased permeability.
- Peripheral Zone: Since the prior exam, the prostate is smaller in appearance with more diffuse decreased T2 signal, most consistent with posttreatment change. There is persistent low signal in the posterior apex on T2-weighted imaging, without associated low ADC. By strict scoring, this likely represents a PI-RAD 2 lesion, but is at the known site of prior PI-RADS 5 lesions, consistent with posttreatment response.
- Seminal vesicles: The seminal vesicles are normal and symmetrical bilaterally.
- Extracapsular extension: The prostatic capsule is preserved. The neurovascular bundles are intact. There is no evidence of tumor in the rectal prostatic angles.
- Bladder: Normal.
- Lymph nodes: The previously visualized areas of right pelvic sidewall adenopathy have resolved. No abnormally enlarged pelvic lymph nodes.

IMPRESSION:

- PI-RADS: Category: post treatment change with visible reduction in size and restricted diffusion in the posterior apical known prostate cancer. The overall prostate size is reduced in the signal intensity is decreased nearly diffusely on T2-weighted imaging. The pelvic lymphadenopathy has also resolved. There is no focal area in the peripheral zone meeting current PIRADS 4 or 5 rating. The inferior right pubic ramus lesion appears unchanged. The central zone demonstrates restricted diffusion but appears symmetric and is indeterminant (PI-RADS 3).

CASE STUDY Ulcerative Colitis

Here we have a 28-year-old female patient with severe Ulcerative Colitis which began in November of 2020 and confirmed via Colonoscopy in October 2022. The patient complained of blood and mucus in the stool which occurred 15 or more times a day. She experienced frequency/urgency of bowel movements and diarrhea accompanied by sharp abdominal left lower pain daily. She also experienced hair loss, achy joints, anxiety, GERD, bloating, depression, anemia, eczema, chronic fatigue, shortness of breath, and headaches with poor concentration and brain fog. She had been taking Vyvanse for 8 years for ADHD, Xyzal for 8 years for allergies, Omeprazole for 2 years for GERD, and Ogestrel for 2 years for irregular menses. Her ability to eat a variety of foods without experiencing acute symptoms was very limited and despite this limitation she was unable to lose weight and weighed 165lbs.

CASE STUDY Ulcerative Colitis

10/2/2023 - We began Transformation's Thrive in 63 Phase 1 protocol which consists of 3 DigestZyme and 1 PureZyme before each meal and 3 GastroZyme after each meal along with 3 Plantadophilus and 3 PureZyme at bedtime.

10/30/2023 - Substituted the PureZyme and GastroZyme for the more potent formula of 1 Protease and 1 Gastro, respectively, at the same dosing times as well as the bedtime PureZyme to Protease.

11/3/2023 - Protocol changed to 1 Digest and 1 Protease before each meal and 1 Gastro after each meal along with 3 Plantadophilus and 2 Protease at bedtime.

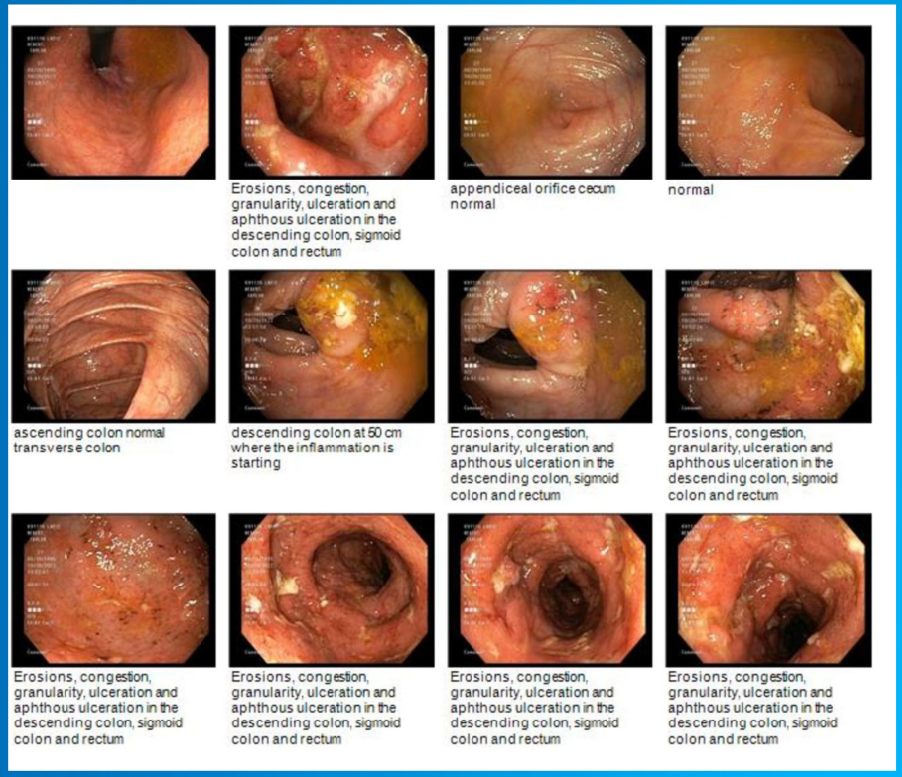
12/5/2023 - Changed the 3 Plantadophilus to 1 Probiotic at bedtime and the rest of the dosing schedule remained the same.

1/9/2024 - Patient discontinued the Omeprazole for the first time in 2 years and discontinued and the Ogestrel for the first time after 8 years.

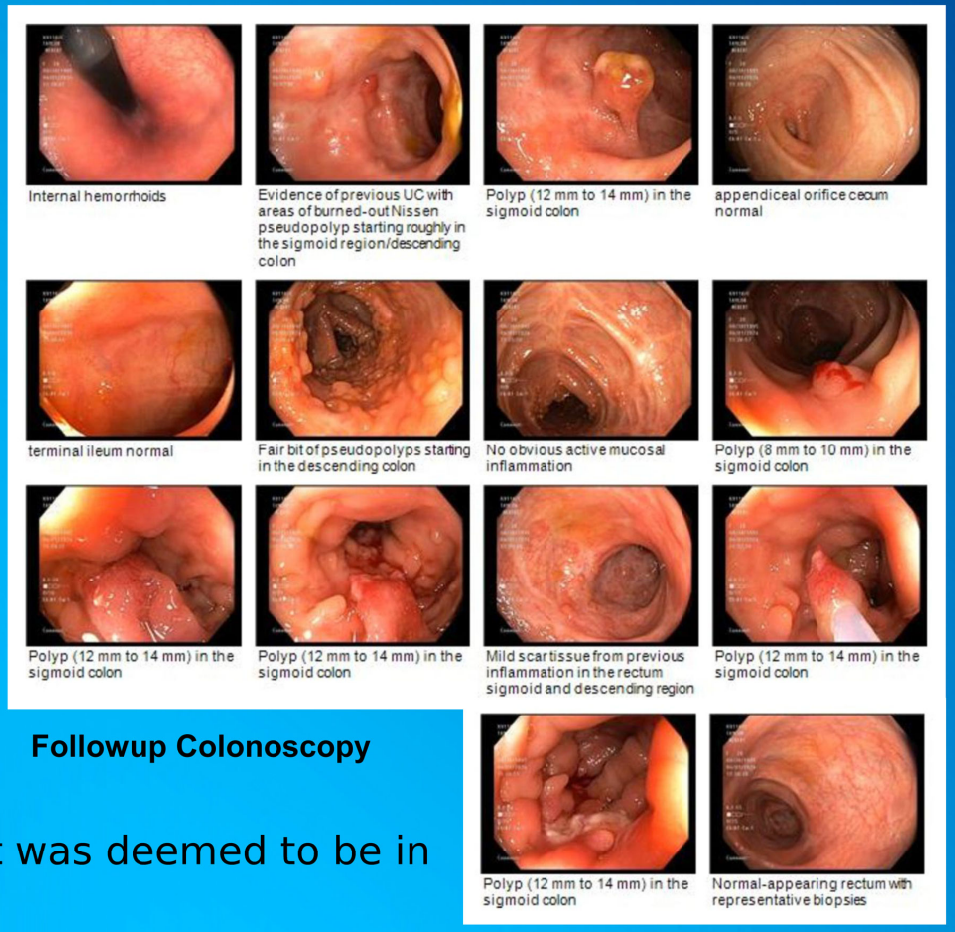
1/11/2024 - Patient started on 1 Probiotic morning and night, 1 Digest before meals, 2 Gastro after each meal, and 2 Protease 3 times a day on an empty stomach.

2/25/2024 - Patient continued with the digestive enzymes with each meal and the probiotic in the morning and night and added 5 grams of powdered protease 3 times a day until 4/20/2024 when we concluded the study.

CASE STUDY Ulcerative Colitis



Initial Colonoscopy



Followup Colonoscopy

Upon follow up colonoscopy the patient was deemed to be in endoscopic remission

CASE STUDY Ulcerative Colitis

We observed through imaging studies healing of the ulceration and decrease GI inflammation as well as improvement of bowel movements from constant bloody diarrhea to normal fecal matter, decrease pain, and improved tolerance to a variety of foods without causing distress.

The patient reported not having to take Omeprazole after not being able to live without it for 2 years and she also discontinued the Ogestrel for the irregular menstrual cycles she experienced in the past.

The patient was able to return to a daily exercise regimen at the gym, has lost 23 lbs, and states she feels “great.”

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CASE STUDY Osteoarthritis of the Knee

In this present case study, we have a 49-year-old male patient with severe osteoarthritis of the right knee who is a dedicated CrossFit® athlete and trains up to 5 times a week using heavy weight on all gym movements ranging from 100 to 300 lbs to include squatting, cleaning, snatching, overhead lifting, etc. The patient walks with a limp and has limited ROM in all planes. He had been dealing with right knee pain for over 8 years and underwent knee arthroscopy in 2016.

5/2021 through 6/2021: The patient received four Orthovisc® 30mg/2mL injections which contained Hyaluronan. This innovative knee injection is made from Hyaluronan, a natural and non-animal substance found in high amounts in joint tissues and the fluid that fills the joints that acts as a lubricant and shock absorber in the joint, helping it function correctly. This treatment reduces bone friction and alleviates pain and stiffness in knee osteoarthritis. Injecting Orthovisc® into the knee joint enhances joint function by restoring synovial fluid's natural shock absorbing properties and improving mobility.

The patient returned to his orthopedic doctor with pain and tenderness of the lateral patellar facet, the lateral joint line, and the medial joint line with flexion at 135 degrees and extension at -5 degrees. He had mild knee effusion, pain at extreme limits of range, positive McMurray's and Apley's comprehension tests, crepitus, and symptoms of locking, pulling, inability to straighten knee, and increased pain with planting/twisting. The patient was given an MRI for suspicion of meniscal tear but showed severe degeneration, multiple osteophyte formation, chondrosis, cartilage thinning and fissuring, subchondral edema, and moderate joint effusion.

CASE STUDY Osteoarthritis of the Knee

MRI of Right Knee Impression:

1. Mild intrasubstance degeneration and fraying in the menisci. No large tear.
2. There is mucoid degeneration of the anterior cruciate ligament. Osteophytes mildly encroach on the cruciate ligaments. No acute sprain.
3. There are degenerative changes/chondromalacia in all 3 compartments with small to moderate osteophytes. Focal area of cartilage delamination in the posterior non weightbearing medial femoral condyle without definitive articular surface extension roughly measuring 8X11mm with mild subchondral edema. Small area of grade 3 to 4 chondrosis elsewhere.
4. No acute contusion or fracture. Mild subcutaneous edema. Moderate joint effusion.

CASE STUDY Osteoarthritis of the Knee

5/9/2023: The patient received a cortisone injection with a mixture of 20mg Kenalog® and 2mL 0.25%Sensorcaine®.

5/12/2023 The patient presented with decreased pain and was referred to physical therapy to improve ROM and gait without success so was given another round of Visco-supplementation.

5/2023 through 7/2023: The patient was given three injections with TriVisc® 10mg/mL at 2.5mL and was released with recommendations to take Naproxen 500mg in the morning and at night. Throughout all this knee discomfort the patient never stopped exercising, continued with heavy lifting, and pushed through the pain.

CASE STUDY Osteoarthritis of the Knee

The patient started with 5 grams three times a day of Transformation's Professional Protocol™ Protease powder for 5 days and then pushed up to 10 grams three times a day for approximately 6 months. Our objectives were to improve inflammation, edema, and pain as well as halt/slow the knee joint degeneration. We did not expect to reverse the OA findings since there was a great deal of degeneration in the cartilage, synovium, and many osteophytes present. The patient also did not want to stop his CrossFit® routine and continued heavy weightbearing exercises throughout the study which is not beneficial for his clinical status.

8/17/2023: The patient started the protocol and was at ROM flexion 130 degrees and extension 15 degrees with pain (normal 135 degrees flexion to 0 degrees extension). The week of the 21st went to his normal biweekly Chiro/rehab treatment for preventative maintenance. Upon the doctor starting light stretching he felt a release in the bottom of his knee to where his leg fully extended for a significant amount of time. This had not happened before starting the powder. While he was still not fully extended, he did notice seeing that it was becoming far easy to be extended while stretching and by simply slowing the leg to fully relaxed in a straight leg position with minimal down force.

9/27/2023: Nothing new but continued flexibility when comes to stretching and rehab treatment. According to the patient, knee felt stronger than previous few months before use and did not flare up with issues at all since starting the powder.

10/15/2023: Walked about 26.5 miles over 5 days while on vacation with no issues. This was not possible before starting the protocol. While he still had some discomfort the following mornings, simple stretching relieved the discomfort. Also, regular treatment by rehab doctor was going well where the doctor was able to compress knee down to 0 degrees with very little pain.

11/7/2023: Patient to continue 30 grams a day and add 1 capsule of Transformation's Professional Protocol™ Joint Health twice a day. This Transformation Enzyme Corporation formula is a unique blend of enzymes and NEM® brand eggshell membrane to supply nourishment for joint mobility and support healthy production of cartilage and connective tissues. Each capsule contains 500mg eggshell membrane which has been shown to be nearly five times more clinically effective than glucosamine and chondroitin.

1/26/2024: ROM flexion 139 degrees and extension 19 degrees. This was the end of the study and wanted to get a follow-up MRI to see any positive changes.

2/9/2024: Patient reports “I hate to say it but coming off the powder, my knee has been more problematic.”

We started another 2 rounds of 30 grams a day of the powder and 1 cap of Joint Health twice a day before getting a second MRI on 4/11/2024.

CASE STUDY Osteoarthritis of the Knee

MRI OF RIGHT KNEE COMPARISON, READ 4/11/2024. Comparison is made to a prior right knee MRI performed at Alliance MRI on 5/3/2023.

1. Again, seen is severe mucoid degeneration of the ACL without a tear. There is mildly increased bone marrow edema adjacent to the tibial attachment of the distal ACL. Also again, seen is mild degeneration of the PCL without a tear.

2. Again, seen is slight intrasubstance degeneration in the posterior horn of the medial meniscus. There is no meniscal tear.

3. Fairly stable mild to moderate chondromalacia along the central and posterior weightbearing portions of the medial femoral condyle as well as a small chondral fissure along the posterior weightbearing portion of the medial femoral condyle. There has been interval development of focal subchondral bone marrow edema in the medial aspect of the medial tibial plateau with suspected overlying chondromalacia. There is stable mild to moderate marginal osteophytosis of the medial compartment.

4. Fairly stable overall mild chondromalacia along the lateral femoral condyle and lateral tibial plateau as well as focally moderate chondromalacia along the central to posterior weightbearing portion of the lateral femoral condyle. There is also stable mild to moderate marginal osteophytosis of the lateral compartment.

5. Stable mild to moderate chondromalacia along the patella and trochlear groove. The previously seen mild subchondral bone marrow edema in the lateral trochlear groove has resolved. There is also stable mild marginal osteophytosis of the patellofemoral compartment.

6. Stable minor patellar tendinosis without a tear.

7. Mildly decreased now moderate joint effusion. There may be some loose chondral bodies located posterior to the posterior lateral femoral condyle on axial PD FS.

CASE STUDY Osteoarthritis of the Knee

CONCLUSION: Here we have a 49-year-old male patient with severe OA of the right knee who is a dedicated CrossFit ® athlete and trains up to 5 times a week using heavy weight on all gym movements ranging from 100 to 300lbs to include squatting, cleaning, snatching, and overhead lifting among other high intensity movements.

The patient was given adjunct support with 30 grams of Protease powder blend and 2 capsules of Joint Health daily along with his chiropractic rehabilitative care to improve symptoms of OA.

All end points of reducing pain, inflammation, and slowing down the degenerative components of OA were met as the patient reported significant differences while on the protocol in terms of mobility and tolerating heavy exercise with minimal discomfort.

The patient's follow up MRI also showed improvement in terms of the previously seen mild subchondral bone marrow edema in the lateral trochlear groove which had completely resolved.

Even with this patient's intense exercise regimen with heavy weightbearing movements, according to the radiologist the MRI findings remained stable, e.g., the findings have not progressively gotten worse from the previous MRI findings.

It is important to understand that while proteolytic enzymes will not reverse OA, they will improve quality of life and reduce inflammation and symptoms enough to be able to perform activities of daily living without the side effects of steroids, pain meds, or NSAIDS.

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