Beyond The Basics

Advanced insights to functional bloodwork and specialty testing Tracey Stroup, ND

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Current state of health

- Chronic Inflammation
- Immune system dysregulation
- Cancer Turbo
- Spectrum cases climbing
- MCAS Mast Cell Activation Syndrome
- "Chronic" infections
- Hormone issues infertility and beyond
- Neurotransmitter issues mass psychosis



You are only as young as your immune system

Getting Foundational

- Lifestyle Nutrition, hydration, movement, sleep, elimination, emotional and spiritual wellness
- Ultimate Shake
- Pro Lean Greens





The "Kill it Mentality"

The Kill it or quiet it mentality

- Antibiotic
- Chemotherapy
- Steroids



Injury Healing Process

- Acute injury Viral, bacterial, injury (trauma/jab) – requires an immune action
- Kill mentality & Repress mentality antibiotics, NSAIDS, Steroids, Immune repression, chemotherapy
- Always leaves a scar when unsupported UNHEALED TISSUE
- PAMP/DAMP = CHRONIC UNDERLYING INFLAMMATION/IMMUNE DYSREGULATION
- THE IMMUNE SYSTEM RESPONDS CORRECTLY
 MAY NOT RESOLVE CORRECTLY



Regenerative Healing

- Stops "treating" the chronic infection
- STARTS STRENGTHENING and TREATING THE IMMUNE SYSTEM
- What we are really seeing is:
 - Chronic inflammation
 - Immune system dysregulation
 - Lack of P53 activation APOPTOSIS



What happens when full healing does not occur



Yousefzadeh, Matt et al. "DNA damage-how and why we age?." *eLife* vol. 10 e62852. 29 Jan. 2021, doi:10.7554/eLife.62852

Pathogen-Associated Molecular Patterns (PAMP)

- These are signals that indicate the presence of harmful invaders, such as bacteria, viruses, or other pathogens. Imagine these as red flags that tell the immune system, "Hey, there's a bad guy here, we need to defend ourselves!" When cells detect PAMPs, they trigger an immune response to fight off the invaders and protect the body from infection.
- Issue The infection or invader is never handled or overcome completely
- Reason No nutraceutical support, repression therapy, protocol not taken long enough, continuous exposure.
- Result Complete healing does not occur

Damage-Associated Molecular Patterns (DAMP)

- These are signals that cells release when they're damaged or stressed, but not necessarily because of an infection. Think of DAMPs as distress signals that cells send out when they're injured or undergoing stress, saying, "Help! Something's wrong here, and we need assistance!" These can result from various sources, including physical injury, toxins, or even metabolic stress. When the immune system detects DAMPs, it responds by initiating repair processes to heal the damaged tissues and restore normal function.
- Issue chronic or sustained release of DAMPs can lead to persistent inflammation, which is implicated in the development and progression of many chronic inflammatory diseases, autoimmunity, cancer, neurodegeneration, tissue fibrosis, cardiovascular disease, diabetes and disease of the bones.
- Reason NOT ENOUGH fuel or TOO MUCH Toxicity
- Result Cellular Senescence or SICK CELLS Chronic Inflammation, Immune dysregulation, DIS-ease

Sterile Chronic Inflammation – No infection

Exposure to PAMPS

It is established that PAMPs mediate the production of cytokines by binding to PRRs such as Toll-like receptors (TLR) on immune cells. Galectins (Gal) are carbohydrate-binding proteins that when expressed play essential roles in the resolution of infectious and metabolic diseases. Are PAMPs inflammatory? PAMP and DAMP-mediated signaling and induction of an innate immune response usually results in resolution of infection, but may also cause chronic inflammation or autoimmunity by altering various cell death and survival mechanisms.

DAMPs endogenous

Cellular stress, damage, inflammation, and necrotic cell death cause release of endogenous damage-associated molecular pattern (DAMP) molecules or alarmins, which alert the host of danger by triggering immune responses and activating repair mechanisms through their interaction with pattern recognition receptors. Damage-associated molecular patterns (DAMPs) are endogenous danger molecules that are released from damaged or dying cells and activate the innate immune system by interacting with pattern recognition receptors (PRRs). Although DAMPs contribute to the host's defense, they promote pathological inflammatory responses

DAMPs are molecules that have a physiological role inside the cell, but acquire additional functions when they are exposed to the extracellular environment: they alert the body about danger, stimulate an inflammatory response, and finally promote the regeneration process.

What is a Senescent Cell ?

- Cell cycle arrest phase G0
- Can't divide but still viable
- Apoptosis does <u>not</u> occur





Cellular Senescence as a Therapeutic Target for Age-Related Diseases: A Review



4 Cycles of p53 Activation

P53 is a transcriber Codes over 100 genes for four mechanism

When P53 is activated, it becomes stable

Enters the nucleus of the cell, binds promotors and turns on genes in 4 categories to help the cell respond to a stressful situation

Cellular Arrest

DNA repair

Feedback Regulation

Apoptosis - Cell Death What encompasses a stressful situation

- Low Oxygen Levels
- DNA Damage
- Low Nutrient Levels
- Abnormal Cell Cycle

Cellular Senescence



THERE ARE NO FENCES IN THE BODY

Immune system circulates

- Blood vessels
- Vasculature
- Lymphatics



Signaling in the body

- All types of signaling in the body – Ligands transmit signals between cells (extra and intra cellular communication)
- Ligands interact with proteins
 - Paracrine other cells
 - Autocrine same cell
 - Neurotransmitter
 - Endocrine



Paracrine Signaling

Types of Signaling

1. Paracrine signaling/ Short Range Signaling

They involve **cells** within a **local** neighborhood. These signaling events are mediated by regional chemical factors and mechanical forces.

Examples include *Fibroblast growth factor*

which stimulate proliferation and

differentiation and *interferon* response

during viral infections



Autocrine Signaling

2. Autocrine Signaling

Autocrine signaling is a form of cell signaling in which a cell secretes a hormone or chemical messenger (the autocrine agent) that binds to autocrine receptors on that same cell, leading to changes in the cell. This is in contrast

with paracrine or endocrine signaling.



Examples: cytokines/immune cells, growth factors

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Fatty Liver





Paracrine & Autocrine - DAMP



Autocrine Example

Examples

The cytokine Interleukin-1 in monocytes. When interleukin-1 is produced in response to external stimuli, it can bind to cell-surface receptors on that same cell.

In activated T cell, the cell that releases IL-2 binds to its IL-2 receptors, causing self-stimulation and ultimately a monoclonal population of T cells is produced.

One approach used by tumors to upregulate growth and survival is through autocrine production of growth and survival factors.

Cancer is a metabolic issue



Paracrine & Autocrine - DAMP



Let's go beyond the bloodwork

High Monocytes/Low Lymphocytes

- Low grade sterile inflammation
- Naïve T cell production decreases over time
- Memory T Cells increase but are old



Thymic Involution



Chronic Ear Infections in Kids



When a baby is young, they have a lot of Naïve T cells...

However, reoccurring infections begin to create senescent cells...

Oxidative stress, inflammation, immune dysregulation

Most cases I have seen begin with underlying strep

KILL MENTALITY

Antibiotics...antibiotics...antibiotics...

532	\$5.00	Complete Blood Count (CBC) With Differential (005009)
513	\$6.00	Antistreptolysin O (ASO) Antibodies (006031)
1054	\$36.00	Anti-DNase B (Streptococcal) Antibodies (096289)

Certain Infections Are More Frequently Associated with Autoimmune Encephalopathies and Neuropsychiatric Symptoms

- Group A streptococci
- Influenza A
- Varicella (chickenpox)
- Mycoplasma
- Lyme disease
- Babesia
- Bartonella
- Coxsackie virus
- Others

PAMP & DAMP

- Antibiotics unsupported
- Not enough "other" nutrition to overcome
- "Other" Toxicity in the way
- Environmental Influences Childhood vaccine schedule

Antibodies Recognize "Epitopes" on Infectious Agents





The Immune system gets Confused

Autoimmune response through "Molecular Mimicry"



"The IgM anti-B. burgdorferi ... cross-reacted with S. pyogenes M and myosin, both of which share sequence homology with B. burgdorferi OspA, <u>suggesting a role for</u> <u>molecular mimicry in the generation of these Ab reactivities</u>



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Simple scheme of the hypothalamus–pituitary–thyroid axis. The hypothalamus produces thyrotropin-releasing hormone (TRH), which stimulates the pituitary to release thyrotropin (thyroid-stimulating hormone, TSH). TSH is released in circulation and stimulates the thyroid gland to produce thyroid hormones (THs) (Ortiga-Carvalho et al. 2014). The thyroid produces the main THs, thyroxine (T4) and triiodothyronine (T3). TSH stimulates all the steps of TH biosynthesis and release, as well as the expression and activity of several proteins: the solute carrier family 5A (also known as sodium-iodide symporter (NIS)), pendrin (PDS), dual oxidase type 2 (DUOX), thyroid peroxidase (TPO), thyroglobulin (Agic et al. 2007) and deiodinases type 1 (D1, DIO1), 2 (D2, DIO2) and 3 (D3, DIO3). In physiologic balance, T4 and T3 (3) regulate their own concentrations in the blood by negative feedback acting at the hypothalamic (1) and pituitary (2) levels (Ortiga-Carvalho et al. 2016). BPA, bisphenol A; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; PBDE, polybrominated diphenyl ether.

Viruses lay latent until something tips the immune system

Hashimoto's is a great example of a latent virus destroying a function over time. Epstein-Barr (EBV) is a virus that causes mononucleosis (also known as "mono" or "glandular fever" in the UK).

A 2015 Polish study found the Epstein-Barr virus in the thyroid cells of 80 percent of people with Hashimoto's and 62.5 percent of people with Graves'.

Specific immune cells known as CD8+T cells are needed to fight off the Epstein-Barr virus. However, some individuals may have a low baseline level of these types of immune cells.CD8+T cells decrease with age, are lower in women, and are also decreased when vitamin D intake is low.

When levels of these fighter cells are insufficient, the Epstein-Barr virus may take up residence in the thyroid and essentially hijack it to help the virus hide and multiply. Add poor Lifestyle, SAD diet, deficiencies and toxicity. It's the perfect storm.

Begin PAMP & DAMP!


Probiotics can enhance the antitumor immune response of CD8⁺T cells. It can play a synergis tic antitumor role. On the one hand, its mechanism is through regulating intestinal flora, and on the other hand, through regulating the antitu mor immune function of CD8⁺T cells.

Cell

L-Arginine Modulates T Cell Metabolism and Enhances Survival and Anti-tumor Activity

Graphical Abstract



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In Brief

Metabolomic and proteomic profiling unveil intracellular L-arginine as a cruc regulator of metabolic fitness, survival capacity, and anti-tumor activity of central memory T cells.

Regenology Pyramid



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Inflammation and Immune Modulation Protocols

- SPM
- CBD
- Xflame
- InFlam
- Turmeric Plus

They are called 'resolving mediators' because of their role in facilitating natural resolution of the inflammatory response.

Examples of SPMs include resolvins, lipoxins, protectins, and maresins.



Resolution of Inflammation



THE BODY'S ENDOCANNABINOID SYSTEM





Turmeric

Curcumin can also modulate the expression of genes involved in inflammation. It inhibits the activation of transcription factors such as nuclear factor-kappa B (NF- κ B), which regulates the expression of pro-inflammatory genes. By suppressing NF- κ B activation, curcumin reduces the production of inflammatory cytokines such as tumor necrosis factor-alpha (TNF- α), interleukin-1 beta (IL-1 β), and interleukin-6 (IL-6), which are key mediators of inflammation

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P53 Modulation and APOPTOSIS

EnerDMG Resveratrol EGCG – Pro Oranges Nutraglutide Quercetin Peptides

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You must balance blood sugar for OPTIMAL P53 Activation

• P53 can influence the expression of genes encoding glucose transporters (e.g., GLUT1) and enzymes involved in glycolysis (the breakdown of glucose), such as hexokinase and phosphofructokinase. By modulating the expression of these genes, P53 can affect the uptake and utilization of glucose by cells

• Dysregulation of P53 function is commonly observed in cancer and metabolic disorders, including diabetes and obesity. Altered glucose metabolism and insulin signaling pathways can impact P53 activity and expression, while aberrant P53 function may contribute to metabolic abnormalities and insulin resistance.



Cancer is a metabolic issue

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Peptides to learn about

PEA



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KPV

Specific Protocol to Educate and Eliminate

ImmuneBoost Probiotics (Super) Immunomax Peptides Nosodes - Specific

Gut Health

- GI COMPLETE sooths and cools digestive tract enhances integrity of the lining of GI tract
- PROBIOITICS Microbiota balance and proper signaling and defense against inflammatory pathogens
- IGG Modulation of immune response, neutralizes pathogens, supports gut barrier function, potential to manage food sensitivities.

Poor gut health is connected to chronic inflammation,

Neurological issues, metabolic syndrome and more



One offs to Consider

- PowerFuel
- CircuCore
- BCAAs



ATP Production



Proper AA metabolism



Vascular Integrity

.....

.....

Rebuild what has been damaged

Nutritional Frontiers Solutions

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Testing Beyond The Baseline



Inflammation Blood Panel

The most frequently used inflammatory markers include acute-phase proteins, essentially CRP, serum amyloid A, fibrinogen and procalcitonin, and cytokines, predominantly TNFα, interleukins 1β, 6, 8, 10 and 12 and their receptors and IFNγ.

- \$9.00 C-Reactive Protein (CRP), Quantitative (006627)
- \$7.00 Ferritin (004598)
- \$50.00 Fibrinogen Antigen (117052)
- \$50.00 Interleukin-06 (IL-6), Serum (140916)
- \$35.00 Tumor Necrosis Factor-a (140673)
- \$50.00 Interleukin-08 (IL-8), Serum (140918)
- \$50.00 Interleukin-10 (IL-10), Serum (140920)
- \$7.00 Sedimentation Rate, Modified Westergren (ESR) (005215)

EBV (always test Strep too!)

532	\$5.00	Complete Blood Count (CBC) With Differential (005009)
513	\$6.00	Antistreptolysin O (ASO) Antibodies (006031)
1105	\$16.00	Epstein-Barr Virus (EBV) Antibodies to Viral Capsid Antigen (VCA), IgM (096735)
5128	\$34.00	EBV-VCA and EA, IgG Antibody Profile (096255)
1054	\$36.00	Anti-DNase B (Streptococcal) Antibodies (096289)

MCAS Panel

Serum Tryptase: Tryptase is a marker of mast cell activation and is released into the bloodstream during mast cell degranulation. Measuring serum tryptase levels can help assess the extent of mast cell activation. However, it's important to note that tryptase levels may be normal or only transiently elevated in some individuals with MCAS, so a normal result does not necessarily rule out the diagnosis.

Histamine: Histamine is one of the primary mediators released by activated mast cells. Measuring histamine levels in the blood or urine may provide additional evidence of mast cell activation. However, histamine levels can fluctuate rapidly and may not always correlate with symptoms.

Prostaglandin D2 (PGD2): PGD2 is another mediator released by mast cells during activation. Elevated levels of PGD2 in the blood or urine may indicate mast cell activation and contribute to the diagnosis of MCAS.

N-Methylhistamine (NMH) and 11 β -Prostaglandin F2 α (PGF2 α)**: These are metabolites of histamine and PGD2, respectively, and their levels in urine can provide indirect evidence of mast cell activation.

Complete Blood Count (CBC): A CBC may reveal abnormalities such as eosinophilia (elevated eosinophil count), which can be associated with allergic or inflammatory conditions, including MCAS.

Inflammatory Markers: Tests such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) may be elevated in individuals with inflammatory conditions, although they are not specific to MCAS.

Specific IgE and IgG Testing: Allergy testing, including specific IgE and IgG testing for common allergens or triggers, may be helpful in identifying potential triggers for mast cell activation in some individuals.

Specialty Tests – Food Sensitivity

Gut Barrier Panel					
	lgG1-4+C3d	lgA1-2			
Candida	Negative	Negative			
Zonulin	Negative	Negative			
Occludin	Negative	Negative			
LPS	Positive	Negative			

KBMO or Blood Gut barrier panel

Serum – EBV – Current "Medical" Interpretation

VCA-IgM	VCA- IgG	EA-D, IgG	EBNA, IgG	Possible Interpretation
Negative	Negative	Negative	Negative	No infection, symptoms due to another cause, susceptible to EBV infection
Positive	Positive	Negative	Negative	Early, primary infection
Negative or positive	Positive	Positive	Negative	Active infection, though EA-D IgG may persist for life in about 20% of people
Negative	Positive	Negative	Positive	Past infection
Vegative	Positive	Positive	Positive	May indicate reactivation of virus



From the Newfoundland and Labrador Public Health Laboratory.

Figure 20. Shifts in EBV antibodies over time. Source: Newfoundland and Labrador Public Health Library Serum – EBV – the way you should look at it

- Each antibody has a different pattern of response time
- Some people are symptomatic with only on type of antibody flaring

Serum - Mold

Components:

M001-IgG Penicillium chrysogen M005-IgG Candida albican M009-IgG Fusarium proliferatum M207-IgG Aspergillus niger M003-IgG Aspergillus fumigatus M007-IgG Botrytis cinerea M011-IgG Rhizopus nigricans M002-IgG Cladosporium herbarum M006-IgG Alternaria alternata M008-IgG Setomelanomma rostart M012-IgG Aureobasidi pullulans M004-IgG Mucor racemosus M010-IgG Stemphylium herbarum M014-IgG Epicoccum purpur Mold testing generally refers to environmental testing (for the presence of mold in a home or building), while mycotoxin testing refers to tests that look at the presence or effects of mycotoxins in the body.

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Specialty Tests - Mycotoxins

- Mycotoxins are certain toxins that are naturally produced by mold and other kinds of fungi. Humans may be exposed to mycotoxins through the air in mold-affected buildings or homes and through certain kinds of foods.
- Mycotoxin exposure can lead to illness, the symptoms and severity of which vary significantly from person to person





GI Map

• The GI-MAP[®] includes pathogens (bacterial, parasitic and viral) commonly known to cause gastroenteritis

Specialty Test -Micronutrient

- Spectra Cell
- May need to partner with a clinic to do this test





Specialty Test - Neurotransmitter

ZRT Labs

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Serum – Vit D, Omega, Fasting Glucose, A1C

Vitamin D, 25-Hydroxy				
Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
 Vitamin D, 25-Hydroxy⁰¹ 27.0 Low Vitamin D deficiency has been defined by the Institute of Medicine and an Endocrine Society practice guideline as a level of serum 25-OH vitamin D less than 20 ng/mL (1,2). The Endocrine Society went on to further define vitamin D insufficiency as a level between 21 and 29 ng/mL (2). 1. IOM (Institute of Medicine). 2010. Dietary reference intakes for calcium and D. Washington DC: The National Academies Press. 2. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. JCEM. 2011 Jul; 96(7):1911-30. 				30.0-100.0
Magnesium				
Test	Current Result and Flag	Previous Result and Date	Units	Reference Interval
Magnesium ⁰¹	1.9		mg/dL	1.6-2.3

Serum – Vit D, Omega, Fasting Glucose, A1C

▼	Arachidonic Acid/EPA Ratio ⁰²	2.0	Low	20.4	06/29/2020		3.7-40.7
V	Omega-6/Omega-3 Ratio ⁰²	2.6	Low	11.1	06/29/2020		3.7-14.4
	Omega-3 total ⁰²	11.2		3.4	06/29/2020	% by wt	
	EPA ⁰²	4.1	High	0.5	06/29/2020	% by wt	0.2-2.3
	DPA ⁰²	1.8		0.9	06/29/2020	% by wt	0.8-1.8
	DHA ⁰²	5.3	High	2.0	06/29/2020	% by wt	1.4-5.1
	Omega-6 total ⁰²	29.4		37.6	06/29/2020	% by wt	
		Cleveland Heart with AA and LA	Lab measures the two	a number of om most abundant	ega-6 fatty acid forms reported.	S	
▼	Arachidonic Acid ⁰²	8.1	Low	10.2	06/29/2020	% by wt	8.6-15.6
	Linoleic Acid ⁰²	19.4		24.4	06/29/2020	% by wt	18.6-29.5
			• • • •				

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Serum – Vit D, Omega, Fasting Glucose, A1C

22 y/o F Insulin Labs: Normalized



The Tick-Borne Panel

Serum – Lyme and Co– Infections

Interpretation of the Western blot—More is not necessarily better.						
		lgG	lgG	IgM	IgM	
Band	Band importance	Ma et al.	CDC	Ma et al	CDC	
kDa		2 of 6	5 of 10	2 of 5	2 of 3	
18	Thought to be specific					
22	Thought to be specific					
23-25	OSP-C highly specific					
28	Notspecific					
30	Thought to be specific					
31	OSP-A highly specific					
34	OSP-B highly specific					
37	Thought to be specific					
39	Thought to be specific					
41	Non-specific flagella					
45	Non-specific					
58	Non-specific					
66	Non-specific					
73	Non-specific					
88	Thought to be specific					
93	Thought to be specific					
Engstrom found 2 of 5 bands to be highly sensitive and specific for Lyme disease						
(Engstrom 1995), while 46 of 66 symptomatic pediatric patients with a history of bulls						
eye rash and tick bite were negative by CDC criteria (Fawcett 1995 Rheumatology						
Symposia Abstract #1254.) The CDC criteria are intended only for surveillance						
purposes, not diagnosis. Many physicians interpret the Western blot based on the						
number and specificity of the patient's bands. See also (Ma et al. 1989).						

Specialty Tests – Diurnal Cortisol

- Saliva is easiest Collected at 4 points through the day
- Can do an am/pm
 - Miss the CAR
 - The change in cortisol concentration that occurs in the first hour after waking from sleep.
 - 50-100% rise 30 min after waking



Data from 15 studies with 104,623 salivary cortisol samples of 18,698 individuals by Miller et al in 'The Reference ranges and seasonal changes in diurnal salivary cortisol derived from a meta-data field studies', Psychoneuroendocrinology, Nov 2016, 73, pages 16-23.

Factors affecting Cortisol:

- The early morning cortisol is affected by several factors:
- The exact *time of collection* after waking up—levels are flat for first 15 minutes but then quickly change in next 30 to 60 minutes.
- Darkness or dim *light* or full exposure to sunlight after waking up—the peak levels are higher with more light.
- Season of the year—which again correlates to the amount of light; late sunrise time (in winter) gives higher levels in morning according to an <u>Australian study</u>.
- Increases with age; Women have a higher surge than men on average with CAR



Data from an Australian study of 27,569 serum samples collected over 13 years by Hadlow et al in 'The effects of season, daylight saving and time of sunrise on serum cortisol in a large population', Chronobiology International, 2014 vol. 31(2): pages 243–251 ©TraceyStroup, ND AI

Blood or Dutch



Accession # 00287454 Female Sample Report 123 A Street Sometown, CA 90266

Ordering Physician: Precision Analytical

DOB: 1976-01-01 **Age:** 42 **Gender:** Female



Last Menstrual Period:

2017-12-26 Collection Times: 2018-01-24 08:00AM 2018-01-24 10:00AM 2018-01-24 05:00PM 2018-01-24 11:00PM

Hormone Testing Summary


Continuous Glucose Monitor

Practitioner: https://join.theiahealth.ai/partners?r eferrer=traceystroupnd

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Signaling in the body

- All types of signaling in the body – Ligands transmit signals between cells (extra and intra cellular communication)
- Ligands interact with proteins
 - Paracrine other cells
 - Autocrine same cell
 - Neurotransmitter
 - Endocrine



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You are only as young as your immune system

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Questions

LAB RESOURCE: Evexia Diagnostics: https://www.evexiadiagnostics.com/

www.traceystroupnd.com



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