Peptides for Autoimmune diseases

Dr. Luis Martinez
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Objectives

DESCRIBE IMMUNE DYSREGULATION IN AUTOIMMUNE DISEASES

DISCUSS MECHANISMS OF ACTION FOR IMMUNE MODULATION AS EXERTED BY MULTIPLE PEPTIDES

DISCUSS CASES AND PROTOCOLS FOR INCORPORATING PEPTIDES IN THE MANAGEMENT OF IMMUNE DISEASES.

Autoimmune disease statistics

50 million Americans with ADs

80-100 different autoimmune diseases identified with evidence suggesting 40 more

ADs share close genetic relationships

Common immunosuppressants lead to marked side effects

New treatment options are required to address ADs

Autoimmune Disorders- affected systems

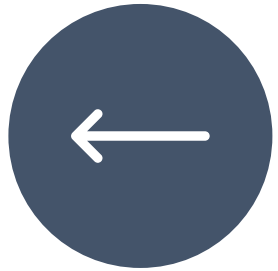
- Thyroid: Graves disease, Hashimoto's
- Bones: Rheumatoid arthritis, ankylosing spondylitis
- Brain/Nervous system: MS, ALS, GBS
- Gastrointestinal system: Crohn's disease, Ulcerative colitis
- Skin: Vitiligo, psoriasis

Peptides and ADs

CAN MODULATE IMMUNE SYSTEM

INCREASED TREGS

TH1-TH2 SHIFTS



CYTOKINE MODULATION

Peptide based immunotherapy

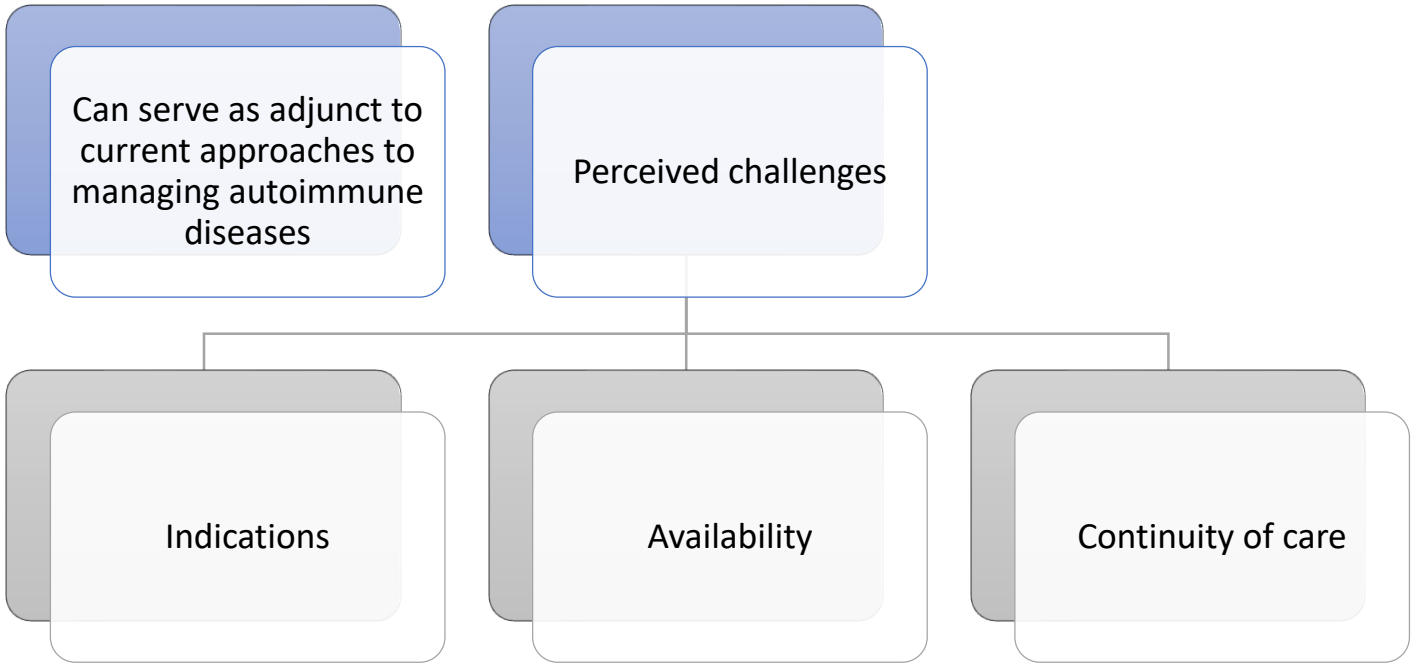
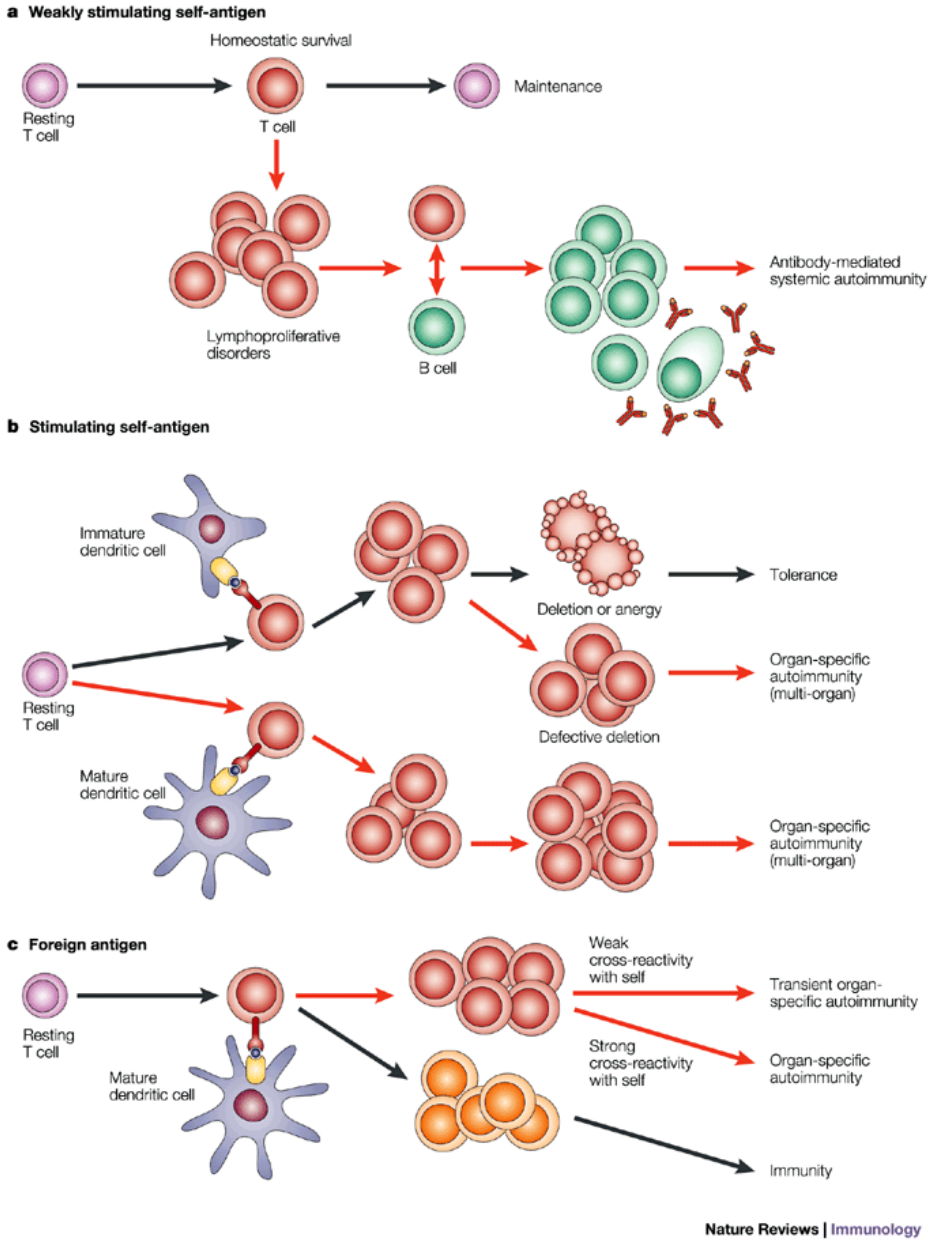


Table 1 Types of regulatory T cells involved in immune tolerance: phenotype, function and origin

Treg cell type	Origin	Phenotype	Suppressive mechanism
Natural Treg cells	Thymus	CD4 $CD25^{high}$ $FoxP3^{+}$ $GITR^{+}$ $CTLA4^{high}$ $CD45RB^{low}$ $CD127^{low}$	Cell-contact (CTLA4) dependent (most studies) and IL10/TGFβ1 (in vivo studies)
Expanded natural Treg cells	Expansion of natural Treg cells in periphery	CD4 $CD25^{high}$ $FoxP3^{+}$ $CD69^{+}$	Cell-contact (CTLA4) dependent
Th3 cells	Periphery	CD4 $FoxP3^{+/-}$	TGFβ1
Induced Treg cells	Generation and/or expansion of non-regulatory CD4 T cells	CD4 $CD25^{high}$ $FoxP3^{+}$ $GITR^{+}$ $CTLA4^{high}$ $CD45RB^{low}$	Cell-contact (CTLA4) dependent and in some cases TGFβ1
Tr1 cells	Induced by tolerogenic DCs in the periphery	CD4 $CD25^{+}FoxP3^{+/-}$	IL10 and/or TGFβ1
CD8 Treg cells	Induced by tolerogenic DCs in the periphery	CD8 $CD28^{+/-}$	IL10, cell-contact dependent, ILT3 and ILT4

For simplicity, a consensus of the most widely accepted characteristic of Treg cells is shown.
CTLA4, cytotoxic T-lymphocyte antigen 4; DCs, dendritic cells; GITR, glucocorticoid-induced tumour necrosis factor receptor-related protein; ILT, immunoglobulin-like transcript; TGFβ1, transforming growth factor β1; Tr1, T regulatory 1.

Key Concepts in Autoimmunity



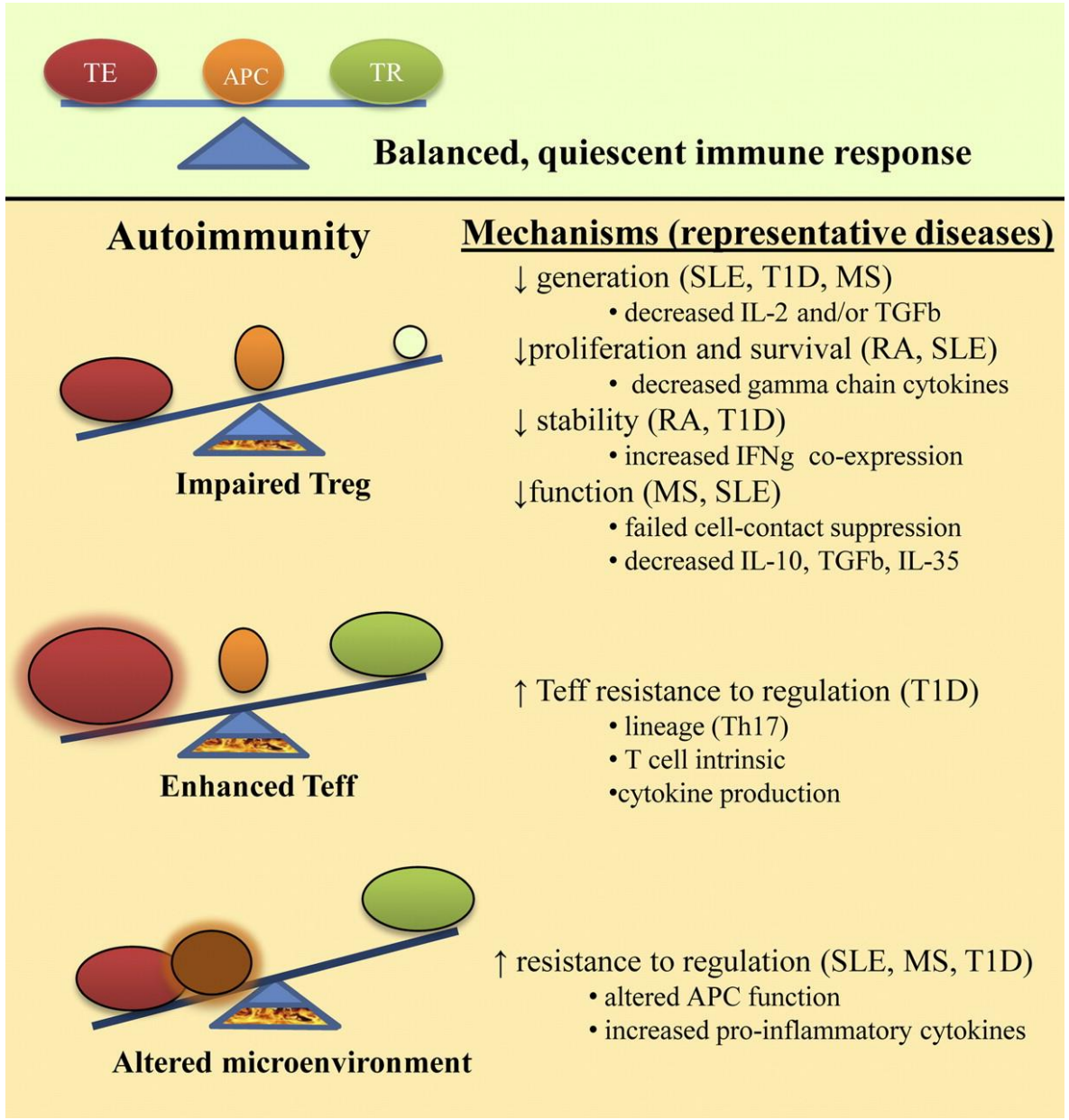
Self vs Non Self

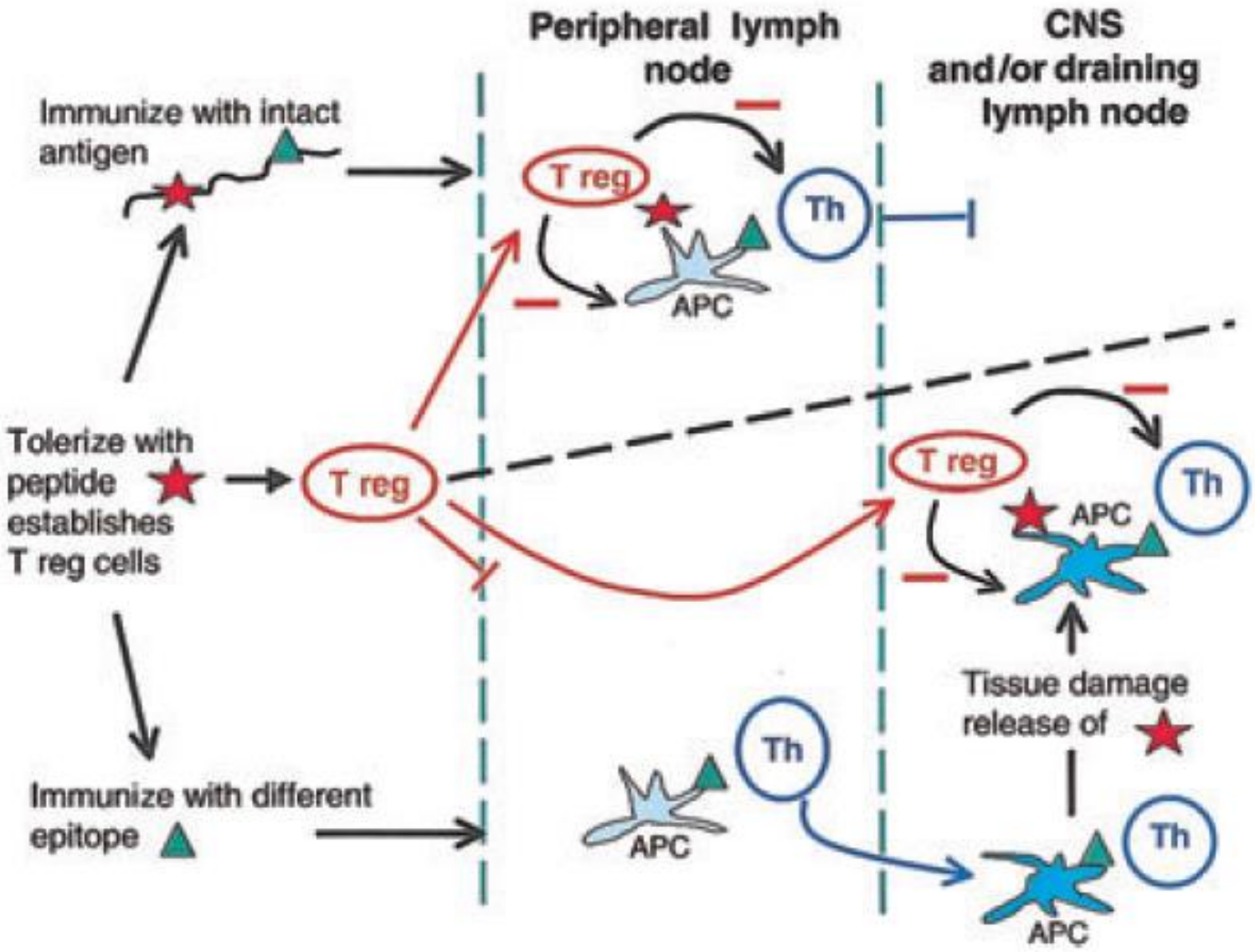
Antigens Identification

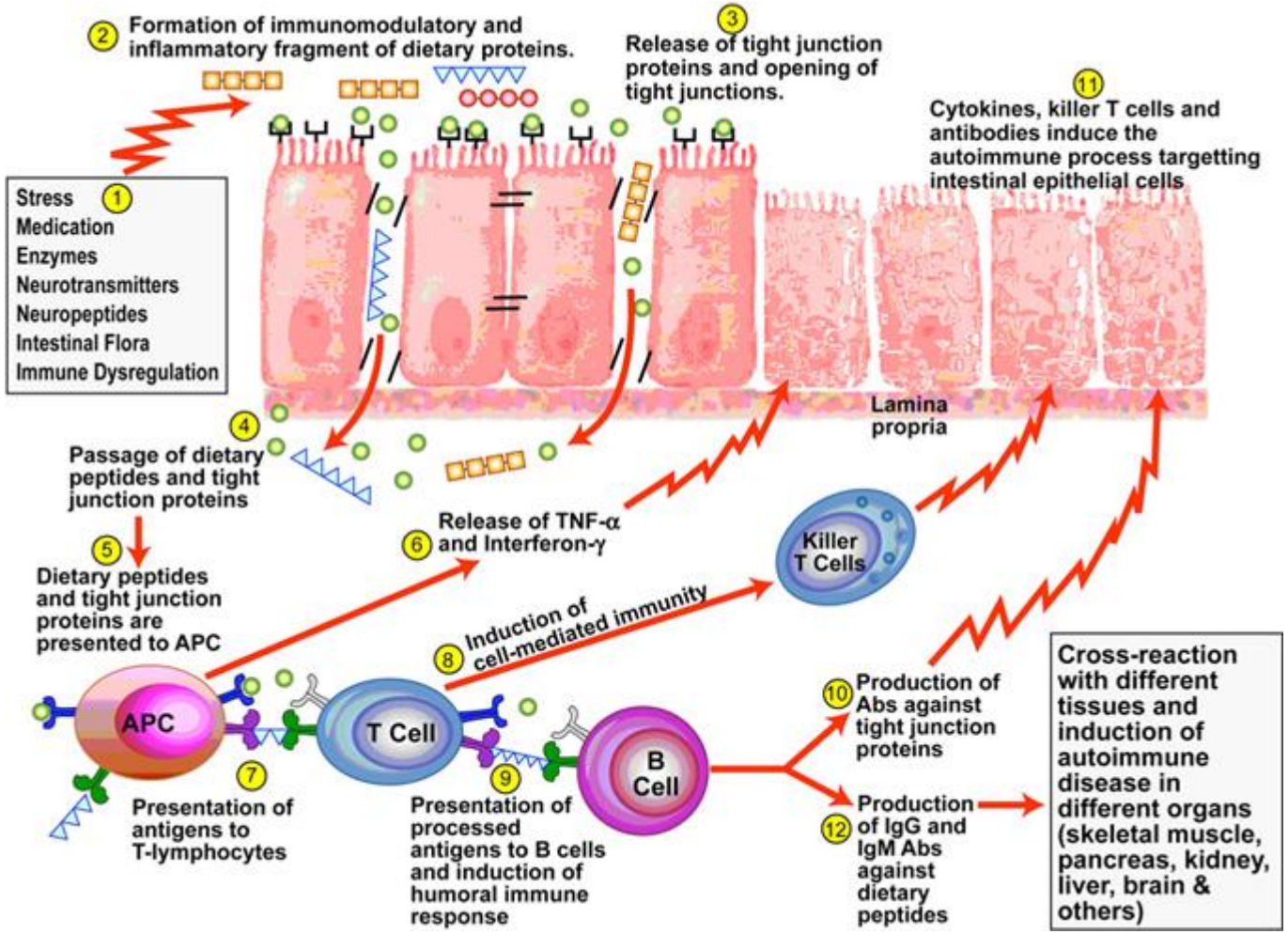
http://drugline.org/img/term/autoimmunity-1507_1.gif

TE vs TR

It is all in the balance




Peripheral lymph node
CNS and/or draining lymph node
Immunize with intact antigen
T reg
Th
APC
Tolerize with peptide establishes T reg cells
T reg
T reg
Th
APC
Tissue damage release of
Immunize with different epitope
Th
APC
Th
APC



Leaky gut and autoimmunity

Is it all in the gut?

http://sanjosefuncmed.com/wp-content/uploads/2013/05/pathogenesis-leaky-gut-autoimmune-connection.jpg

Central Tolerance

The regulatory environment

Tolerance and Autoimmunity

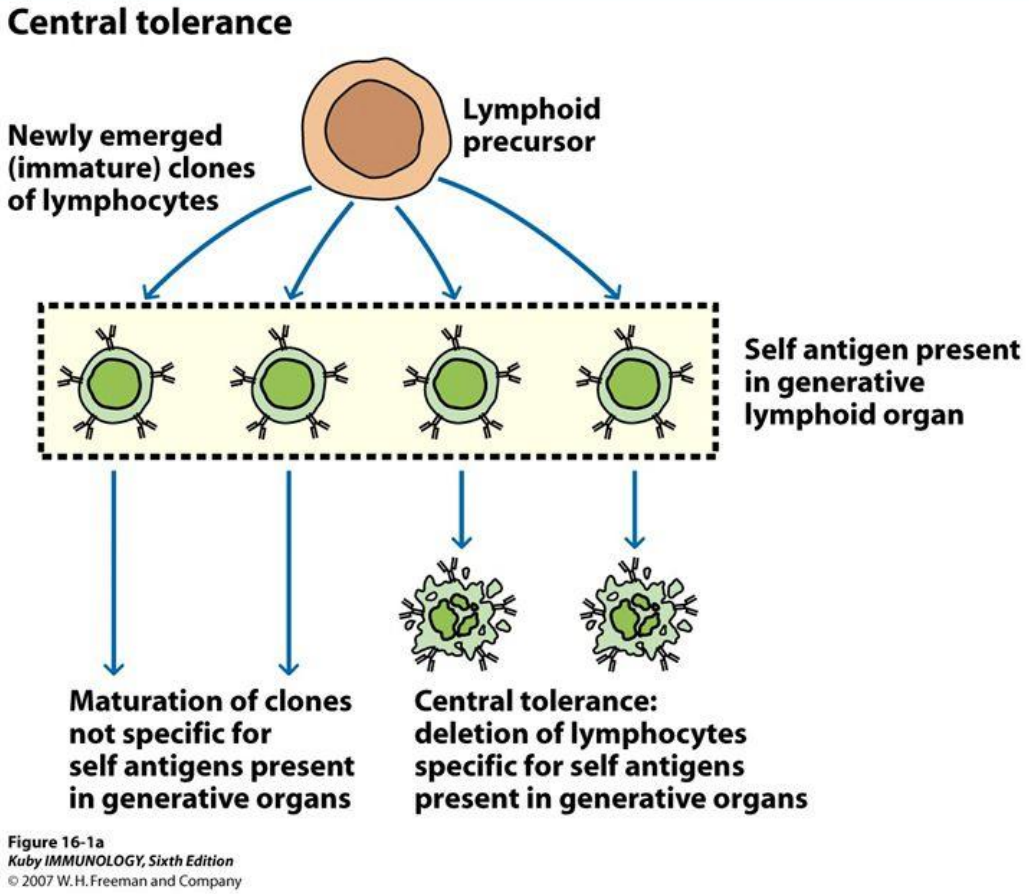
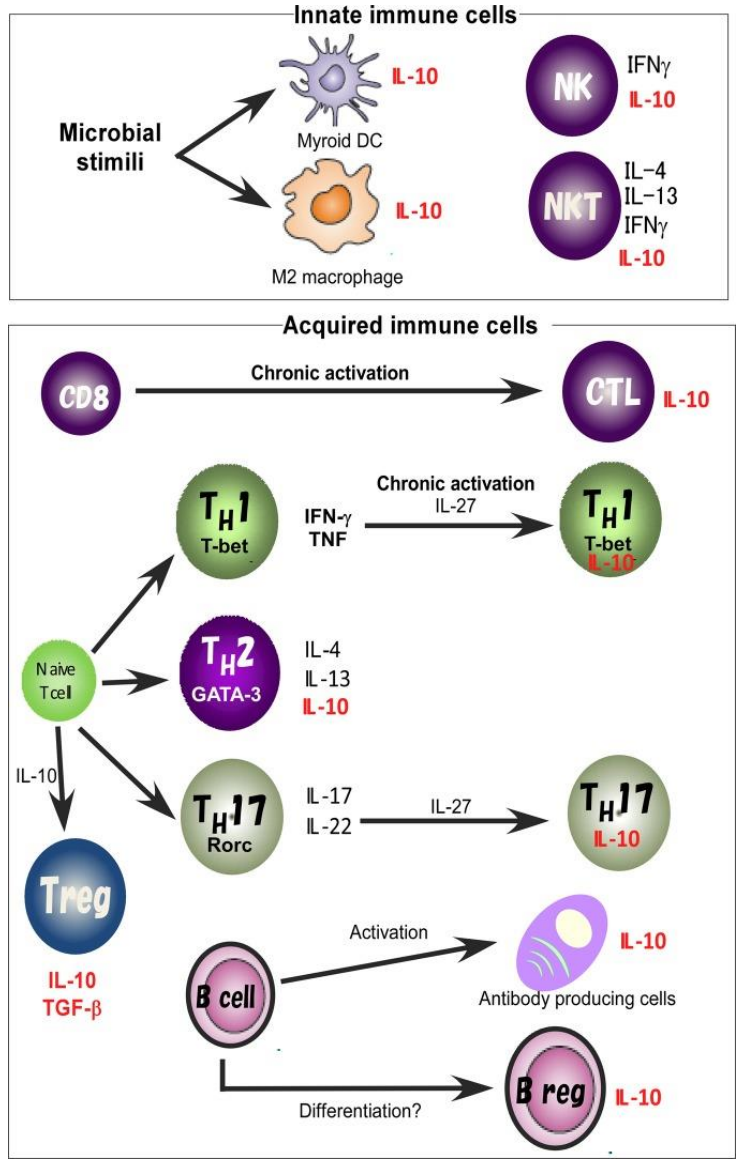
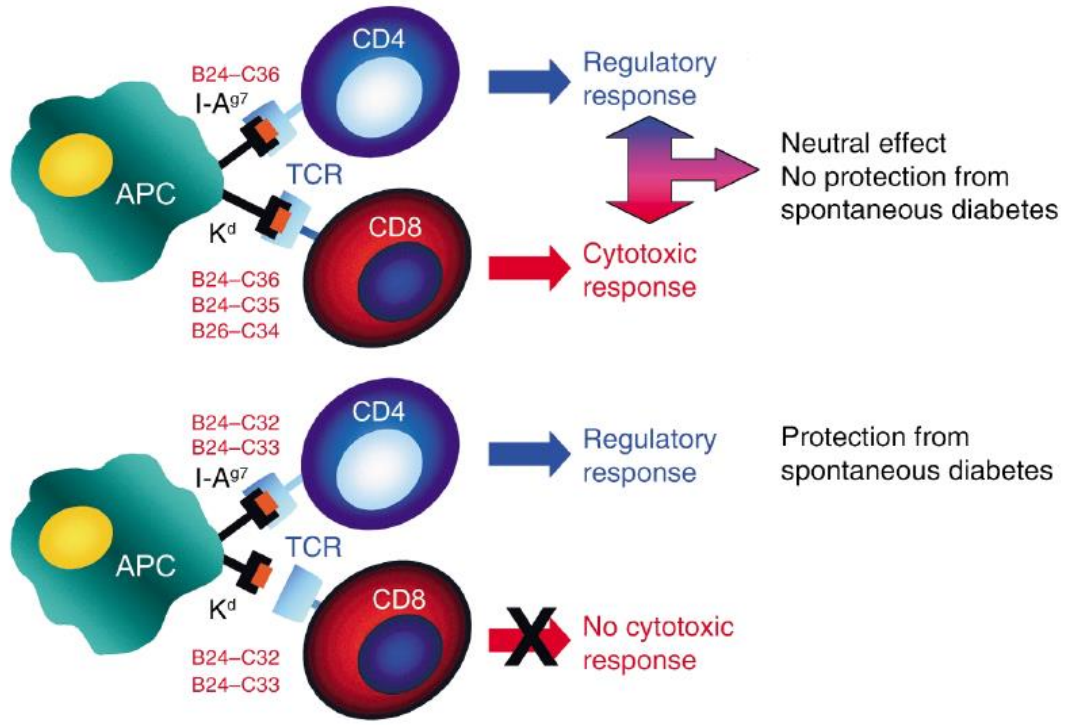


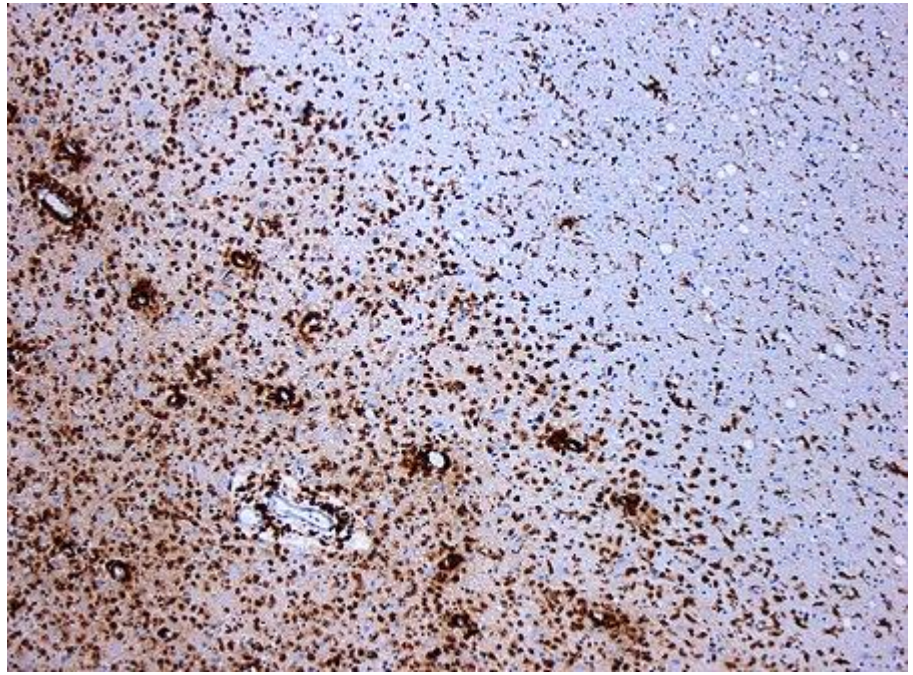
Figure 16-1a
Kuby IMMUNOLOGY, Sixth Edition
© 2007 W.H. Freeman and Company


Innate immune cells
Microbial stimili
IL-10
Myroid DC
IL-10
M2 macrophage
NK
IFNγ
IL-10
NKT
IL-4
IL-13
IFNγ
IL-10
Acquired immune cells
CD8
Chronic activation
CTL
IL-10
TH1
T-bet
IFN-γ
TNF
Chronic activation
IL-27
TH1
T-bet
IL-10
Naive Tcell
TH2
GATA-3
IL-4
IL-13
IL-10
IL-10
TH17
Rorc
IL-17
IL-22
IL-27
TH17
IL-10
Treg
IL-10
TGF-β
Activation
B cell
IL-10
Antibody producing cells
Differentiation?
B reg
IL-10


CD4
B24–C36
I-Ag7
APC
TCR
Kd
CD8
B24–C36
B24–C35
B26–C34
Regulatory response
Cytotoxic response
Neutral effect
No protection from spontaneous diabetes
CD4
B24–C32
B24–C33
I-Ag7
APC
TCR
Kd
CD8
B24–C32
B24–C33
Regulatory response
No cytotoxic response
Protection from spontaneous diabetes

Multiple Sclerosis

- Demyelinating disease
- Affects brain and spinal cord
- T cells penetrate BBB
- Initiate myelin attack
- Autoreactive lymphocytes
- Treatment options limited



Demyelination by MS. The CD68 colored tissue shows several macrophages in the area of the lesion

The Peptides

Opioid Growth Factor (OGF)

- Opioid Growth Factor (OGF) known as Metkephalin (Met5)
- Endogenous pentapepide
- OGF activates a specific receptor called Opioid Growth Factor receptor (OGFr or ζ-opioid receptor).
- OGF and OGFr axis regulates cell growth in normal and abnormal cells

OGF and Immunity

OGF blocks release of proinflammatory cytokines including Interleukins IL6 and IL12, TNFα, NF-κB (nuclear factor kappa light chain enhancer of activated B cells)

Can alter T and B lymphocyte production

Modulates immune response TH2/TH1

Biphasic response

Increased regulatory T cells

Brain Res. 2012 Sep 7;1472:138-48. doi: 10.1016/j.brainres.2012.07.006. Epub 2012 Jul 20.

Opioid growth factor arrests the progression of clinical disease and spinal cord pathology in established experimental autoimmune encephalomyelitis.

Campbell AM[1], Zagon IS, McLaughlin PJ.

Author information

Abstract

An endogenous neuropeptide, opioid growth factor (OGF), chemically termed [Met(5)]-enkephalin, arrested the progression of established disease in a mouse model of multiple sclerosis (MS) called experimental autoimmune encephalomyelitis (EAE). This study treated mice who demonstrated 2 consecutive days of behavioral decline following injections of myelin oligodendrocyte glycoprotein (MOG) with daily injections of OGF (10mg/kg) or saline (0.1ml) for 40 days. Within 6 days of OGF treatment, mice initially demonstrating clinical signs of EAE had significant reductions (45% reduction) in their behavioral scores relative to EAE mice receiving saline. Behavior was attenuated for the entire 40-day period with mice receiving OGF showing only limp tails and wobbly gait in comparison to saline-treated EAE mice who displayed paralysis of one or more limbs. Neuropathological studies revealed that OGF treatment initiated after the appearance of disease reduced the number of activated astrocytes and damaged neurons, decreased demyelination, and inhibited T cell proliferation. These results demonstrate that OGF can halt the progression of established EAE, return aberrant pain sensitivity to normal levels, inhibit proliferation of T cells and astrocytes, and prevent further spinal cord pathology. The data extend our observations that OGF given at the time of disease induction prevented disease onset, reduced the severity of clinical signs of disease, and reversed neurological deficits in a non-toxic manner. Our data substantiate the role of the OGF-OGFr axis in EAE and support the use of OGF as a biotherapy for MS.

Exp Biol Med (Maywood). 2017 Sep;242(15):1524-1533. doi: 10.1177/1535370217724791. Epub 2017 Aug 2.
Featured Article: Serum [Met5]-enkephalin levels are reduced in multiple sclerosis and restored by low-dose naltrexone.
Ludwig MD1, Zagon IS1, McLaughlin PJ1.
Author information
Abstract

Low-dose naltrexone is a widely used off-label therapeutic prescribed for a variety of immune-related disorders. The mechanism underlying low-dose naltrexone's efficacy for fatigue, Crohn's disease, fibromyalgia, and multiple sclerosis is, in part, intermittent blockade of opioid receptors followed by upregulation of endogenous opioids. Short, intermittent blockade by naltrexone specifically blocks the opioid growth factor receptor resulting in biofeedback events that increase production of the endogenous opioid growth factor (OGF) (chemically termed [Met5]-enkephalin) facilitating interactions between opioid growth factor and opioid growth factor receptor that ultimately, result in inhibited cell proliferation. Preclinical studies have reported that enkephalin levels are deficient in animal models of experimental autoimmune encephalomyelitis, a mouse model of multiple sclerosis. Our hypothesis is that serum enkephalin levels are diminished in humans with multiple sclerosis and experimental autoimmune encephalomyelitis mice, and that change in serum opioid growth factor levels may serve as a reasonable candidate biomarker for the onset of experimental autoimmune encephalomyelitis and response to therapy. To address this, we designed a two-part study to measure endogenous opioids in multiple sclerosis patients, and to investigate the temporal pattern of decline in serum enkephalin concentrations in mice with chronic progressive experimental autoimmune encephalomyelitis and treated with low-dose naltrexone. For comparison, we investigated whether low-dose naltrexone exposure in normal mice also resulted in altered enkephalin levels. In both animal models, we monitored tactile and heat sensitivity, as well as differential white blood cell counts as indicators of inflammation. Serum [Met5]-enkephalin levels were lower in humans with multiple sclerosis relative to non-multiple sclerosis patients, and low-dose naltrexone restored their levels. In experimental autoimmune encephalomyelitis mice, [Met5]-enkephalin levels were depressed prior to the appearance of clinical disease, and were restored with low-dose naltrexone treatment. Low-dose naltrexone therapy had no effect on serum [Met5]-enkephalin or β-endorphin in normal mice. Thus, [Met5]-enkephalin (i.e. opioid growth factor) may be a reasonable candidate biomarker for multiple sclerosis, and may signal new pathways for treatment of autoimmune disorders. Impact statement This report presents human and animal data identifying a novel biomarker for the onset and progression of multiple sclerosis (MS**). Humans diagnosed with MS have reduced serum levels of OGF (i.e. [Met5]-enkephalin) relative to non-MS neurologic patients, and low-dose naltrexone (LDN) therapy restored their enkephalin levels**. Serum OGF levels were reduced in mice immunized with MOG35-55 prior to any clinical behavioral sign of experimental autoimmune encephalomyelitis, and LDN therapy restored their serum OGF levels. β-endorphin concentrations were not altered by LDN in humans or mice. Thus, blood levels of OGF may serve as a new, selective biomarker for the progression of MS, as well as response to therapy.

Thymosin Alpha 1 (TA-1)

- Endogenous human peptide
- Derived from prothymosin
- 28 aa fragment
- Helps restore immune function (remember thymic involution and aging)
- Enhances cell mediated immunity
- Increases efficiency of antigen presenting cells

Mult Scler. 2018 Feb;24(2):127-139. doi: 10.1177/1352458517695892. Epub 2017 Feb 1.

Thymosin-α1 expands deficient IL-10-producing regulatory B cell subsets in relapsing-remitting multiple sclerosis patients.

Giacomini E[1], Rizzo F[1], Etna MP[1], Cruciani M[1], Mechelli R[2], Buscarinu MC[2], Pica F[3], D'Agostini C[4], Salvetti M[2], Coccia EM[1], Severa M[1].

Author information

Abstract

BACKGROUND:

B cells are key pathogenic effectors in multiple sclerosis (MS) and several therapies have been designed to restrain B cell abnormalities by directly targeting this lymphocyte population.

OBJECTIVES:

Moving from our data showing a Toll-like receptor (TLR)7-driven dysregulation of B cell response in relapsing-remitting multiple sclerosis (RRMS) and having found a low serum level of Thymosin-α1 (Tα1) in patients, we investigated whether the addition of this molecule to peripheral blood mononuclear cells (PBMCs) would influence the expansion of regulatory B cell subsets, known to dampen autoimmune inflammation.

METHODS:

Serum Tα1 level was measured by enzyme immunoassay. Cytokine expression was evaluated by Cytometric Bead Array (CBA), enzyme-linked immunosorbent assay (ELISA), and real-time reverse transcription polymerase chain reaction (RT-PCR). B cell subsets were analyzed by flow cytometry.

RESULTS:

Tα1 pre-treatment induces an anti-inflammatory status in TLR7-stimulated RRMS PBMC cultures, reducing the secretion of pro-inflammatory interleukin (IL)-6, IL-8, and IL-1β while significantly increasing the regulatory IL-10 and IL-35. Indeed, Tα1 treatment enhanced expansion of $CD19^{+}CD24^{+}CD38^{hi}$ transitional-immature and $CD24^{low/neg}CD38^{hi}$ plasmablast-like regulatory B cell subsets, which likely inhibit both interferon (IFN)-γ and IL-17 production.

CONCLUSION:

Our study reveals a deficient ability of B cells from MS patients to differentiate into regulatory subsets and unveils a novel anti-inflammatory and repurposing potential for Tα1 in MS targeting B cell response

Clin Exp Immunol. 2016 Oct;186(1):39-45. doi: 10.1111/cei.12833. Epub 2016 Aug 1.

Serum thymosin α 1 levels in patients with chronic inflammatory autoimmune diseases.

Pica F[1], Chimenti MS[2], Gaziano R[1], Buè C[1], Casalinuovo IA[1], Triggianese P[2], Conigliaro P[2], Di Carlo D[1], Cordero V[3], Adorno G[3], Volpi A[4], Perricone R[2], Garaci E[1,5].

Author information

Abstract

Thymosin alpha 1 (Tα1) is a powerful modulator of immunity and inflammation. Despite years of studies, there are a few reports evaluating serum Tα1 in health and disease. We studied a cohort of healthy individuals in comparison with patients affected by chronic inflammatory autoimmune diseases. Sera from 120 blood donors (healthy controls, HC), 120 patients with psoriatic arthritis (PsA), 40 with rheumatoid arthritis (RA) and 40 with systemic lupus erythematosus (SLE), attending the Transfusion Medicine or the Rheumatology Clinic at the Policlinico Tor Vergata, Rome, Italy, were tested for Tα1 content by means of a commercial enzyme-linked immunosorbent assay (ELISA) kit. Data were analysed in relation to demographic and clinical characteristics of patients and controls. A gender difference was found in the HC group, where females had lower serum Tα1 levels than males ($P < 0{\cdot}0001$). Patients had lower serum Tα1 levels than HC ($P < 0{\cdot}0001$), the lowest were observed in PsA group ($P < 0{\cdot}0001$ versus all the other groups). Among all patients, those who at the time of blood collection were taking disease-modifying anti-rheumatic drugs (DMARD) plus steroids had significantly higher Tα1 levels than those taking DMARD alone ($P = 0{\cdot}044$) or no treatment ($P < 0{\cdot}0001$), but not of those taking steroids alone ($P = 0{\cdot}280$). **However, whichever type of treatment was taken by the patients, serum Tα1 was still significantly lower than in HC and there was no treatment-related difference in PsA group**. Further prospective studies are necessary to confirm and deepen these observations. They might improve our understanding on the regulatory role of Tα1 in health and disease and increase our knowledge of the pathogenesis of chronic inflammatory autoimmune diseases.

Multiple sclerosis: II. Effects of prothymosin α on the autologous and allogeneic MLR in patients with multiple sclerosis

G. J. RECLOS, C. N. BAXEVANIS, C. SFAGOS*, C. PAPAGEORGIOU*, G. C. TSOKOS† & M. PAPAMICHAIL *Department of Immunology, Hellenic Anticancer Institute, Athens, *Neurology Department, Medical School, University of Athens, and †Metabolic Diseases Branch, National Institute of Diabetes Digestive and Kidney Diseases, National Institute of Health, Bethesda*

SUMMARY

We have recently demonstrated that peripheral blood monocytes from patients with multiple sclerosis (MS) have a defect in stimulating autologous and allogeneic T lymphocytes. This defect was found to correlate with disease activity. In this report we demonstrate that prothymosin α (ProTα), a rat thymus fraction 5 polypeptide, restores the MS monocyte stimulatory defect. The concentrations of ProTα which induced optimal enhancement of the mixed lymphocyte responses (MLR) were significantly higher when monocytes from patients with active disease were used as stimulators than when monocytes from patients with inactive disease were used. $T4^+$ cells tested with autologous stimulatory monocytes harvested from an inactive stage of MS exhibited considerably higher proliferative responses than when stimulated with autologous monocytes obtained from an acute relapse. The decreased autologous proliferation of $T4^+$ cells in MS patients was restored to normal levels after preincubation with ProTα in the environment of autologous monocytes. Our results demonstrate that ProTα is capable of fully restoring the deficient stimulatory function of MS monocytes and monocyte-associated functional defects of MS-derived $T4^+$ cells.

BPC 157

- Composed of 15 amino acids
- Partial sequence of body protection peptide
- Can heal digestive system
- Leaky gut = antigen release into blood stream
- Reduce leaky gut = control source of immune dysregulation
- Additionally beneficial in GI autoimmune diseases (UC/Crohn’s)

TB4

- 43 aa sequence
- Actin sequestering protein
- Essential for protection, repair and regeneration of tissues
- Broad activity as shown in multiple clinical trials
- Ophthalmic, cardiac, PNS, CNS and dermal indications
- Lowers proinflammatory cytokines

Neurobiol Dis. 2016 Apr;88:85-95. doi: 10.1016/j.nbd.2016.01.010. Epub 2016 Jan 12.

Thymosin beta4 promotes oligodendrogenesis in the demyelinating central nervous system.

Zhang J[1], Zhang ZG[2], Li Y[2], Lu M[3], Zhang Y[2], Elias SB[2], Chopp M[4].

Author information

Abstract

Multiple sclerosis (MS) is a demyelinating disease of the central nervous system (CNS). No effective remyelination therapies are in use. We hypothesized that thymosin beta4 (Tβ4) is an effective remyelination treatment by promoting differentiation of oligodendrocyte progenitor cells (OPCs), and that the epidermal growth factor receptor (EGFR) signaling pathway contributes to this process. Two demyelination animal models were employed in this study: 1) experimental autoimmune encephalomyelitis (EAE), an animal model of MS. EAE mice were treated daily for 30days, with Tβ4 or saline treatment initiated on the day of EAE onset; and 2) cuprizone diet model, a non-inflammatory demyelination model. The mice were treated daily for 4weeks with Tβ4 or saline after fed a cuprizone die for 5weeks. Immunofluorescent staining and Western blot were performed to measure the differentiation of OPCs, myelin and axons, respectively. To obtain insight into mechanisms of action, the expression and activation of the EGFR pathway was measured. AG1478, an EGFR inhibitor, was employed in a loss-of-function study. Data revealed that animals in both demyelination models exhibited significant reduction of myelin basic protein (MBP(+)) levels and CNPase(+) oligodendrocytes. Treatment of EAE mice with Tβ4 significantly improved neurological outcome. Double immunofluorescent staining showed that Tβ4 significantl increased the number of newly generated oligodendrocytes identified by BrdU(+)/CNPase(+) cells and MBP(+) mature oligodendrocytes, and reduced axonal damage in the EAE mice compared with the saline treatment. The newly generated mature oligodendrocytes remyelinated axons, and the increased mature oligodendrocytes significantly correlated with functional improvement ($r=0.73$, $p<0.05$). Western blot analysis revealed that Tβ4 treatment increased expression and activation of the EGFR pathway. In the cuprizone demyelination model, Tβ4 treatment was confirmed that significantly increased OPC differentiation and remyelination, and increased the expression of EGFR and activated the EGFR pathway in the demyelinating corpus callosum. In cultured OPCs, blockage of the activation of the EGFR pathway with AG1478 abolished the Tβ4-increased OPC differentiation. Collectively, these findings indicate that: 1) Tβ4 increases proliferation of OPCs and the maturation of OPCs to myelinating oligodendrocytes which in concert, likely contribute to the beneficial effect of Tβ4 on EAE, 2) EGFR upregulated and activated by Tβ4 may mediate the process of OPC differentiation, and 3**) Tβ4 could potentially be developed as a therapy for MS patients, and for other demyelinating neurological**

Vasoactive Intestinal Peptide (VIP)

28 aa peptide

Belongs to glucagon/secretin superfamily

Produced in many tissues and organs

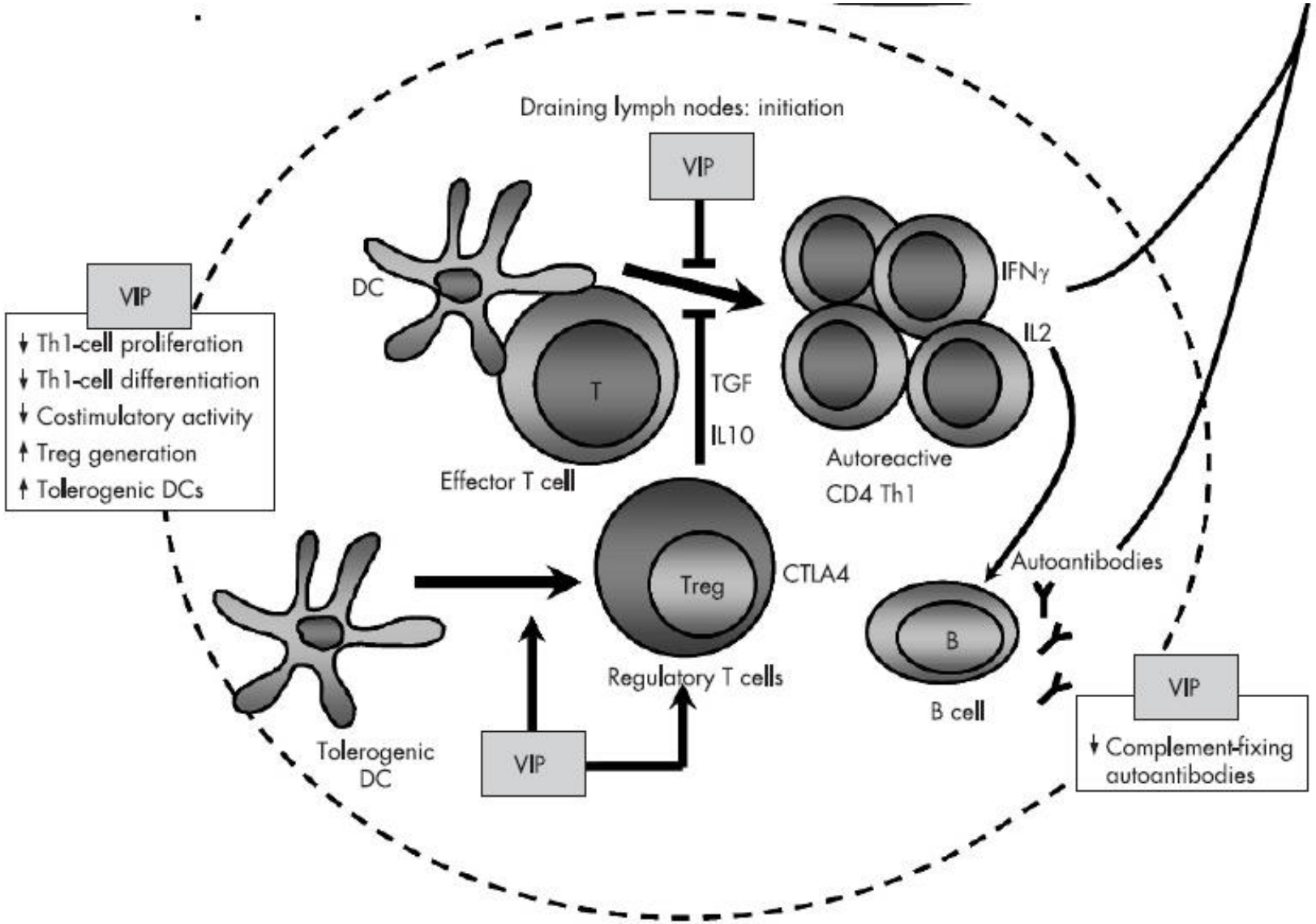
Multiple functions (vasodilation, glycogenolysis, increases heart contractility)

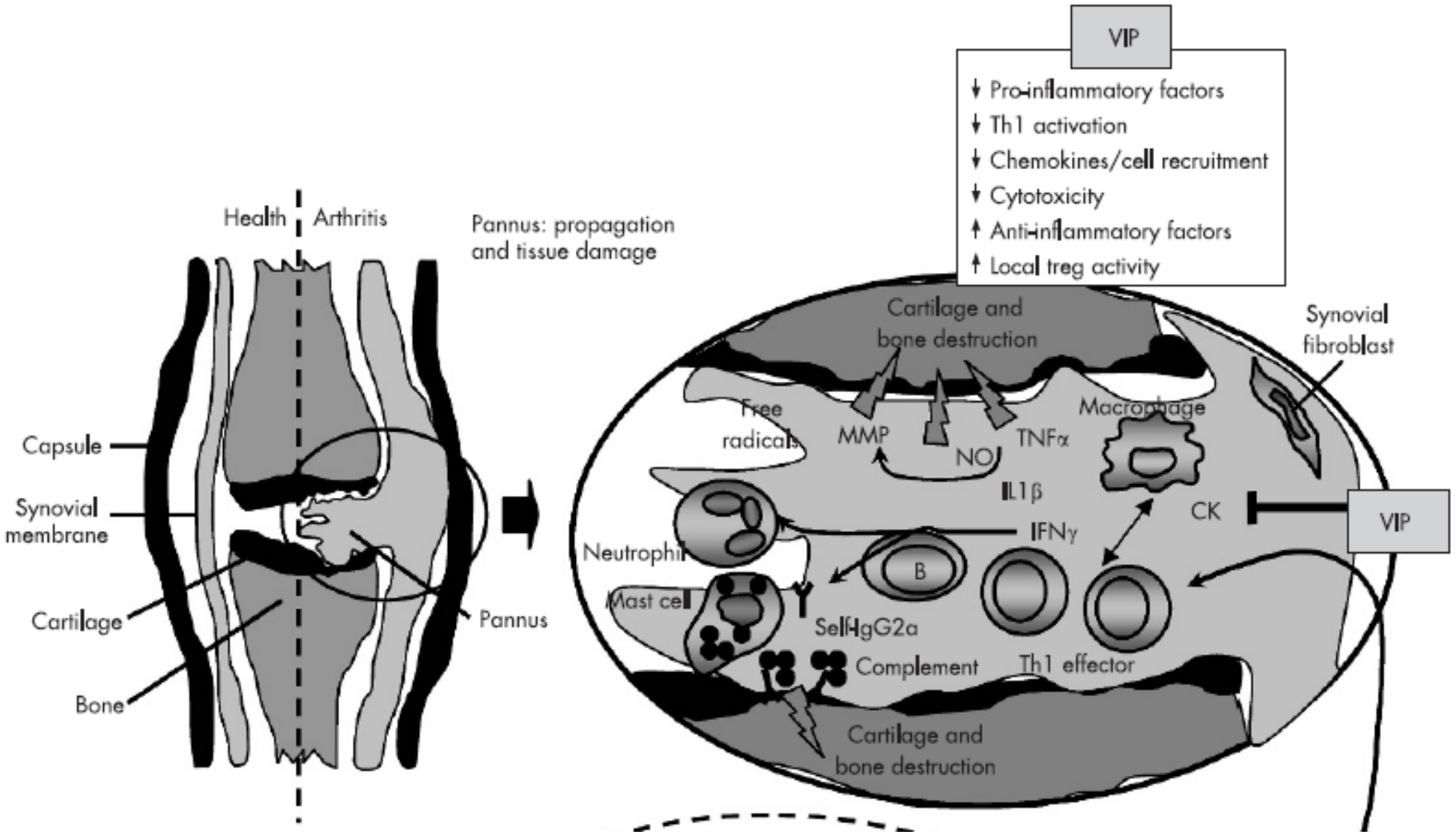
Short half life

Has shown promise in regulating autoimmunity

VIP and innate immune cell function

- Mostly excitatory effects on mast cells
- Inhibitory effects on macrophages and monocytes (VPAC 1 receptor)
- Stimulation of IL10
- Down regulation of Toll like receptors
- Increased Tregs
- Decreased TH1 cytokine expression


Draining lymph nodes: initiation
VIP
DC
T
Effector T cell
TGF
IL10
IFNγ
IL2
Autoreactive
CD4 Th1
VIP
↓ Th1-cell proliferation
↓ Th1-cell differentiation
↓ Costimulatory activity
↑ Treg generation
↑ Tolerogenic DCs
Treg
CTLA4
Regulatory T cells
Autoantibodies
B
B cell
Tolerogenic
DC
VIP
VIP
↓ Complement-fixing
autoantibodies


VIP
Pro-inflammatory factors
Th1 activation
Chemokines/cell recruitment
Cytotoxicity
Anti-inflammatory factors
Local treg activity
Health
Arthritis
Pannus: propagation and tissue damage
Capsule
Synovial membrane
Cartilage
Bone
Pannus
Cartilage and bone destruction
Synovial fibroblast
Free radicals
MMP
NO
TNFα
Macrophage
IL1β
CK
VIP
IFNγ
Neutrophil
B
Mast cell
SelfIgG2a
Complement
Th1 effector
Cartilage and bone destruction

THE NEUROPEPTIDE VIP: DIRECT EFFECTS ON IMMUNE CELLS AND INVOLVEMENT IN INFLAMMATORY AND AUTOIMMUNE DISEASES

Doina Ganea, **Kirsten M. Hooper**, and **Weimin Kong**
Department of Microbiology & Immunology, Temple University School of Medicine, Philadelphia, PA, USA

Abstract

Neuropeptides represent an important category of endogenous contributors to the establishment and maintenance of immune deviation in immune privileged organs such as the CNS, and in the control of acute inflammation in the peripheral immune organs. Vasoactive intestinal peptide (VIP) is a major immunoregulatory neuropeptide widely distributed in the central and peripheral nervous system. In addition to neurons, VIP is synthesized by immune cells which also express VIP receptors. Here we review the current information on VIP production and VIP receptor mediated effects in the immune system, the role of endogenous and exogenous VIP in inflammatory and autoimmune disorders, and present and future VIP therapeutic approaches.

Emerging roles of vasoactive intestinal peptide: a new approach for autoimmune therapy

Elena Gonzalez-Rey, Per Anderson, Mario Delgado

Ann Rheum Dis 2007;**66**(Suppl III):iii70–iii76. doi: 10.1136/ard.2007.078519

See end of article for authors' affiliations

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Accepted 2 July 2007

Identification of the factors that regulate the immune tolerance and control the appearance of exacerbated inflammatory conditions is crucial for the development of new therapies of autoimmune diseases. Some neuropeptides and hormones have emerged as endogenous agents that participate in the regulation of the processes that ensure self-tolerance. Among them, the vasoactive intestinal peptide (VIP), a well-characterised endogenous anti-inflammatory neuropeptide, has shown therapeutic potential for a variety of immune disorders. Here we examine the latest research findings, which indicate that VIP participates in maintaining immune tolerance in two distinct ways: by regulating the balance between pro-inflammatory and anti-inflammatory factors, and by inducing the emergence of regulatory T cells with suppressive activity against autoreactive T cell effectors.

Putting it all together: Integrative Approach

	Immuneregulation:	TA1 OGF/Met Enk VIP
	Neuro repair	TB4
	GI/Leaky gut	BPC 157
	Systemic repair: HGH analogues/secretagogues	

Dosing

Peptide	Dosing	Comments
TA1	450 mcg SQ	Evaluate clinical response and markers; titrate adjustingly
TB 4	750mcg SQ	Alternate dosing after 1st month
VIP	50mcg QID	Alternating nostrils; watch out for adverse effects; taper down post 1 month; check lipase
OGF	250mcg/kg IV	Consider LDN as an option due to current limits with OFG/Met Enk
BPC 157	200 mcg SQ daily; Alt 500 mcg caps PO	

Conclusions

- Autoimmune diseases share some common altered immunological pathways
- TH subset balance, Tregs predominance, chronic inflammation and leaky gut tend to be presentations/causes
- Multiple peptides have shown immunomodulatory as well as anti inflammatory and tissue repairing effects
- Can be considered as part of an integrative approach for the management of autoimmune diseases
- Additional studies will shed new light on future applications and peptides