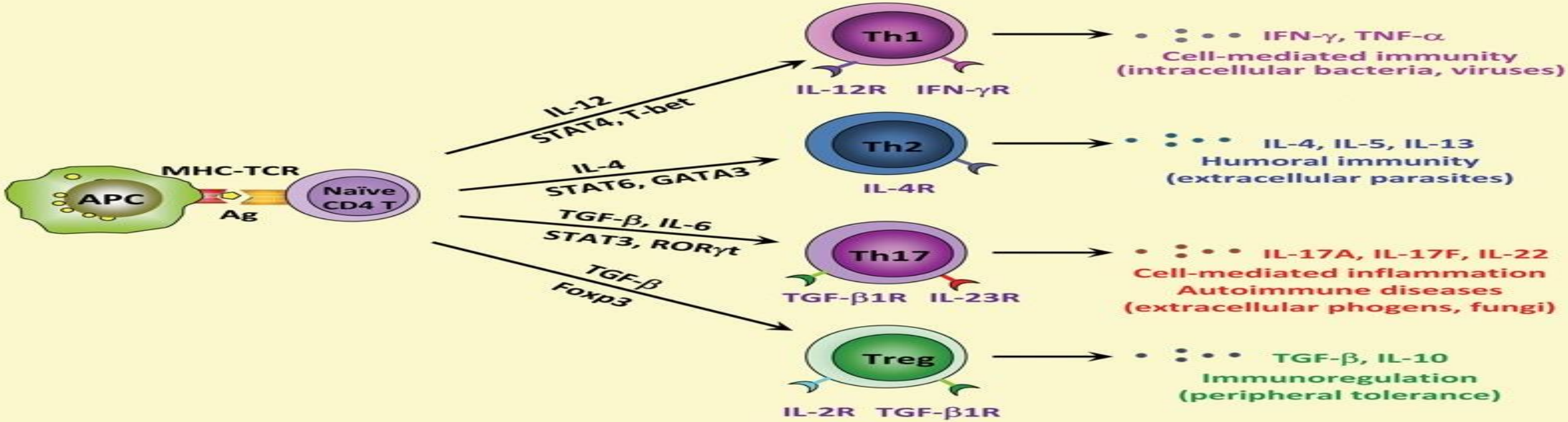
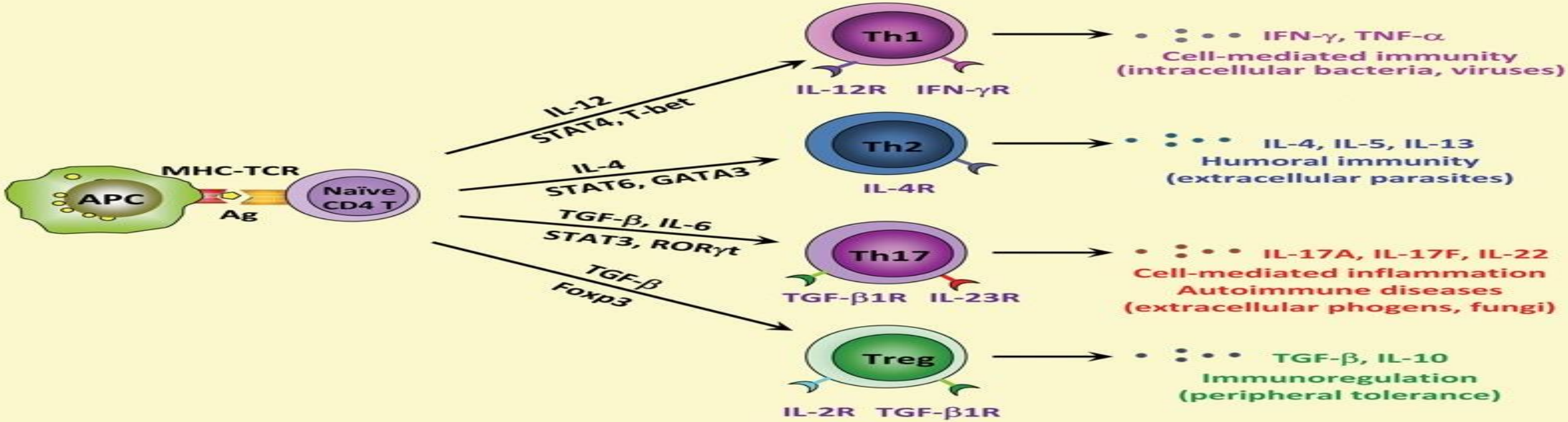


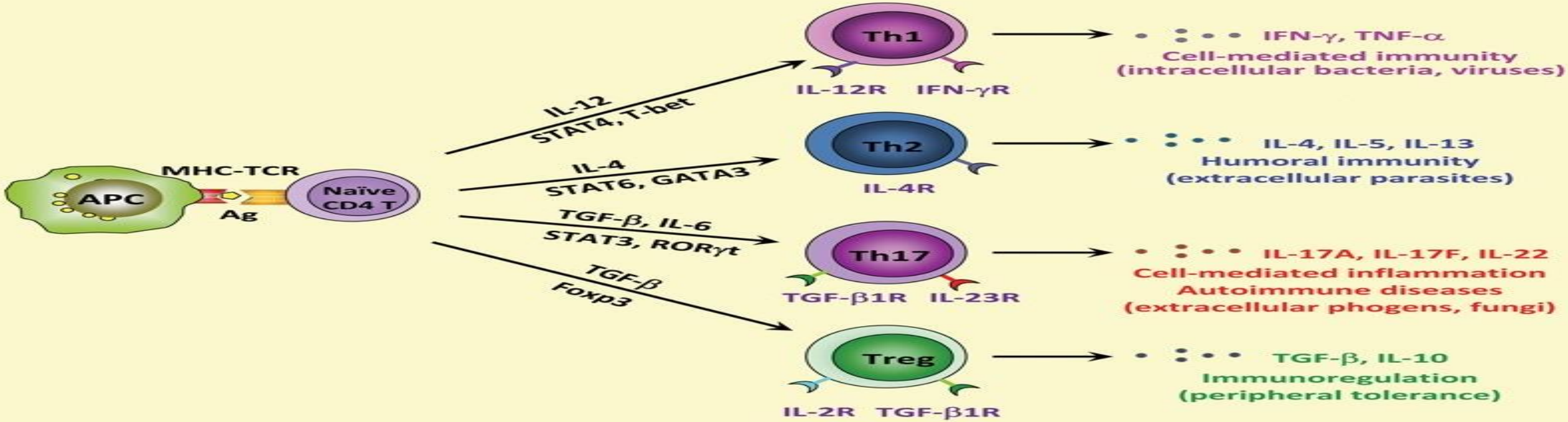
CD4+ T cells play a critical role in regulating human health and disease by orchestrating the immune system against foreign antigens, such as infections or cancer formation.

Before the 1980s, helper T cells were believed to be a single subset among T lymphocytes. Increasing evidence now suggests that there are at least four distinct T helper subsets differentiated in response to particular combinations of cytokines.



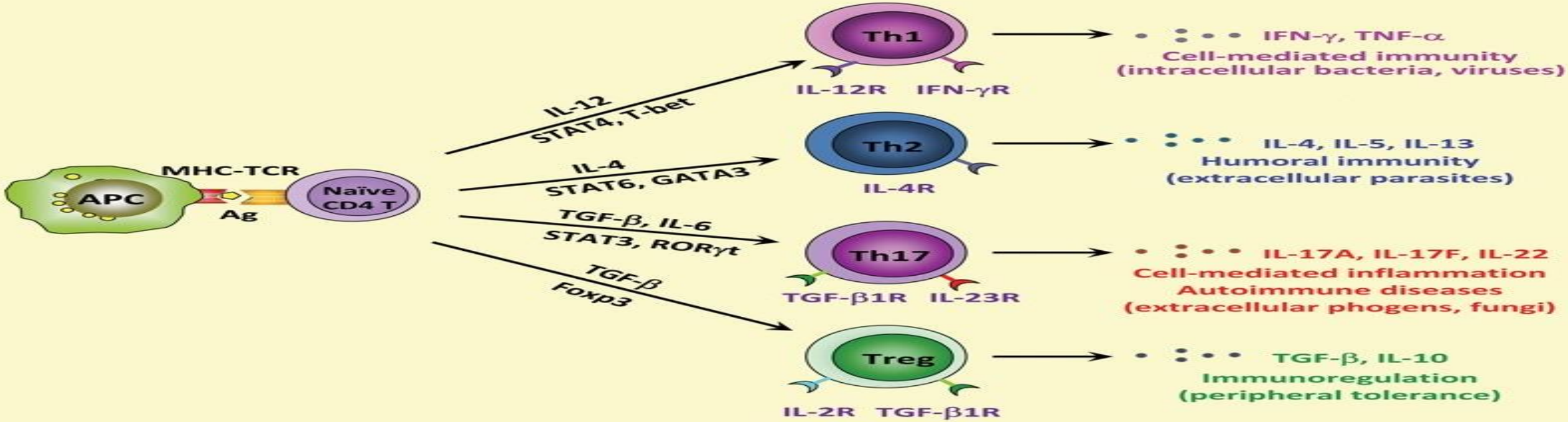
Th1

When Naive macrophages or DCs engulf cancers or virally infected cells, they polarize to M1 or DC1 and secretes IL-12. IL-12 influences Th1 cell development and promotes immunity upon the presence of IFN-γ and eliminate intracellular pathogens and cancers through IFN-γ production, which activates macrophages and cytotoxic T cells to eliminate cancers and infected cells with viruses.



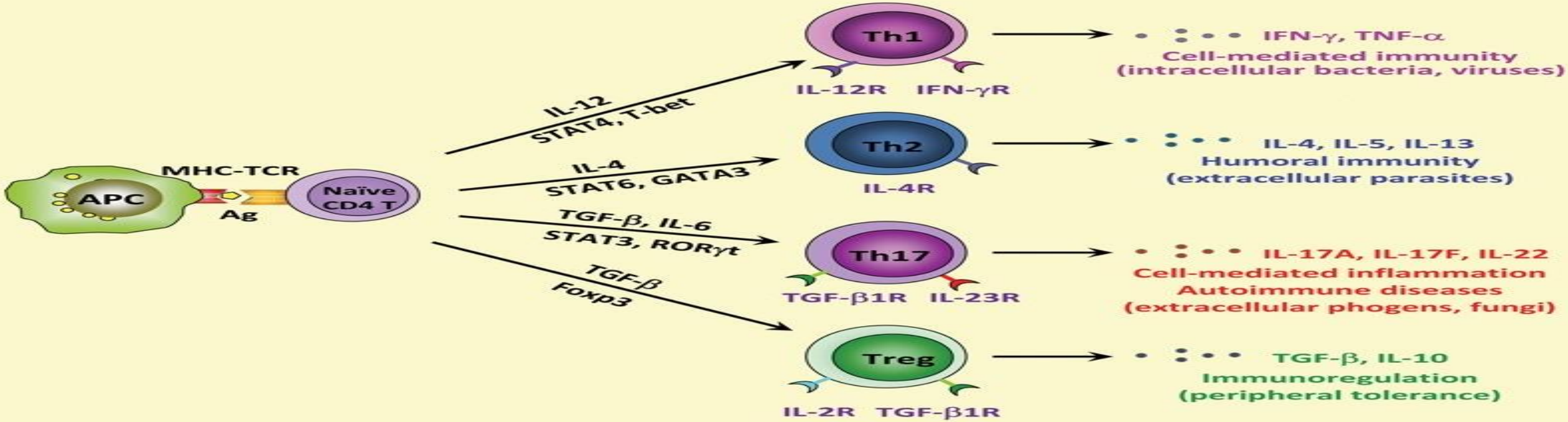
Th2

When Naive macrophages or DCs engulfs parasites or allergens they polarize to M2 or DC2 and secretes IL-4. IL-4 influences Th2 cell development and promotes immunity upon the presence of IL-4, IL-5, IL-13 which activates B lymphocytes and eliminate the parasite and allergens through Ig-E activated basophils, mast cells and eosinophils.



Th17

When Naive macrophages or DCs engulfs extra- cellular pathogens such as bacteria or fungus or viral or cancer antigens they polarize to M17 or DC17 and secretes TGF-β, IL-6.TGF-β, IL-6 influences Th 17 cell development and promotes immunity upon the presence of IL-21. IL-1β, IL-23 , IL -22 and IL-17 and eliminate bacteria and fungus through activated neutrophils and natural killers cells and maintain gut defense through IL-17 which up-regulates claudins for tight junction formation in the intestinal barrier in addition to IL-22 plays a role in epithelial maintenance.



Th17

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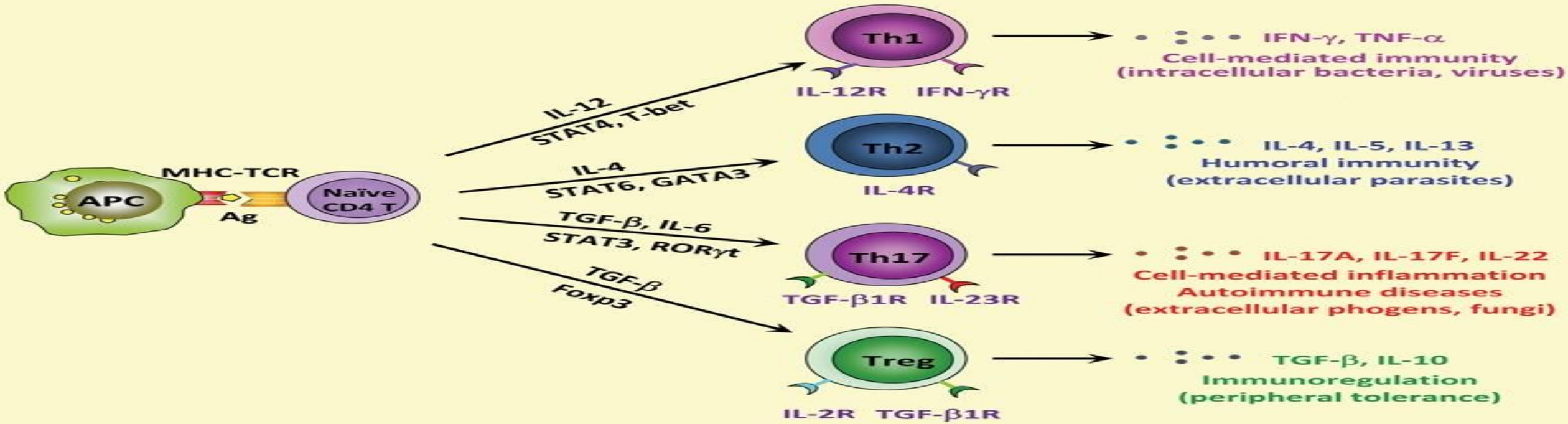


Treg

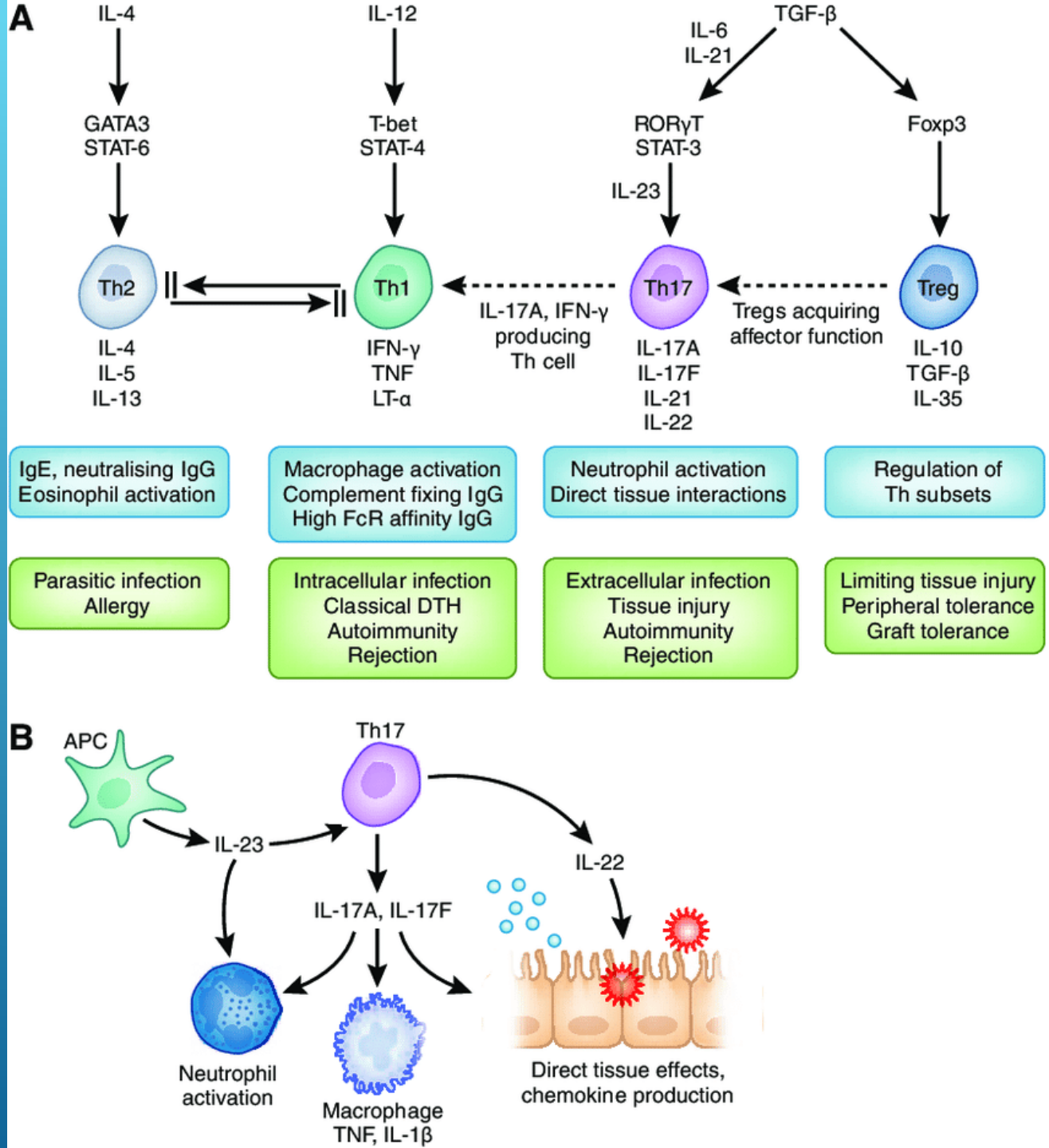
When the Naive macrophages or DCs engulf self-antigens, they polarize to Mregs or DCregs and secretes IL-2 and TGF-β. IL-2 and TGF-β, influences Treg cell development and promotes immune tolerance upon the presence of TGF-β, IL-10 and IL-35 and suppress effector function (Th1/Th17/Th4) through secretion of inhibitory cytokines such as IL-10 and TGF-β.

T helpers in opposition

Our current understanding of T helper function revolves around a theory that subsets are in a state of equilibrium37. Upon activation of one particular subset, other subsets are modulated or inhibited in order to promote the most specific effector response in defense against imminent threat

Historically, this discussion began with the Th1/Th2 hypothesis of distinct opposing T helper subsets, formulated after searching for a T cell responsible for helping antibody production versus one responsible for tissue damage in delayed-type hypersensitivity (DTH)

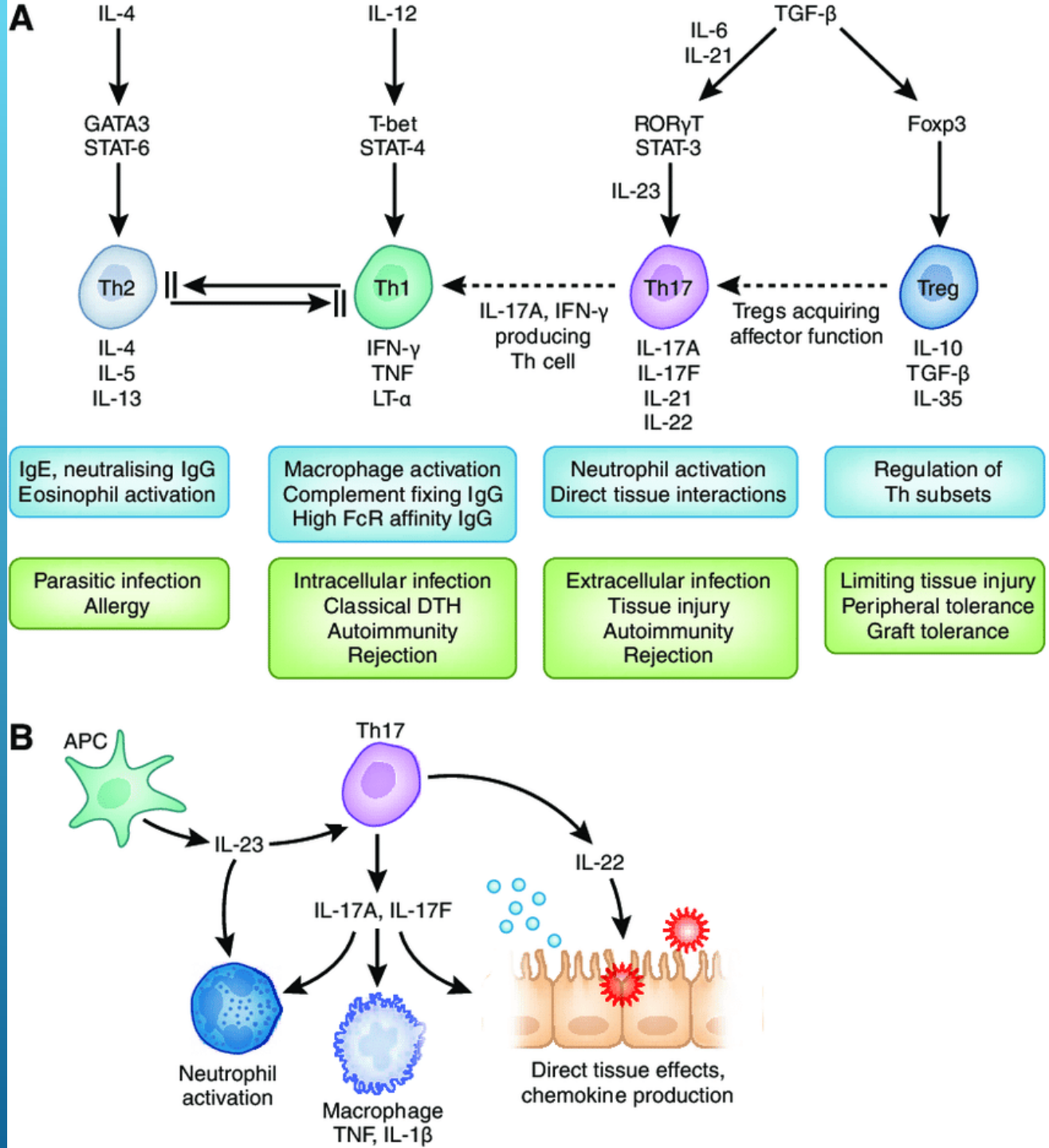
Early studies claimed that Th1 cells mediated tissue damage in DTH, not the antibodies in serum, and would likely be the cell responsible for mediating tissue damage in various autoimmune diseases



T helpers in opposition

After several failed attempts to show that tissue damage in murine experimental autoimmune encephalitis (EAE) was mediated by Th1 cells and their effector cytokine, IFN-γ, the characterization of a novel subset called Th17 cells emerged

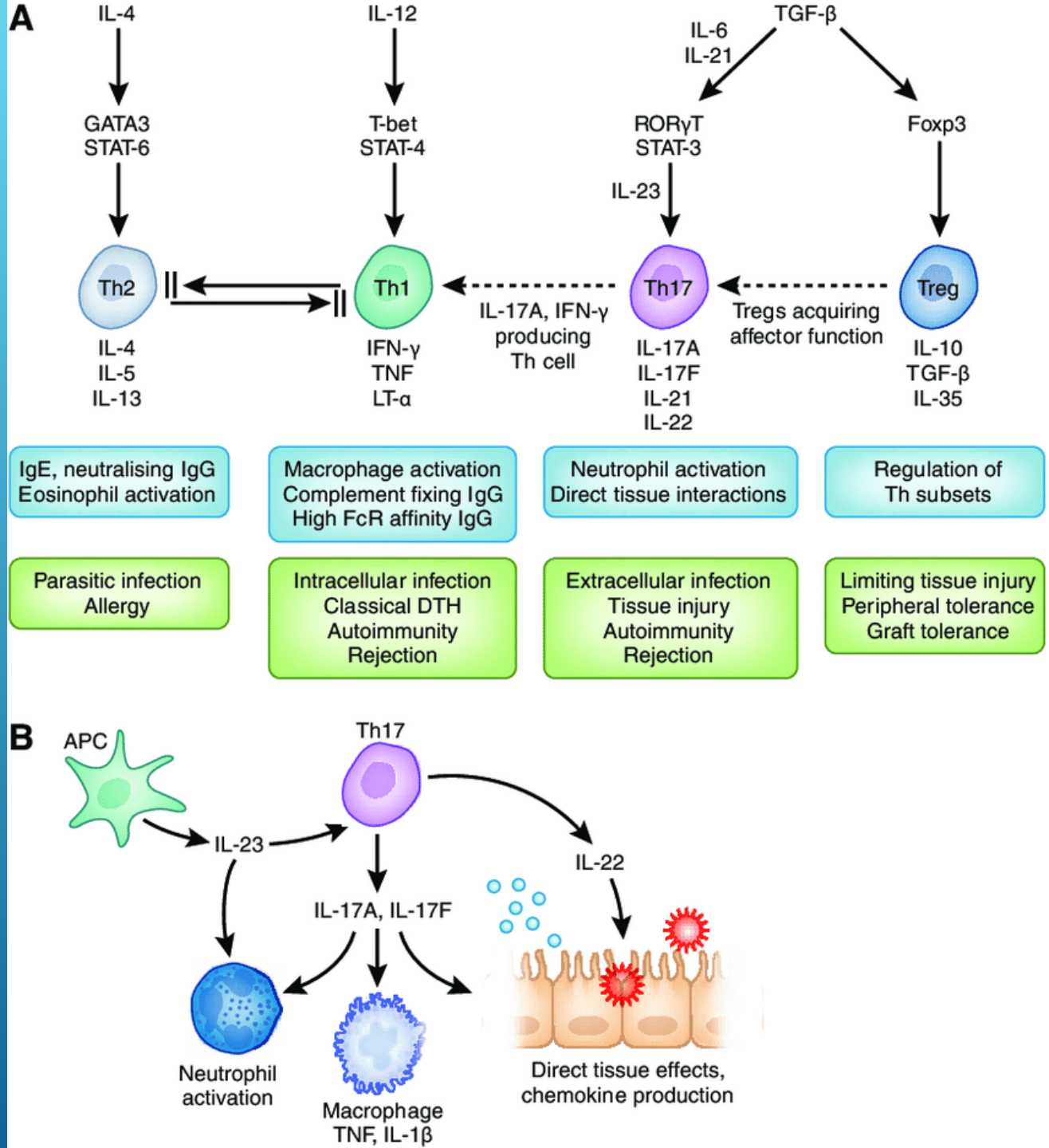
The Th1/Th17 balance developed, recognizing that IFN-γ and IL-17 have antagonistic properties, as blockade of IFN-γ results in increased IL-17 production by T cells. Finally, an antagonistic relationship between Th17 cells and Tregs has been described, as their differentiation is stimulated by similar cytokines yet they have different functions Th17 cells serve as an effector lymphocyte population, while Tregs are suppressor cells



Th1/Th17 plasticity

Th17 cells can acquire Th1-like characteristics after activation, a property that likely plays a role in enhancing autoimmunity and antitumor immunity. Termed ex-Th17 cells, or non-classical Th1 cells, these cells lose their ability to secrete IL-17 while gaining the capacity to secrete IFN-γ in the presence of proinflammatory signals, such exposure to IL-12

They can still be distinguished from classic Th1 cells via unique surface markers, including CD161, CCR6, and IL-17RE. Moreover, these cells are functionally distinct from classic Th1 cells, secreting more TNF, IL-2, GM-CSF, and IFN-γ. Interestingly, proliferation of ex-Th17 cells is not suppressed by Treg cells in direct contrast to classical Th1 and Th17 cells, which are inhibited by Treg cells. These data implicate a possible role for these cells in an unbalanced Th17/Treg autoimmune response. The observed plasticity of Th17 cells occurs only in the direction of Th17 to Th1, as Th1 cells have not been shown to convert to Th17-like T cells



Th17/Treg plasticity

Tregs are able to reacquire characteristics of Th17 cells under a cytokine-driven influence.

When Foxp3+ Tregs are exposed to IL-6 with or without IL-1β and IL-23, Foxp3 becomes down-regulated in favor of expressing Th17 genes including IL-17, IL-22, IL-23R,

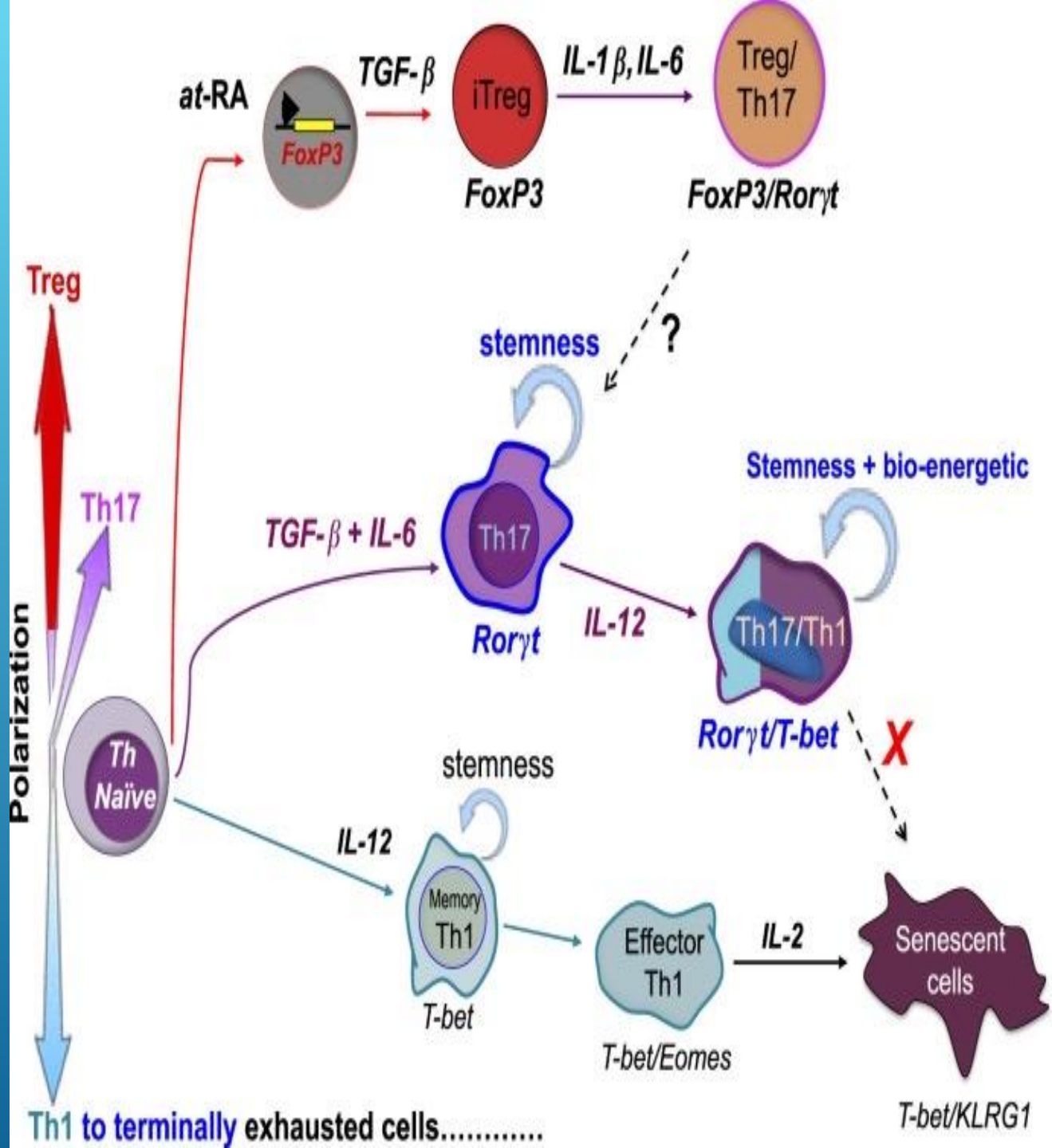
Ex-Tregs have been implicated in the pathogenesis of autoimmune arthritis because they have a reduced ability to suppress cytotoxic CD8+, effector Th17 cells and Th1

Th17/Treg in Autoimmunity

Th17 cell-mediated immunity is important for maintaining mucosal and hematopoietic homeostasis. However, too strong of a Th17 cell response can induce autoimmunity

Likewise, a lack of Tregs can result in lethal autoimmunity in humans.

The altered homeostasis between Th17 and Treg has been implicated in several autoimmune diseases, including multiple sclerosis, psoriasis rheumatoid arthritis inflammatory bowel disease1 and systemic lupus erythematosus



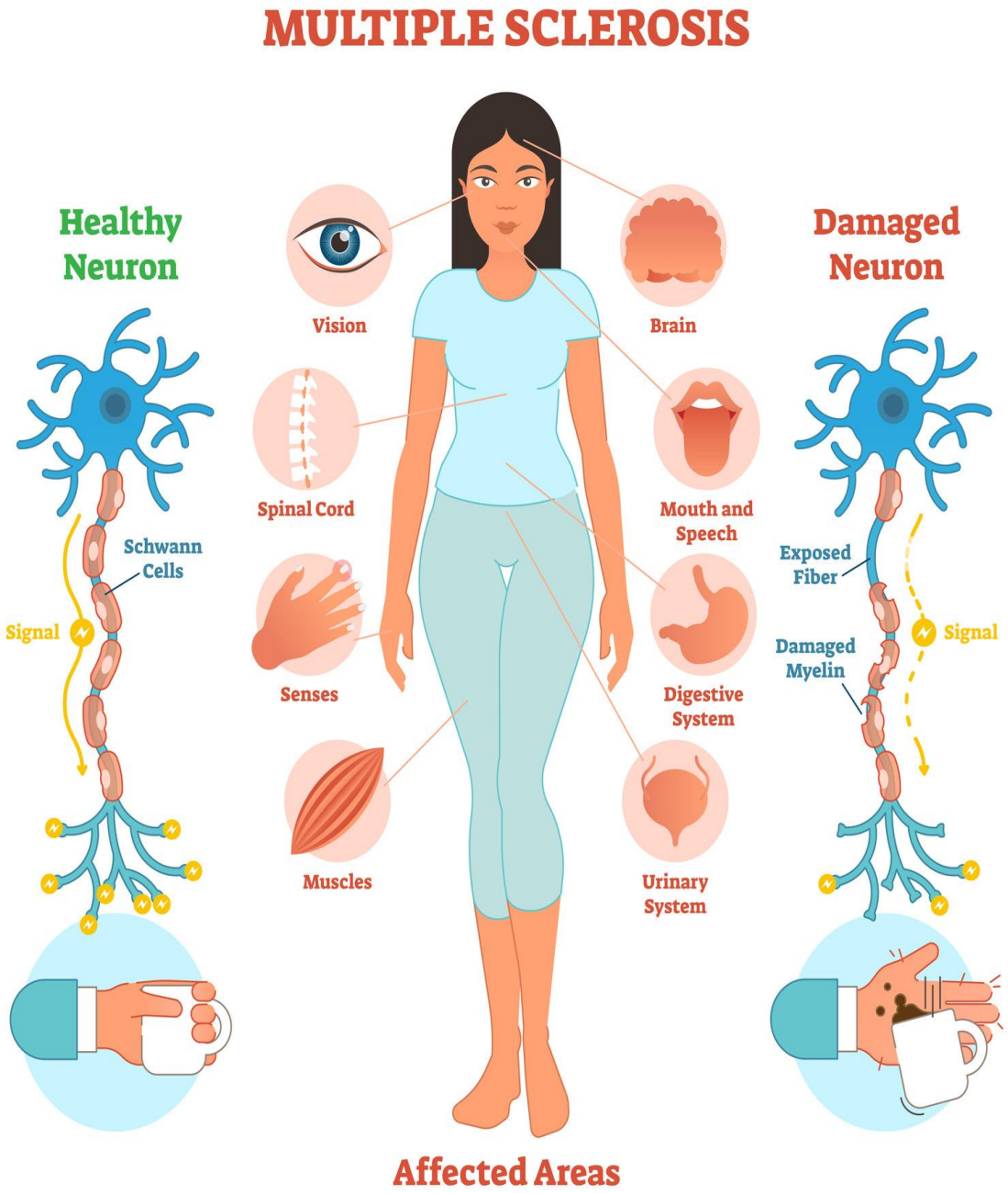
Multiple sclerosis

Multiple sclerosis (MS) is a chronic inflammatory disease involving destruction of myelin in central nervous system white matter.

This disease presents in patients as deficits in sensory or motor function, unilateral vision loss, diplopia, gait disturbance, or loss of bladder control, among other varied symptoms of nervous system malfunction

In MS patients, myelin-reactive T cells not only secrete IL-17 but also secrete IFN-γ and GM-CSF

These data suggest, as in the EAE animal model, that Th17 and Th1 cells play a role in MS in human patients. These data also suggest that these Th17 cells are pathogenic Ex-Th17 due to their ability to cosecrete multiple cytokines

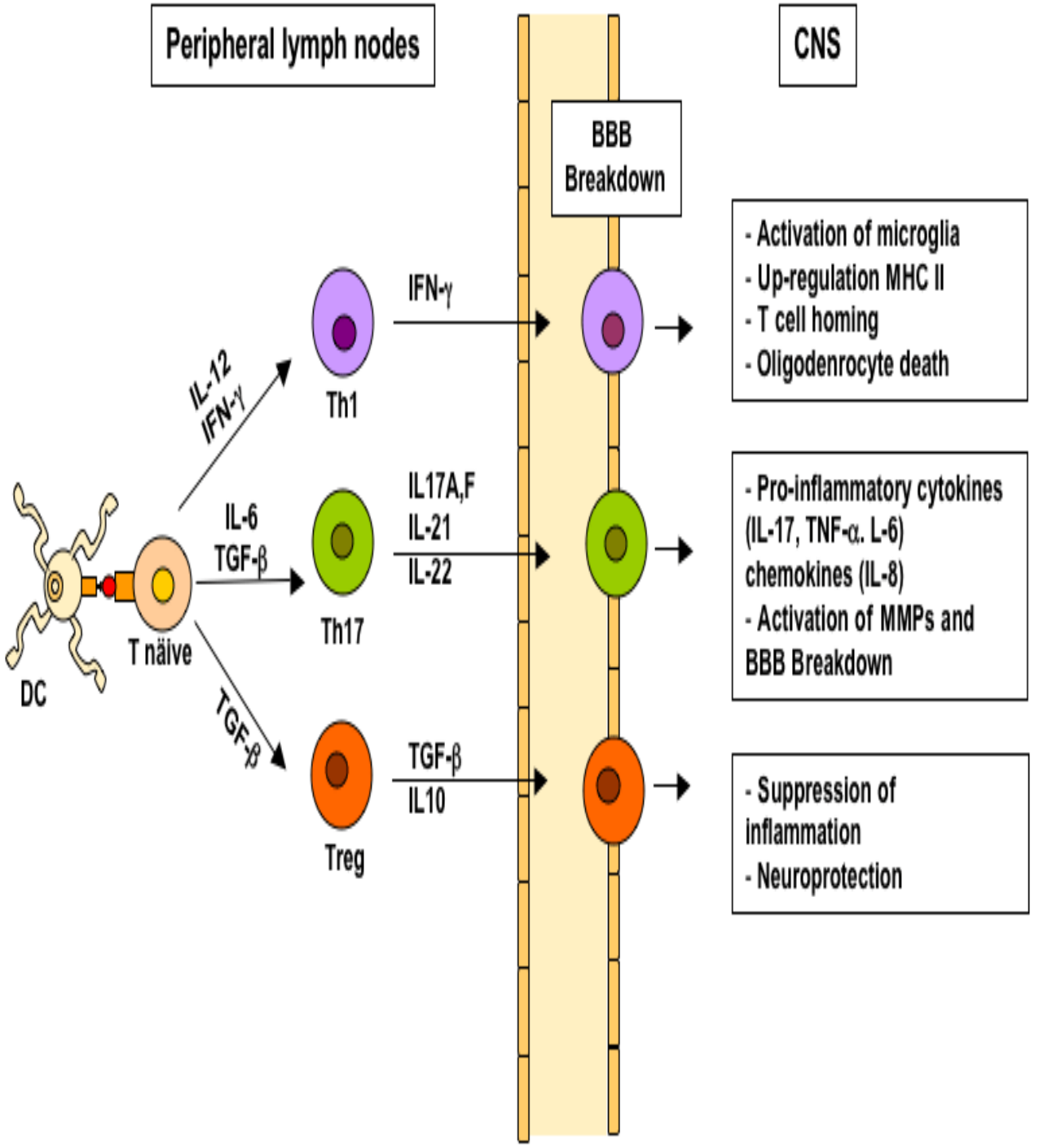


Multiple sclerosis

IL-17 levels have been reported to be increased in the CSF of MS patients during symptomatic relapses, as well as in chronic lesions.

Both the upregulation of IL-17 and IL12 and down-regulation of Treg-mediated immunity likely contribute to the pathogenesis of MS in humans.

Perhaps targeting a combination of both Th17 and Treg pathways through IL-17 and IL-12 blockades and a boost of functional Tregs is necessary for disease control in patients with multiple sclerosis.

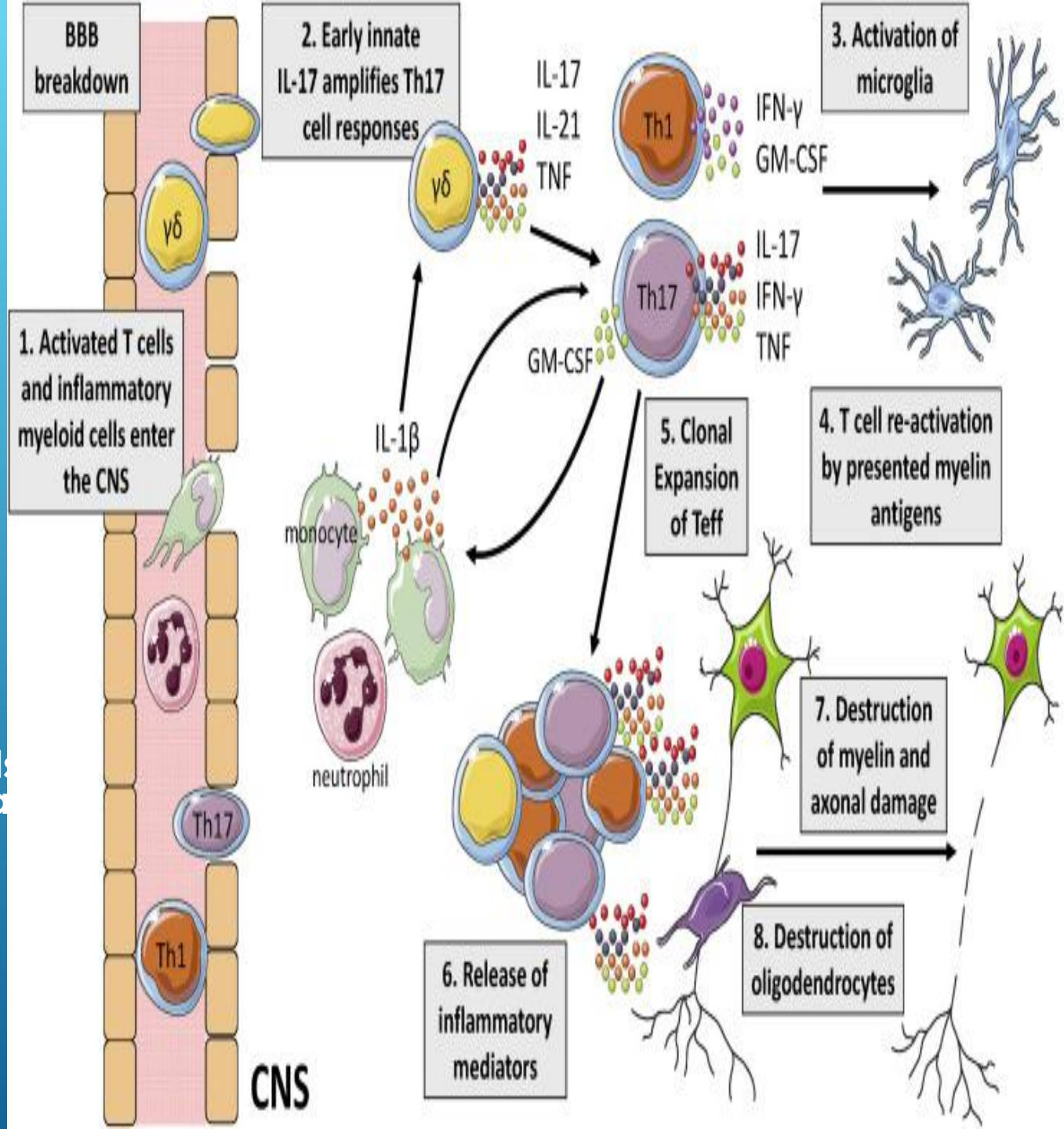


Multiple sclerosis

While an obvious way to treat autoimmunity in patients is by blunting the Th1 and Th17 and IL-12 pathway via IL-17 or IL-12 blockade with FDA-approved drugs such as of IL-17 (secukinumab) or IL-12 (ustekinumab), losartan, methylene blue and ivermectin or supplements such polyphenols and flavonoid ,

Holistic strategies involving simply changing the patient`s diet or modulating the microbiota to dampen Th17-mediated diseases, also using biologics such PRP, stem cells and exosomes and other Nitroredox therapies are becoming increasingly more appreciated.

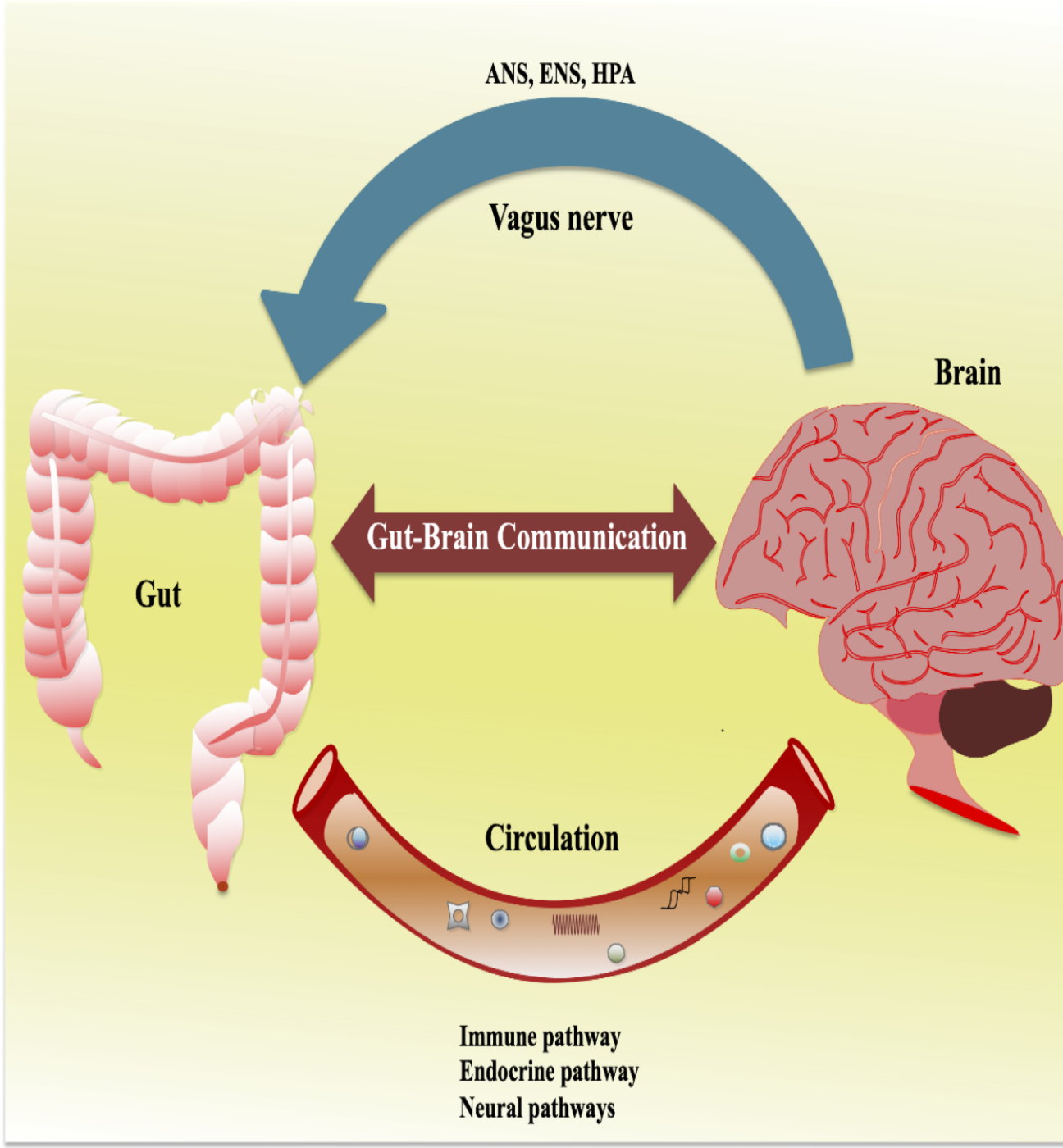
A high-salt diet has been shown to induce Th17 cells and exacerbate EAE This concept is supported by a recent report by Wilck and team, who found that a high-salt diet triggers an increased number of pathogenic Th17 cells in the peripheral blood of mice, correlating with destruction of the *Lactobacillus* species in the gut microbiome and hypertension.



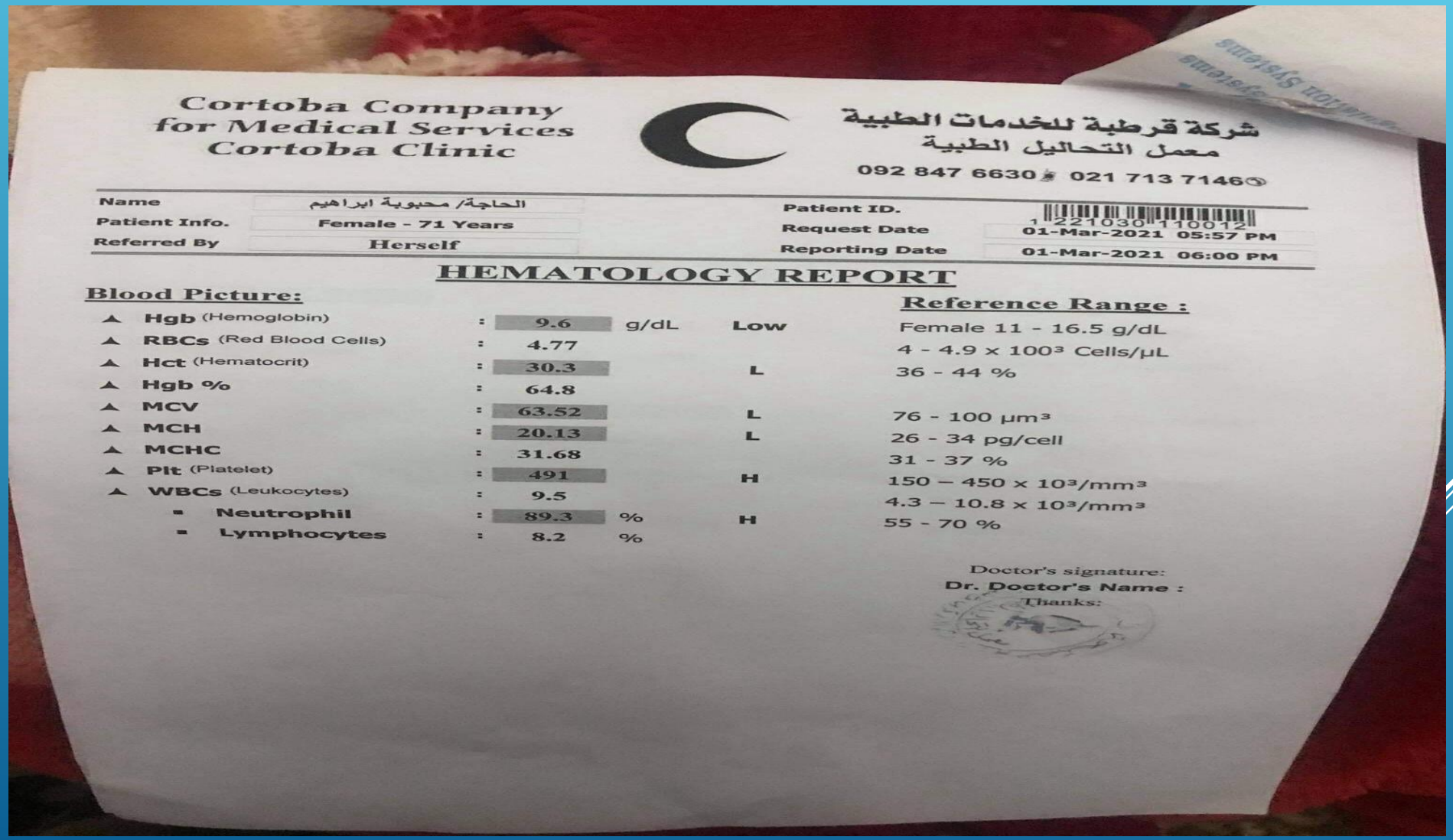
Multiple sclerosis

Repopulating the gut with *Lactobacillus* species was shown to mitigate the severity of EAE and hypertension. The high-salt diet similarly led to an increase in peripheral circulating Th17 cells in a healthy human cohort. In a preclinical arthritis model, the gut microbe segmented filamentous bacterium (SFB) was also found to support Th17 cells and exacerbate autoimmunity.

While probiotics have been shown to reduce SFB and lessen the pathogenesis of Th17and Th1 cells, thus reducing these autoimmune diseases, it is less clear how altering the salt intake or administering probiotics in human patients could impact disease outcome. Regardless, it is now clear that modulating the microbiome can also play a major role in shaping the biology of the Th17/Treg axis. .



LAB RESULTS OF DIABETIC AND HYPERTENSIVE 70 YEARS OLD FEMALE WITH COVID-19 CYTOKINES STORM



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شركة قرطبة للخدمات الطبية
معمل التحاليل الطبية

092 847 6630 021 713 7146

Name	الحاجة/ محبوبة ابراهيم	Patient ID.	1 22103 110012
Patient Info.	Female - 71 Years	Request Date	01-Mar-2021 05:57 PM
Referred By	Herself	Reporting Date	01-Mar-2021 06:00 PM

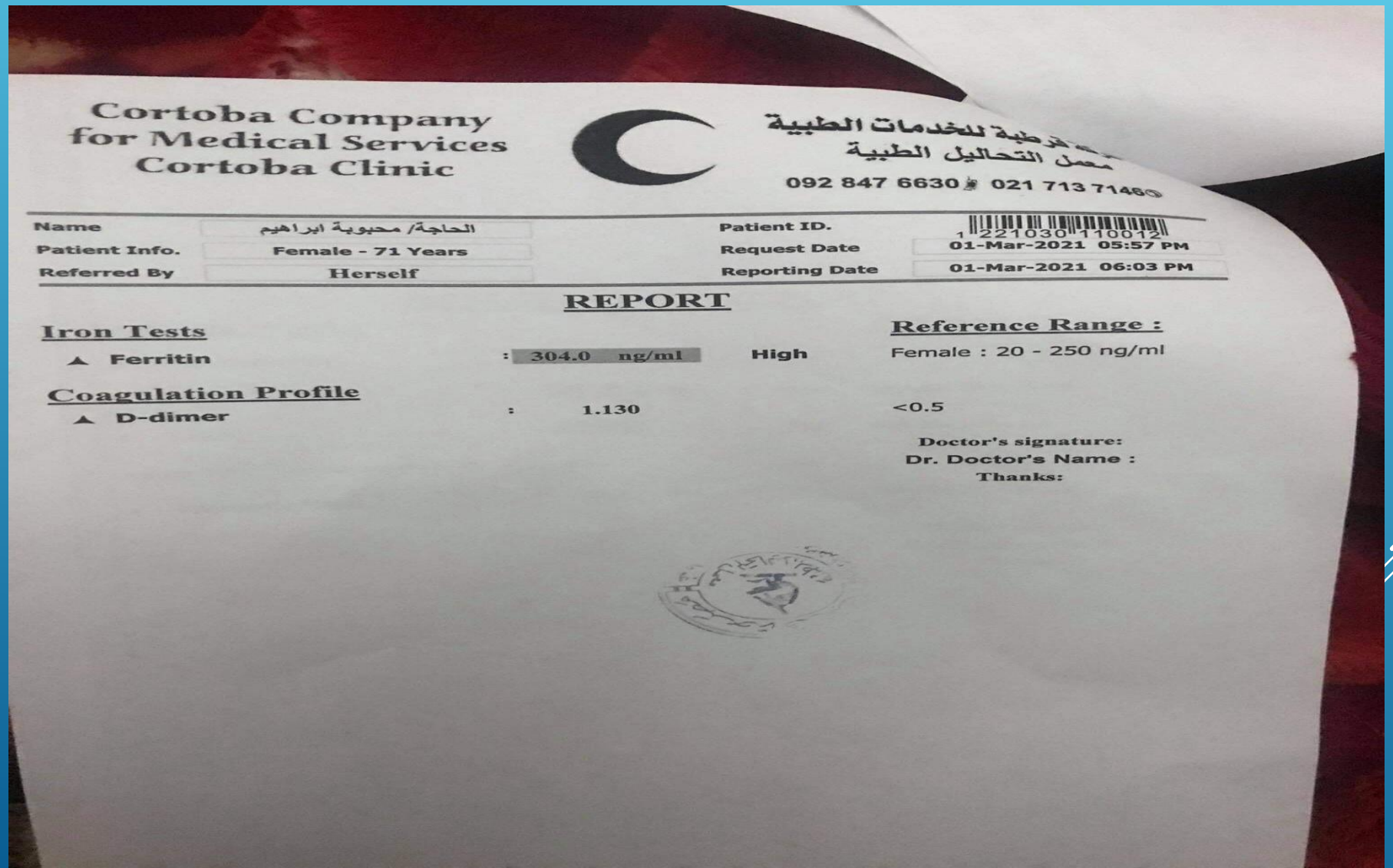
HEMATOLOGY REPORT

Blood Picture:

				Reference Range :
▲ Hgb (Hemoglobin)	9.6	g/dL	Low	Female 11 - 16.5 g/dL
▲ RBCs (Red Blood Cells)	4.77			4 - 4.9 x 10³ Cells/µL
▲ Hct (Hematocrit)	30.3		L	36 - 44 %
▲ Hgb %	64.8			
▲ MCV	63.52		L	76 - 100 µm³
▲ MCH	20.13		L	26 - 34 pg/cell
▲ MCHC	31.68			31 - 37 %
▲ Plt (Platelet)	491		H	150 – 450 x 10³/mm³
▲ WBCs (Leukocytes)	9.5			4.3 – 10.8 x 10³/mm³
▪ Neutrophil	89.3	%	H	55 - 70 %
▪ Lymphocytes	8.2	%		

Doctor's signature:
Dr. Doctor's Name :
Thanks:

LAB RESULTS OF DIABETIC AND HYPERTENSIVE 70 YEARS OLD FEMALE WITH COVID-19 CYTOKINES STORM



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for Medical Services
Cortoba Clinic

قرطبة للخدمات الطبية
معمل التحاليل الطبية

092 847 6630 021 713 7146

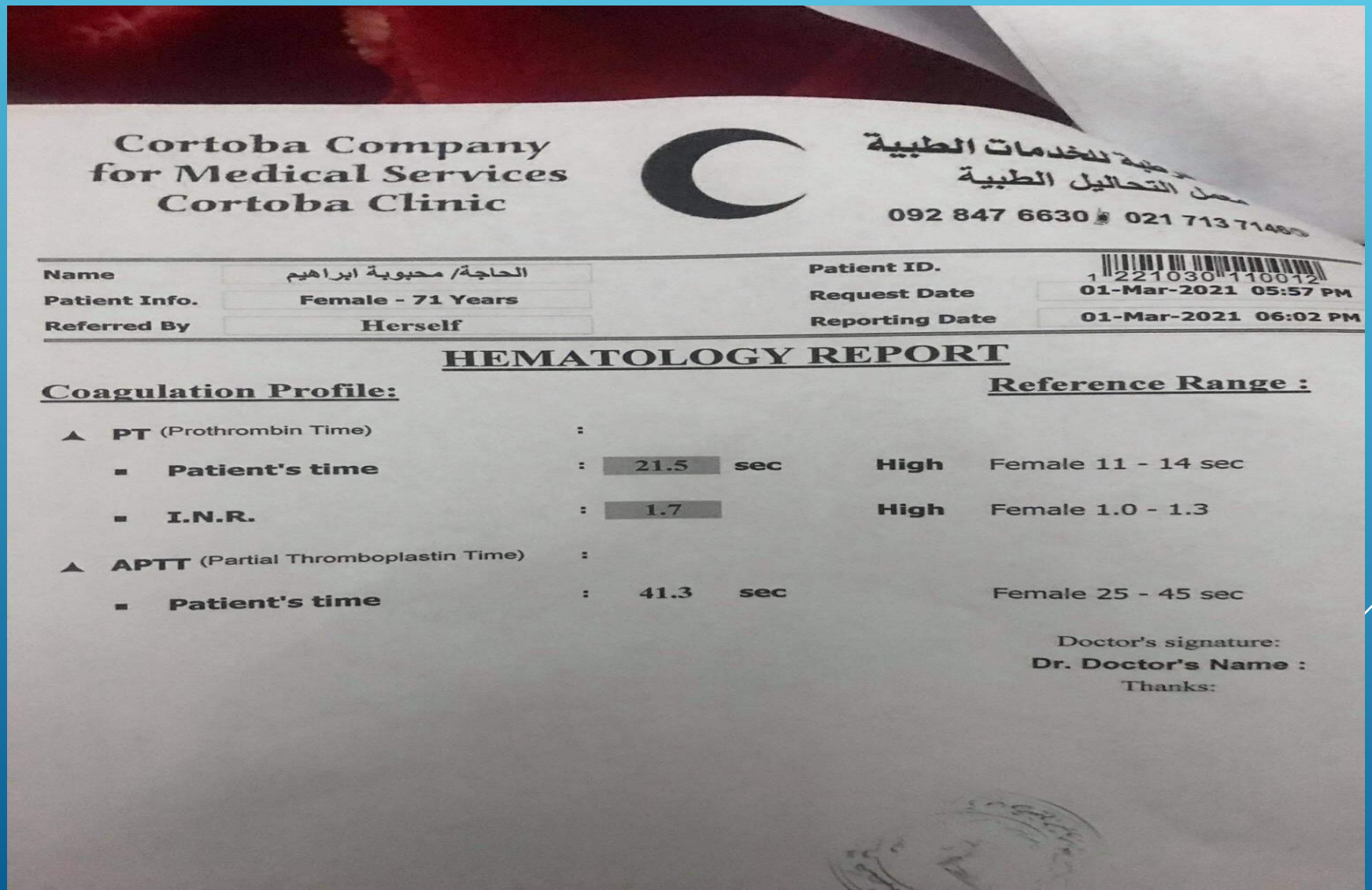
Name	الحاجة/ محبوبة ابراهيم	Patient ID.	1221030110012
Patient Info.	Female - 71 Years	Request Date	01-Mar-2021 05:57 PM
Referred By	Herself	Reporting Date	01-Mar-2021 06:03 PM

REPORT

			Reference Range :
Iron Tests			
▲ Ferritin	: 304.0 ng/ml	High	Female : 20 - 250 ng/ml
Coagulation Profile			
▲ D-dimer	: 1.130		<0.5

Doctor's signature:
Dr. Doctor's Name :
Thanks:

LAB RESULTS OF DIABETIC AND HYPERTENSIVE 70 YEARS OLD FEMALE WITH COVID-19 CYTOKINES STORM



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شركة قرطبة للخدمات الطبية
معمل التحاليل الطبية

092 847 6630 021 713 71480

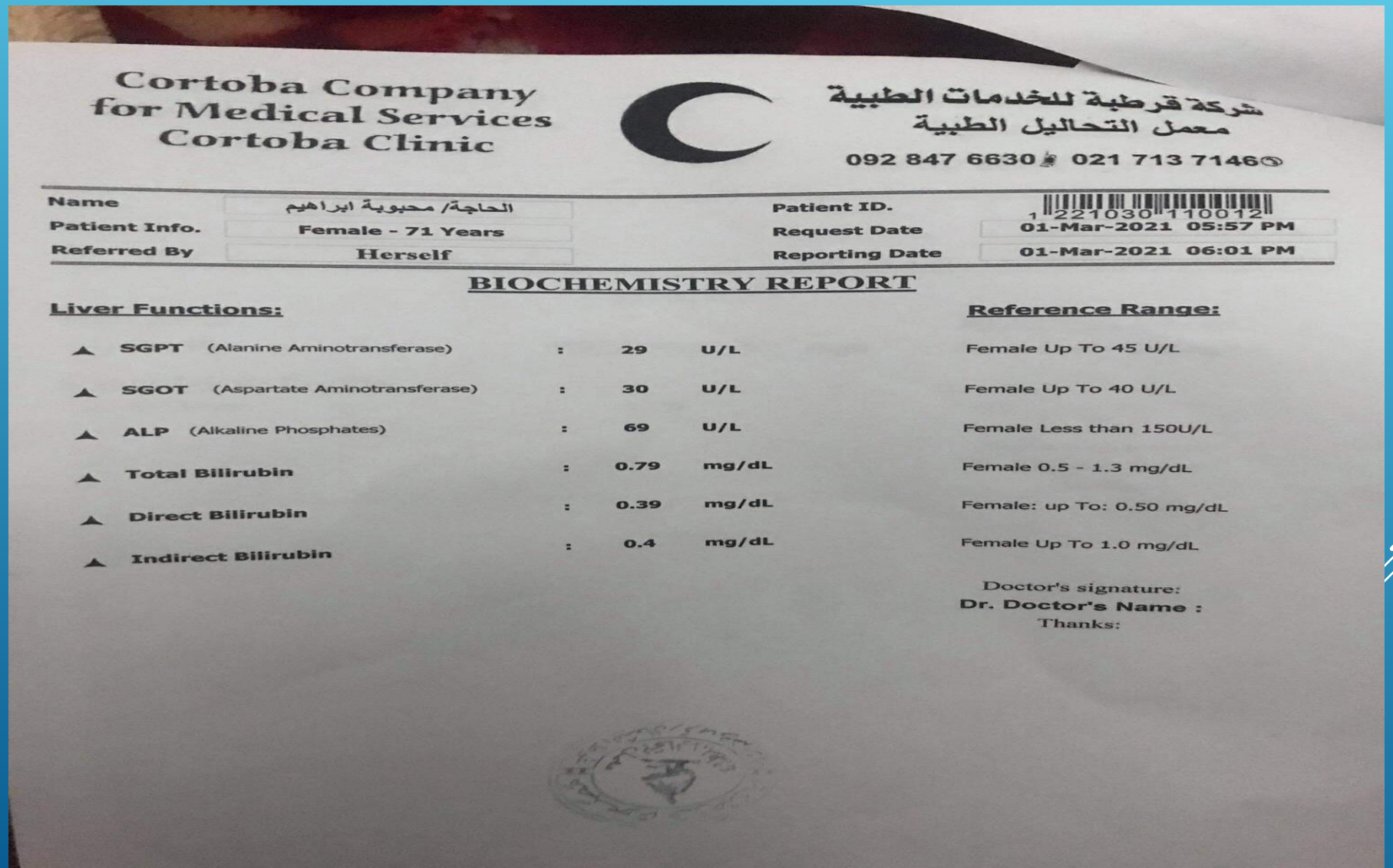
Name	الحاجة/ محبوبة ابراهيم	Patient ID.	1221030110012
Patient Info.	Female - 71 Years	Request Date	01-Mar-2021 05:57 PM
Referred By	Herself	Reporting Date	01-Mar-2021 06:02 PM

HEMATOLOGY REPORT

Coagulation Profile:				Reference Range :
▲ PT (Prothrombin Time)	:			
▪ Patient's time	: 21.5	sec	High	Female 11 - 14 sec
▪ I.N.R.	: 1.7		High	Female 1.0 - 1.3
▲ APTT (Partial Thromboplastin Time)	:			
▪ Patient's time	: 41.3	sec		Female 25 - 45 sec

Doctor's signature:
Dr. Doctor's Name :
Thanks:

LAB RESULTS OF DIABETIC AND HYPERTENSIVE 70 YEARS OLD FEMALE WITH COVID-19 CYTOKINES STORM



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شركة قرطبة للخدمات الطبية
معمل التحاليل الطبية

092 847 6630 021 713 7146

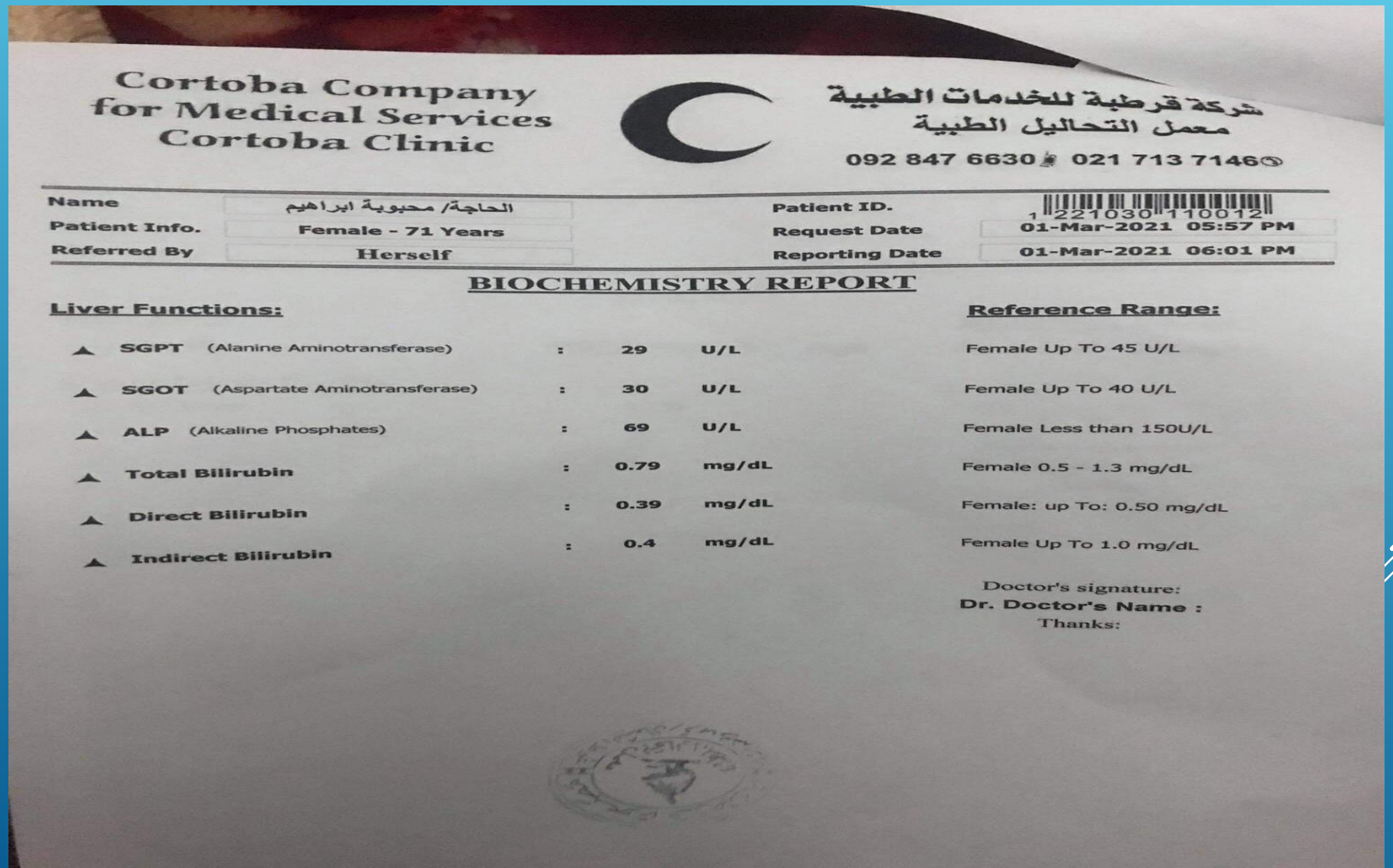
Name	الحاجة/ محبوبة ابراهيم	Patient ID.	1221030110012
Patient Info.	Female - 71 Years	Request Date	01-Mar-2021 05:57 PM
Referred By	Herself	Reporting Date	01-Mar-2021 06:01 PM

BIOCHEMISTRY REPORT

Liver Functions:				Reference Range:
SGPT (Alanine Aminotransferase)	:	29	U/L	Female Up To 45 U/L
SGOT (Aspartate Aminotransferase)	:	30	U/L	Female Up To 40 U/L
ALP (Alkaline Phosphates)	:	69	U/L	Female Less than 150U/L
Total Bilirubin	:	0.79	mg/dL	Female 0.5 - 1.3 mg/dL
Direct Bilirubin	:	0.39	mg/dL	Female: up To: 0.50 mg/dL
Indirect Bilirubin	:	0.4	mg/dL	Female Up To 1.0 mg/dL

Doctor's signature:
Dr. Doctor's Name :
Thanks:

LAB RESULTS OF DIABETIC AND HYPERTENSIVE 70 YEARS OLD FEMALE WITH COVID-19 CYTOKINES STORM



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شركة قرطبة للخدمات الطبية
معمل التحاليل الطبية

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Name	الحاجة/ محبوبة ابراهيم	Patient ID.	1221030110012
Patient Info.	Female - 71 Years	Request Date	01-Mar-2021 05:57 PM
Referred By	Herself	Reporting Date	01-Mar-2021 06:01 PM

BIOCHEMISTRY REPORT

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Direct Bilirubin	:	0.39	mg/dL	Female: up To: 0.50 mg/dL
Indirect Bilirubin	:	0.4	mg/dL	Female Up To 1.0 mg/dL

Doctor's signature:
Dr. Doctor's Name :
Thanks:

LAB RESULTS OF DIABETIC AND HYPERTENSIVE 70 YEARS OLD FEMALE WITH COVID-19 CYTOKINES STORM

1- Prophylaxis

- Vitamin C 500 mg BID and Quercetin 250 mg daily
- Zinc 75-100 mg/day
- Melatonin (slow release): Begin with 0.3mg and increase as tolerated to 2 mg at night
- Vitamin D3 1000-3000 u/day

Health care providers and people who are in contact with covid-19 positive patients
Will add Oral photodynamic methylene blue mouth wash once at night after teeth brush .

2- Asymptomatic patients tested positive for covid-19

#Oral photodynamic methylene blue mouth wash q 6 hours

- Vitamin C 1000 mg BID and Quercetin 500 mg daily
- Zinc 100 mg/day
- Melatonin 10 mg at night
- Vitamin D3 5000 u/day
- Famotidine 40mg bid

LAB RESULTS OF DIABETIC AND HYPERTENSIVE 70 YEARS OLD FEMALE WITH COVID-19 CYTOKINES STORM

3- Mildly Symptomatic patients (at home):
Cough , fever , fatigue and oxygen saturation above 94 %

Oral photodynamic methylene blue mouth wash q 6 hours and oral methylene blue 10 mg bid

■ Vitamin C 2500 mg BID and Quercetin 1000 mg BID
Zinc 100 mg/day
Melatonin 12 mg at night Vitamin D3 10000 u/day
ASA aspirin 81-325 mg/day (unless contraindicated)
■ Famotidine 40mg BID (reduce dose with renal impairment)
In symptomatic patients, monitoring with home pulse oximetry is recommended.
Ambulatory desaturation below 94% should prompt hospital admission
Oral losartan 25-50 mg daily

LAB RESULTS OF DIABETIC AND HYPERTENSIVE 70 YEARS OLD FEMALE WITH COVID-19 CYTOKINES STORM

4- Moderate Symptomatic patients with oxygen saturation above 84% and below 94%

Intranasal oxygen therapy

- Vitamin C 5000 mg PO q 6 hourly and Quercetin 500 mg BID (if available)
- Zinc 100 mg/day
- Melatonin 12 mg at night
- Vitamin D3 50000 IU single oral dose. Calcifediol 500 ug is an alternative. This should be followed by 20 000u D3 (or 200ug calcifediol) weekly until discharged from hospital.
- Enoxaparin 60 mg daily
- Famotidine 40mg BID (reduce dose with renal impairment

Oral or inhaled losartan 25-50 mg daily !!

LAB RESULTS OF DIABETIC AND HYPERTENSIVE 70 YEARS OLD FEMALE WITH COVID-19 CYTOKINES STORM

5- Sever symptomatic patients with oxygen saturation below 84%

Oral photodynamic methylene blue mouth wash q 6 hours
Oxygen therapy (intranasal or ventilation)
Intravenous vitamin C 50 mg/kg q 6 hours
Intravenous methylene blue 1 mg/kg q12 hours
Intravenous or oral dexamethasone 6 mg/day for a week or Methylprednisolone 40 mg q 12 hourly; increase to 80 mg q 12 if poor response for a week.
Intravenous Covid-19 Convalescence plasma or monoclonal antibody
Intravenous Calcifediol 500 ug
Oral Zinc 100 mg daily
Intravenous quercetin 100 mg daily or or 500 mg orally bid
Remdisivir 200 mg on Day 1 followed by once-daily maintenance doses of 100 mg for 5 days .
Aspirin 81-325 mg daily
Famotidine 40 mg bid
Enoxaparin 60 mg daily
Oral or inhaled losartan 25-50 mg daily