# ISI Symposium 2017

Immunology 101 Eric Serrano

#### THANK YOU

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# Definition

#### Two systems:

- 1. Innate
- 2. Humoral



#### Innate

- Born with it
- Consists of three parts:
  - 1. Cellular-macrophages
  - 2. Chemical-binding proteins, interleukins
  - 3. Physical Barrier-lining of intestine



#### umoral

ns

#### Adaptive immunity

#### Specialized cells



**Innate Immunity** 

(Rapid response)

Mast cell

yố T cell

Dendritic cell

Macrophage

Natural

killer cell

Adaptive Immunity

B cell

(Slow response)

ytokine	Source	Biologic Activities (Selected)
terleukin-2	T lymphocytes	T-cell growth factor
	(TH0 and TH1 subtypes)	Induction of cytokines
terferon- $\gamma$	T lymphocytes	Antiviral activity
	(TH1 subtype)	Activation of macrophages
	Natural killer cells	Regulation of lymphokine secretion
terleukin-4	T lymphocytes	T-cell growth factor
	(TH2 subtype)	Enhancement of immunoglobulin production
		Suppression of cytokine production by monocytes
terleukin-5	T lymphocytes (TH2 subtype)	Induction of eosinophilia
terleukin-1	Monocytes or macrophages	T-cell costimulatory activity
	Endothelial cells	Endogenous pyrogen, proinflammatory activity, fibroblast proliferation
terleukin-6	Monocytes or macrophages	Induction of acute-phase response
	Fibroblasts	Enhancement of antibody production
	Endothelial cells	
	(? human T and B cells)	
ranulocyte-macrophage-colony	Macrophages	Growth, differentiation, and survival factor for
stimulating factor	T lymphocytes	hematopoietic progenitor cells
_	Fibroblasts	Monocyte and granulocyte activation
	Endothelial cells	Chemoattractant
mor necrosis factor- $\alpha$	Monocytes or macrophages	Proinflammatory effects
	T lymphocytes	Mediator of endotoxin-induced shock
		Host response to bacteria
		Regulation of lymphocyte function
ansforming growth factor- $\beta$ 1	Lymphocytes	Suppression of lymphocyte growth
	Monocytes or macrophages	Regulation of extra-cellular matrix
	Fibroblasts	Regulation of tissue repair and wound healing
	Endothelial cells	

#### ppendix. Glossary of Cytokines\*

\* Cytokines are essentially the polypeptide hormones of the immune system. In general, they can be produced by more than one cell type and their nctional profile is pleiotropic. This glossary summarizes the sources and biological activities of cytokines relevant to this study.

#### Cells

- Control adaptive response
- Many
- Best understood Th<sub>1</sub> & Th<sub>2</sub>
- Now Th<sub>17</sub> & Th<sub>reg</sub>





#### ells use Special Receptors for recognition

- Epitopes-processed antigenic portions
- MHC I-II-proteins in the membrane that present epitopes
- HLA-human leukocyte antigen-MHC in humans
- Most famous- HLA-DQ<sub>2</sub> & HLA-DQ<sub>8</sub>
- celiac disease



Antigen presentation by Immense Immunology Insight



Th<sub>1</sub>- secretes IF (interferon gamma)

TNF-alpha (Tumor Necrosis)

Beneficial Vs. virus vs bacteria

Auto Immune

► Th<sub>2</sub> - secretes cytokines, related to allergies

Upregulates B cell production of antibodies

Th<sub>17</sub> – activates neutrophils

# Mitochondrial

- Innate immune system is triggered by a host Pattern Recognition Receptor (PRR) expressed within Macrophages, and other tissues
- Mitochondrial plays an important role in regulating PRR
- Mitochondrial receptors RLR (like Rig-1-like receptor) or Toll like receptors (TLR)
- Dependent on vitamin D



# Mitochondrial support affected by...

- Micronutrient- Alpha Lipoic acid, NAC, Carnitine, Zinc\*
  \*virtually all WBC activity is dependent upon
- 2. Macronutrient- sugars
- 3. Exercise
- 4. HPA axis (stress)- DHEA- 200mg
- 5. Circadian rhythm
- 6. Environment
  - Lactobacillus, Bifidobacterium specifically L. Rhamnosus or L. Reuteri (decrease eczema)
  - Lead, Organochlorine
  - Garlic extract in vitro prevents mercury immune dysfunction

# Pattern Recognition Receptors (PRR) can be affected by...

- 1. Resveratrol
- 2. EGCC
- 3. Quercetin
- 4. Chrysin
- 5. Curcumin
- 6. Feverfew





#### GI & Immune FX

- Physical barrier
- **GALT-** Peyers Patches
- Dendritic cells (antigen presenting)
- M cells- special gut epithelial cells
- controlled passage of antigens
- lgA
- Bacteria





# 4 **R's**

- 1. Remove
- 2. Repair
- 3. Replace
- 4. Re-inoculate



# Anti-inflammatory herbs

- 1. Curcumin
- 2. Devils claw
- 3. Quercetin
- 4. Boswellic acid
- 5. Ginger root
- 6. Bromelain
- 7. Licorice root



# **GI-Specific Nutrients**

- 1. Glutamine
- 2. N-acetyl glucosamine
- 3. Butyrate
- 4. Fiber



# utoimmunity

- 1. Higher percent in women
- 2. Similar pathophysiology
- 3. Genetic predisposition
- Common environmental triggers
- 5. Clustering
- 6. Relapse/Recovery

Rare Monogenic Autoinflammatory Diseases	FMF (Familial Med. Fever), TRAPS (TNF Receptor-Assoc. Periodic Syndrome), HI Blau Syndrome (uveitis)
Polygenic Autoinflammatory Diseases	Crohn's disease, Ulcerative colitis Degenerative diseases, e.g. osteoarthritis Gout/Pseudogout/other crystal arthropathies Some categories of reactive arthritis and Psoriasis/psoriatic arthritis (no MHC a Self-limitinginflammatory arthritis including diseases clinically presenting as Storage diseases/congenital diseases with associated tissue inflammation Non-antibody associated vasculitis including giant cell and Takayasu arteritis Idiopathic uveitis Acne and acneform associated diseases Some neurological diseases, e.g. acute disseminated encephalomyelitis Erythema nodosum associated disease, including sarcoidosis
<b>Mixed Pattern Diseases</b> with evidence of acquired component (MHC class I associations) and autoinflammatory components	Ankylosing spondylitis Reactive arthritis Psoriasis/psoriatic arthritis Behcet's Syndrome Uveitis (HLA-B27 associated)
Classic Polygenic Autoimmune Diseases (organ specific and non-specific)	Rheumatoid arthritis Autoimmune uveitis (sympathetic opthalmia) Celiac disease Primary biliary cirrhosis Autoimmune gastritis/pernicious anaemia Autoimmune thyroid disease Addison's disease Pemphigus, pemphigoid, vitiligo Myasthenia gravis Dermatomyositis, polymyositis, scleroderma Goodpasture syndrome ANCA associated vasculitis Type 1 diabetes Sjögren syndrome Systematic lupus erythematosus
Rare Monogenic Autoimmune Diseases	ALPS- Autoimmune lymphoproliferative syndrome IPEX- Immune polyendocrinopathy X-linked APECED- Autoimmune polyendocrinopathy-candidiasis-ectodermaldystrophy

AUTOINFLAMMATOR)



# nmune Support Through Lifestyle

- 1. Diet & Nutrition
- 2. Physical activity
- 3. Stress modification
- 4. Circulation Rhythm
- 5. Environmental Control
- 6. Hygiene Habits

# iet

- 1. Increase signal to calorie ration, diversity
- 2. Avoid inflammatory foods
- 3. Low Glycemic Index
- 4. Avoid known allergens
- 5. Reduce toxic burden
- 6. Adequate Alpha Linolenic acid & omega 3
- 7. Hydration
- 8. Fermented foods



# icronutrients

- . Vitamin A-10,000
- . Vitamin C-2 grams
- . Vitamin D-5,000 IU's
- . Zinc-50 mg
- . Vitamin E-400-800 IU's
- . NAC- 200mg
- . Lipoic acid-400mg





#### ircadian Rhythm

- Sleep- most important
- Circadian disruptorsinfection, inflammation, pain, work

MELATONIN



# Melatonin





#### Menstrual Cycle



### nvironmental

- Sun light
- Toxic exposure
- EMF (electromagnetic fields)
- Outdoors



#### Hygiene

- Oral/chewing
- Foodborne- chicken, fish, beef, pork

Friendship

The meaning of life is to find your gift. The purpose of life is to give it away.

- Pablo Picasso

## Testing

- Allergy: IGG, IGE, Compliment
- Anti-gliadin, Anti-transglutaminase
- Anti-endomysial
- ► HLA DQ<sub>2</sub>, HLA DQ<sub>8</sub>
- TPO, Anti TSH (TSI), RF, AACA, Anti-CCP
- CRP, RF, Ferritin, IL-6, ESR
- Inflammatory markers





Specific autoantibo	dies with their antigenic determinant	t and clinical disease associations
toantibody	Antigenic determinant	Clinical associations
ti-dsDNA	dsDNA	High specificity for SLE often correlates wire active severe disease
ti-extractable nuclear tigens Anti-Sm Anti- RNP	Smith Proteins containing UI-RNA	High specificity for SLE MCTD (mixed connective tissue disease), SI RA, scleroderma, Sjögren syndrome
ti-SSA (Ro)	RNPs	Sjögren syndrome, SLE (subacute cutaneou lupus), neonatal lupus
ti-SSB (La)	RNPs	Sjögren syndrome, SLE, neonatal SLE
ticentromere	Centromere/kinetochore region of chromosome	Limited scleroderma, pulmonary hypertension, primary biliary cirrhosis
ti-Scl 70	DNA topoisomerase I	Diffuse scleroderma
ti-Jo-1 (anti-synthetase tibodies)	Histidyl tRNA synthetase (other tRNA synthetases)	Inflammatory myopathies with interstitial l disease, fever and arthritis
ti-SRP	Antibody to signal recognition protein	Inflammatory myopathies with poor progno
ti-PM/Scl	Antibody to nucleolar granular component	PM/scleroderma overlap syndrome
ti-Mi-2	Antibodies to a nucleolar antigen of unknown function	DM

#### educing/Repairing Immune System

- Diet-depending tests
- Fish oils
- GLA
- Smoking
- Enzymes
- Curcumin
- Quercetin-inhibits COX<sub>2</sub>, 5LOX
- Boswellia-inhibits COX<sub>2</sub> (1000mg/ day)
- Coffeic acid phenethyl ester-from propolis

- 10. Skull cap (scutellaria baicalensis)
- 11. Ginger
- 12. Devil's claw
- 13. Cat's claw
- 14. Nettles (urtica dioica)
- 15. Feverfew
- 16. Butterbur
- 17. Zinc
- 18. Selenium



#### Butterbur

- Antispasmodic effects on smooth muscle and vascular walls
- Anti-inflammatory: inhibits leukotriene synthesis
- Decrease histamines and leukotrienes
- Decrease priming of mast cells in response to allergens
- Many ingredients- volatile oils, flavinoids, tannins
- Petasine & isopetasine- 8mgms

#### Butterbur

- Safe for use in adults and children > 6y.o
- Be sure extract is free of phrrolizidine alkaloid (PA's)
- Which are hepatotoxic and veno-occlusive
- Avoid in pts on other hepatotoxic drugs or herbs, or products that induce the cytochrome P450 or 3A4 (CYP3A4)

#### Whole root extract

- Decreased both nasal symptoms & nasal inflammatory mediators in pts with allergic rhinitis.
- Reduce response to AMP challenge in patients with allergic rhinitis.

## Allergic Responses

- Sinusitis
- Runny nose
- Bloat
- ADHD
- Joint pain
- Insomnia

# GE

#### Mast cell

- ► Histamine
- $\blacktriangleright$  Th<sub>2</sub>



#### Prevention Treatment

- 1. Avoid
- 2. Drug Therapies
- 3. Immune therapy
- 4. Fish oils
- 5. Probiotics:
  - Alive or dead
  - If pollen: Lactobacillus paracasei
  - L.Casei & Bifidobacterium
  - ►  $Th_2 \downarrow$

- 6. Quercitin-400mg TID
- Butterbur-(petasites) extra Ze 339 (32mg)
- Stinging Nettles-(Urtica Dioica) 100mg
- 9. Tinospora Cordiofolia- 220mg
- 10. MSM (2600)
- 11. Apple polyphenol
- 12. Gingko Biloba

## Tinospora Cordiofolia

- Immunostimulatory effects seen in both water & alcohol extracts-alpha-glucan polysaccharide in-vitro:
  - Activates NK cells, T cells, and B cells
  - Induces prdn of 11-1, 6, 12, 18, interferon-gamma, TNFalpha & MCP-1
- 300 mgms TID x 8 wks decreased sneezing, nasal discharge and osbn compared to placebo

## Quercitin

- Bioflavinoid made from skin of apples and onions
- Anti-inflammatory effects stabilize mast cells



#### Omega 6-Plant based

- Babies with eczema-elevated linoleic acid.
- Error in metabolism of EFA's
- Many studies indicate GLA (Evening Primrose Oil) supplementation shifts profile to anti-inflammatory
  - stimulates c-AMP
  - inhibits phospholipase
  - suppress leukotriene production
  - suppress IL, 2 production

Some  $\alpha$ -Linolenic Acid Deficiency Symptoms

- Weakness
- Edema
- Sticky platelets
- Neuro-behavioral changes
- Tissue inflammation



## Bee Pollen & Propolis

- Produced by anthers of flowering plants, gathered by bees
- Acts as binding substance for beehives
- Reduce inflammatory response from histamines
- Local is best

# Ginger Root

Inhibits leukotrienes

# **Stinging Nettles**

- Preliminary evidence that stinging nettle above ground parts may improve symptoms of allergic rhinitis
- Starting stinging nettle at first sign of symptoms
- Can be made as tea

# atural Immune Modulating Agents

- Echinacea- purpurea,
- angustifolia, pullida, Th<sub>2</sub>, Th<sub>1</sub> **,** IgA
- Andrographis paniculata
- Arabinogalactan-fiber, 4gm
- Elderberry (Sambucus Nigra)-Juice, syrup
- Astragalus
- Pau D'Arco
- Berberine
- Olive leaf extract

- 9. Mushroom extract-250mg/day
- 10. Colostrum GCX10
- 11. Lactoferrin
- 12. Probiotics
  - Bifido bacterium- most abundant
  - Streptococcus Salivarius
  - Streptococcus Thermophiles
  - Spore forming- Bacillus subtilis
  - Yeast Probiotics-boulardii



