

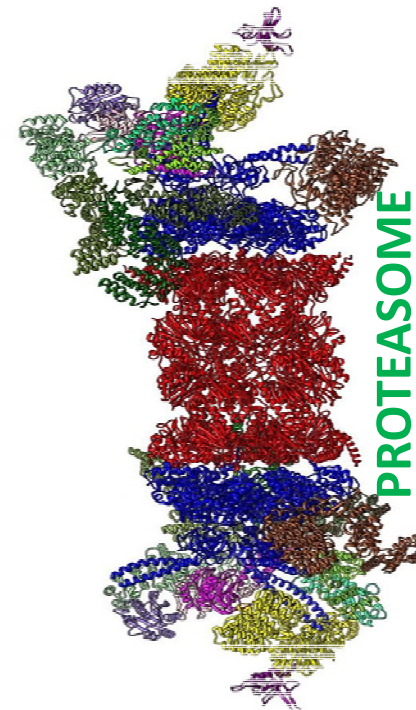


**23^ο ΕΤΗΣΙΟ ΣΕΜΙΝΑΡΙΟ
ΣΥΝΕΧΙΖΟΜΕΝΗΣ ΙΑΤΡΙΚΗΣ ΕΚΠΑΙΔΕΥΣΗΣ
Γ.Ν.Α. «Ο ΕΥΑΓΓΕΛΙΣΜΟΣ»
1 ΜΑΡΤΙΟΥ 2018**

**Νεότερα δεδομένα για την εμμένουσα
πολυοργανική ανεπάρκεια στους χρονίως
βαρέως πάσχοντες ασθενείς: σύνδρομο
PICS**



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Α' ΚΕΘ ΙΑΤΡΙΚΗΣ ΣΧΟΛΗΣ ΕΚΠΑ
ΓΝΑ 'Ο ΕΥΑΓΓΕΛΙΣΜΟΣ'**





23^ο Ετήσιο Σεμινάριο Συνεχιζόμενης
Ιατρικής Εκπαίδευσης
Νοσοκομείου «Ο Ευαγγελισμός»



Αθήνα, 26 Φεβρουαρίου – 2 Μαρτίου 2018

Δεν υπάρχει σύγκρουση συμφερόντων
με τις παρακάτω χορηγούς εταιρείες:

NOVARTIS, JANSSEN ONCOLOGY, ABBVIE,
BRISTOL-MYERS SQUIBB, MEDTRONIC,
TAKEDA, GENESIS, MSD, PFIZER, AMGEN,
ASTELLAS, GILEAD, AENORASIS, BAXTER,
BIANEX, WINMEDICA, ABBOTT, BIOSEP,
SANOFI, ANGELINI, DEMO, ELPEN,
EDWARDS, ROCHE, RONTIS, SPECIFAR, UCB,
ΥΓΕΙΟΔΥΝΑΜΙΚΗ, MAVROGENIS

Persistent Inflammation/Immunoparalysis and Catabolism Syndrome

PICS ≠ Post ICU Syndrome

Synonyms:

- **Chronic Critical Illness Syndrome**
- **Persistent/Chronic MOF**

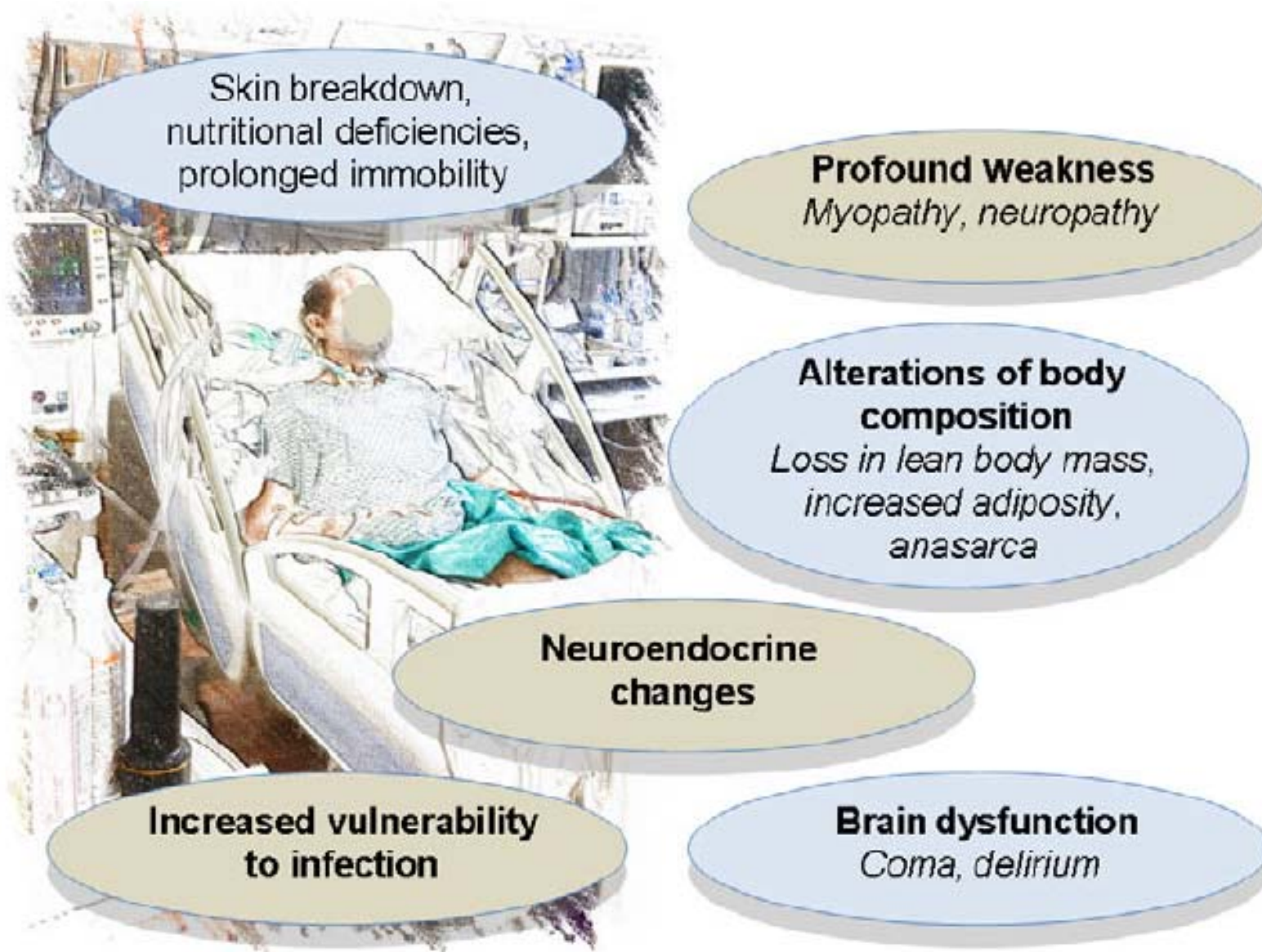
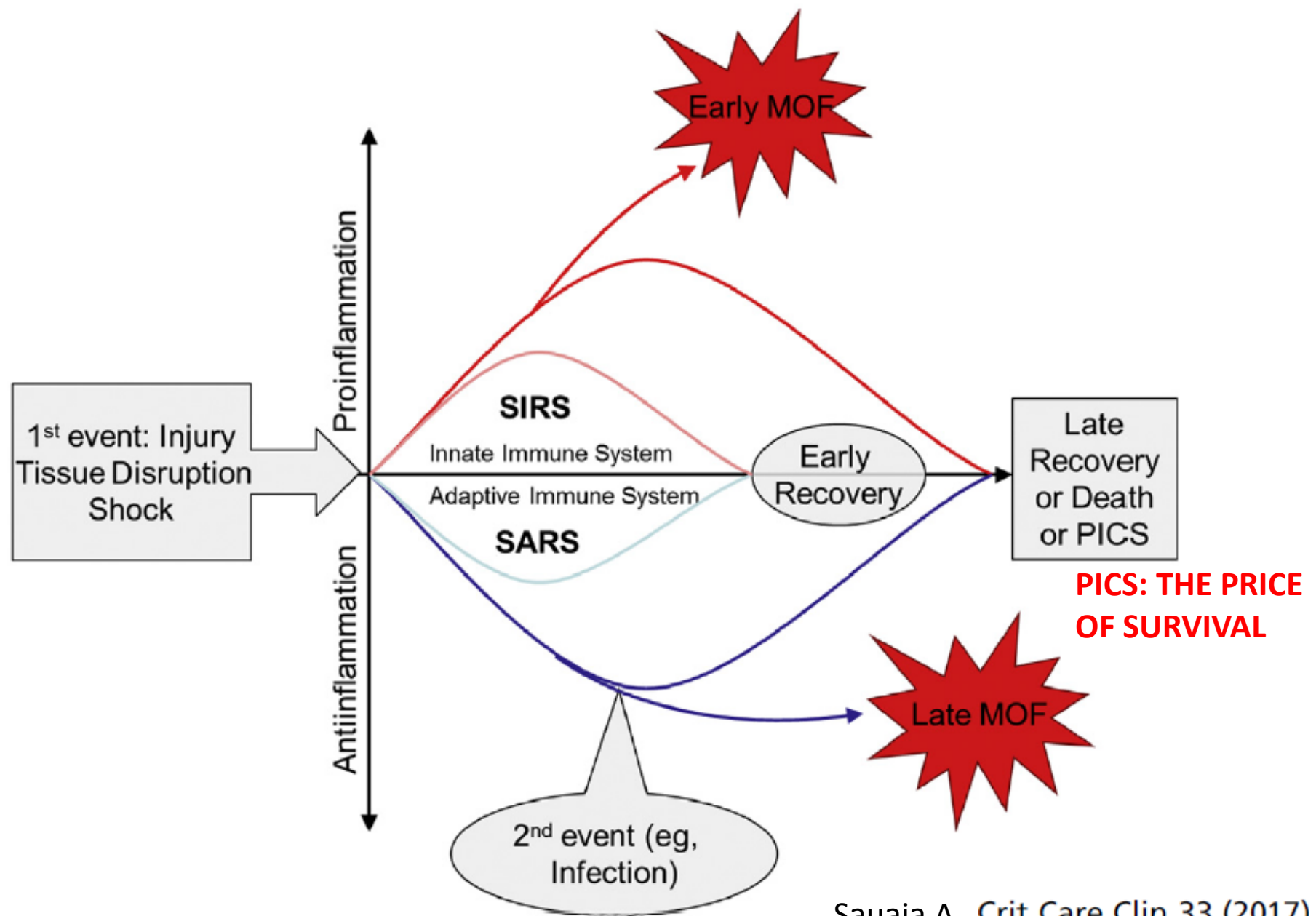


Figure 1 Clinical features of chronic critical illness

PICS: A NEW PHENOTYPE





40 ημέρες μετά

Άνδρας 57 ετών
ΑΙΤΙΑ ΕΙΣΟΔΟΥ: ΔΙΑΤΡΗΣΗ 12/ΛΟΥ...



30 ημέρες μετά

Άνδρας 65 ετών

ΑΙΤΙΑ ΕΙΣΟΔΟΥ: ΡΗΞΗ ΑΝΕΥΡΥΣΜΑΤΟΣ ΚΟΙΛΙΑΚΗΣ ΑΟΡΤΗΣ...

Concise Clinical Review

Chronic Critical Illness

Judith E. Nelson¹, Christopher E. Cox², Aluko A. Hope^{1,3}, and Shannon S. Carson⁴

Am J Respir Crit Care Med Vol 182. pp 446–454, 2010

TABLE 1. OUTCOMES OF CHRONIC CRITICAL ILLNESS RELATIVE TO COHORT DEFINITION*

Cohort Definition	Ventilation for ≥ 14 d	Ventilation for ≥ 21 d		Tracheotomy for Prolonged Mechanical Ventilation	
Study (reference)	Combes <i>et al.</i> (34)	Carson <i>et al.</i> (25)	Cox <i>et al.</i> [†] (24)	Cox <i>et al.</i> [†] (24)	Engoren <i>et al.</i> (14)
n	347	200	114	267	347
Age (yr), median (IQR) or mean $\pm$ SD	63 $\pm$ 14, 67 $\pm$ 13 [‡]	58 (42–69)	66 (47–74)	66 (45–75)	64, 71 [§]
Duration of ventilation, median (IQR) or mean $\pm$ SD	36 $\pm$ 25, 37 $\pm$ 28 [‡]	35 (26–51)	27 (23–36)	16 (10–24)	23–30
Hospital length of stay, median (IQR)	—	51 (36–72)	39 (30–52)	29 (22–38)	28–37
Died in hospital, %	43	41	31	20	22
Discharged home, %	—	11	4	7	—
Alive at 12 mo, %	32	48	42	52	50

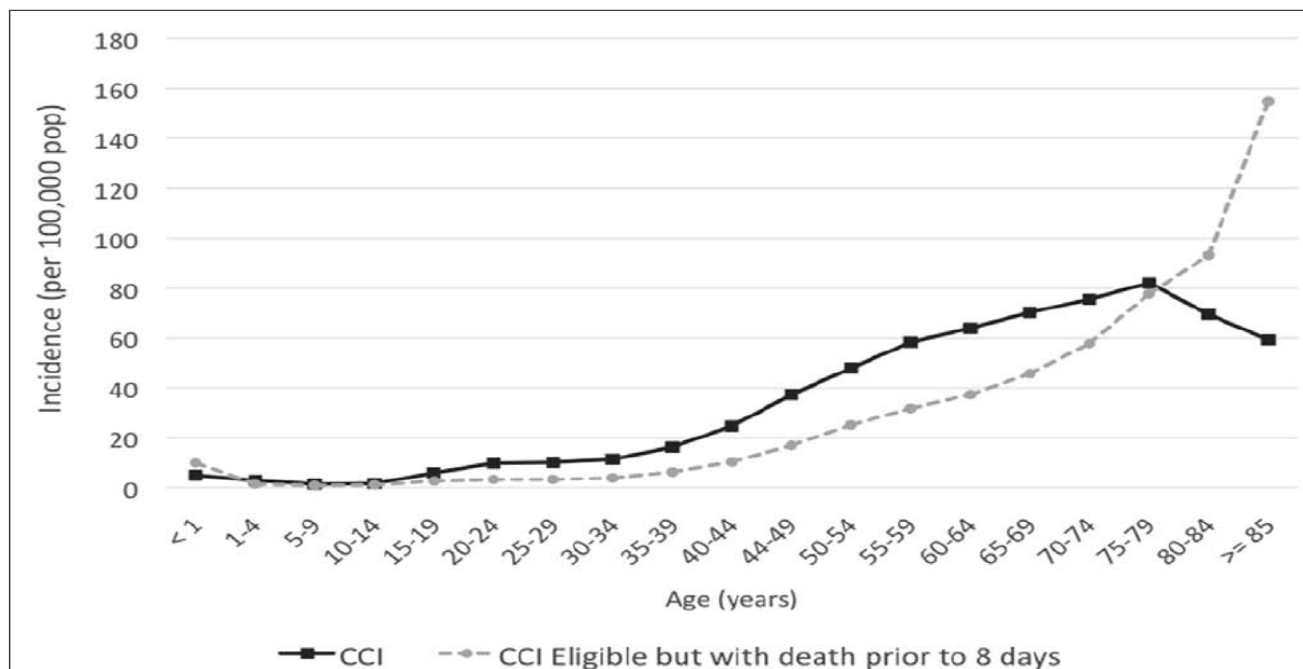
The Epidemiology of Chronic Critical Illness in the United States*

Jeremy M. Kahn, MD, MS^{1,2}; Tri Le, MS²; Derek C. Angus, MD, MPH^{1,2}; Christopher E. Cox, MD, MPH³; Catherine L. Hough, MD, MS⁴; Douglas B. White, MD, MAS¹; Sachin Yende, MD, MS¹; Shannon S. Carson, MD⁵; for the ProVent Study Group Investigators

Critical Care Med 2015

TABLE 2. Estimated Annual Number of Cases, Mortality, and Hospital Costs of Chronic Critical Illness in the United States, by Year

Year	2004	2005	2006	2007	2008	2009
Cases (n)	302,173	317,451	324,790	339,930	365,817	380,001
Mortality, n (%)	100,552 (33.3)	103,357 (32.6)	102,018 (31.4)	104,067 (30.6)	111,348 (30.4)	107,880 (28.3)
Costs (billions) ^a	\$15.6	\$17.5	\$19.4	\$21.8	\$24.7	\$26.0



PICS

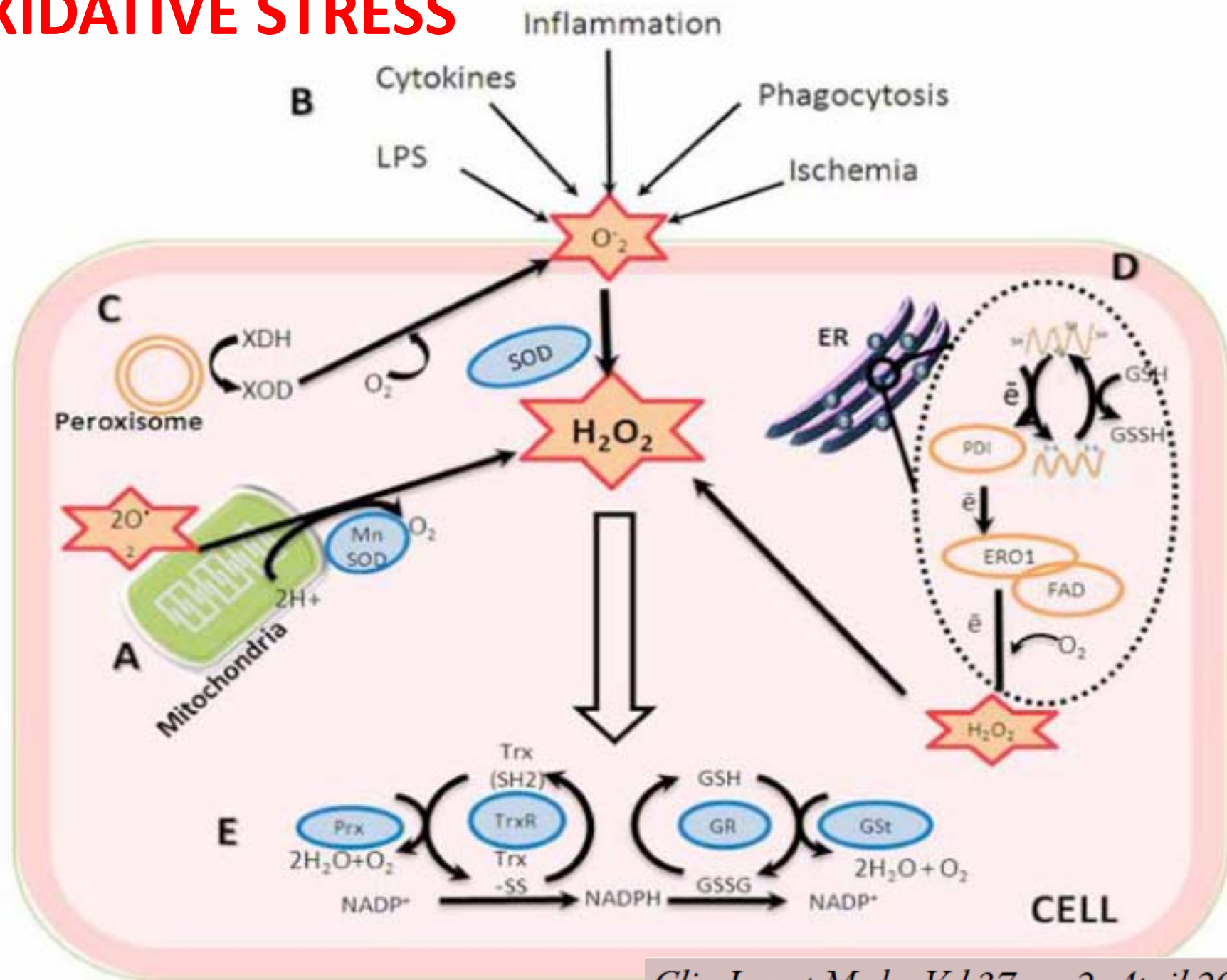
TABLE 3. PICS Criteria

**Clinical Determinants of
PICS**

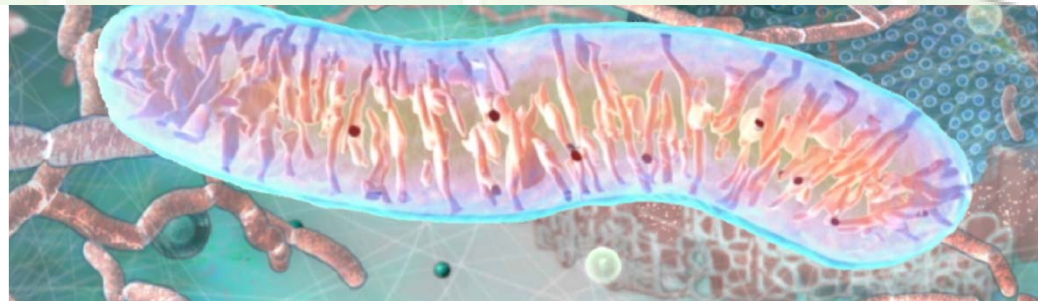
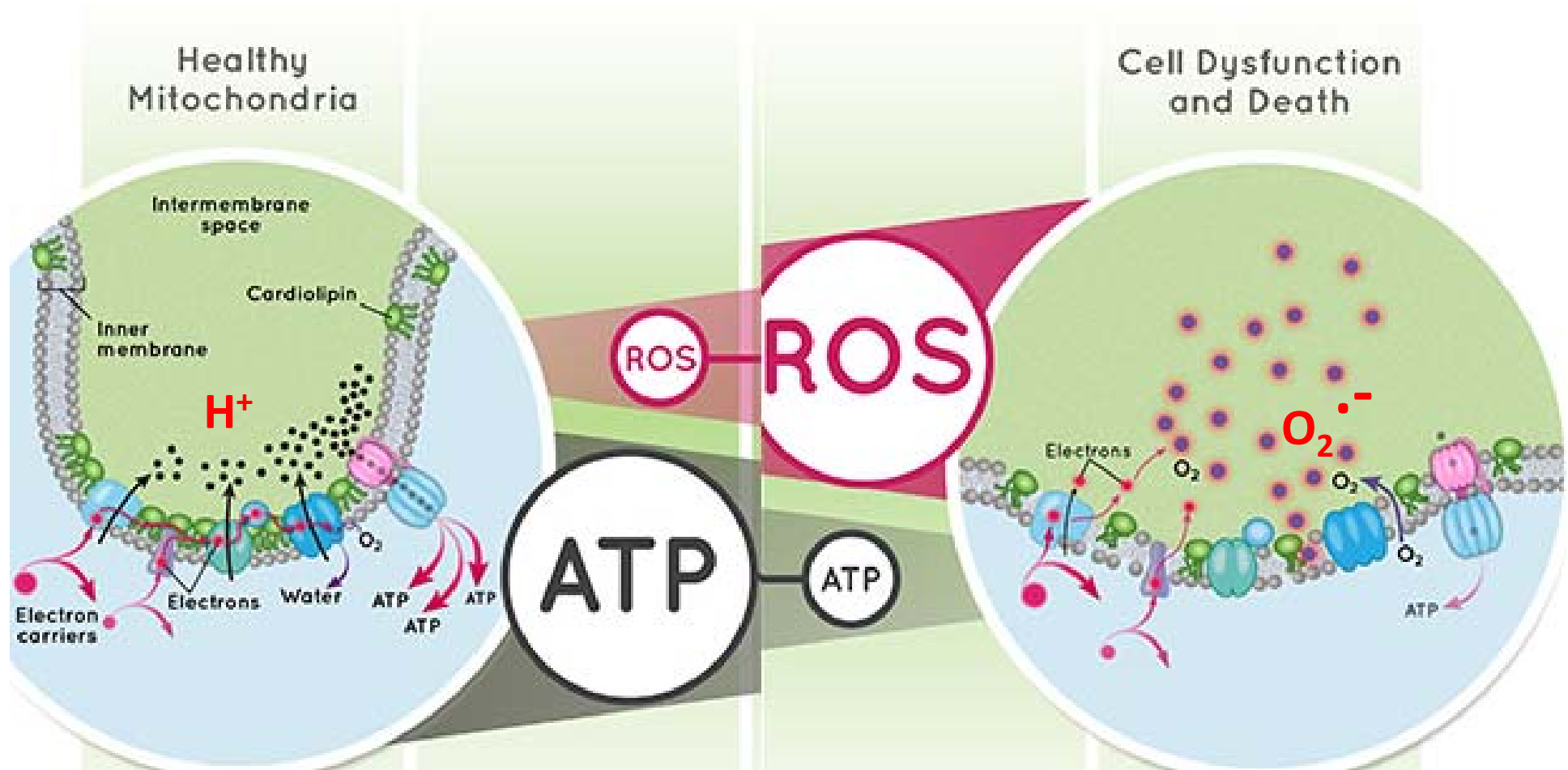
Measurements

Persistent	Prolonged ICU stay >10 d
Inflammation	C-reactive protein >150 µg/dL
Immunosuppression	Total lymphocyte count <0.80 × 10 ⁹ /L
Catabolism	Weight loss >10% during hospitalization or body mass index <18
	Creatinine height index <80%
	Albumin level <3.0 g/dL
	Prealbumin level <10 mg/dL
	Retinol binding protein level <10 µg/dL

OXIDATIVE STRESS



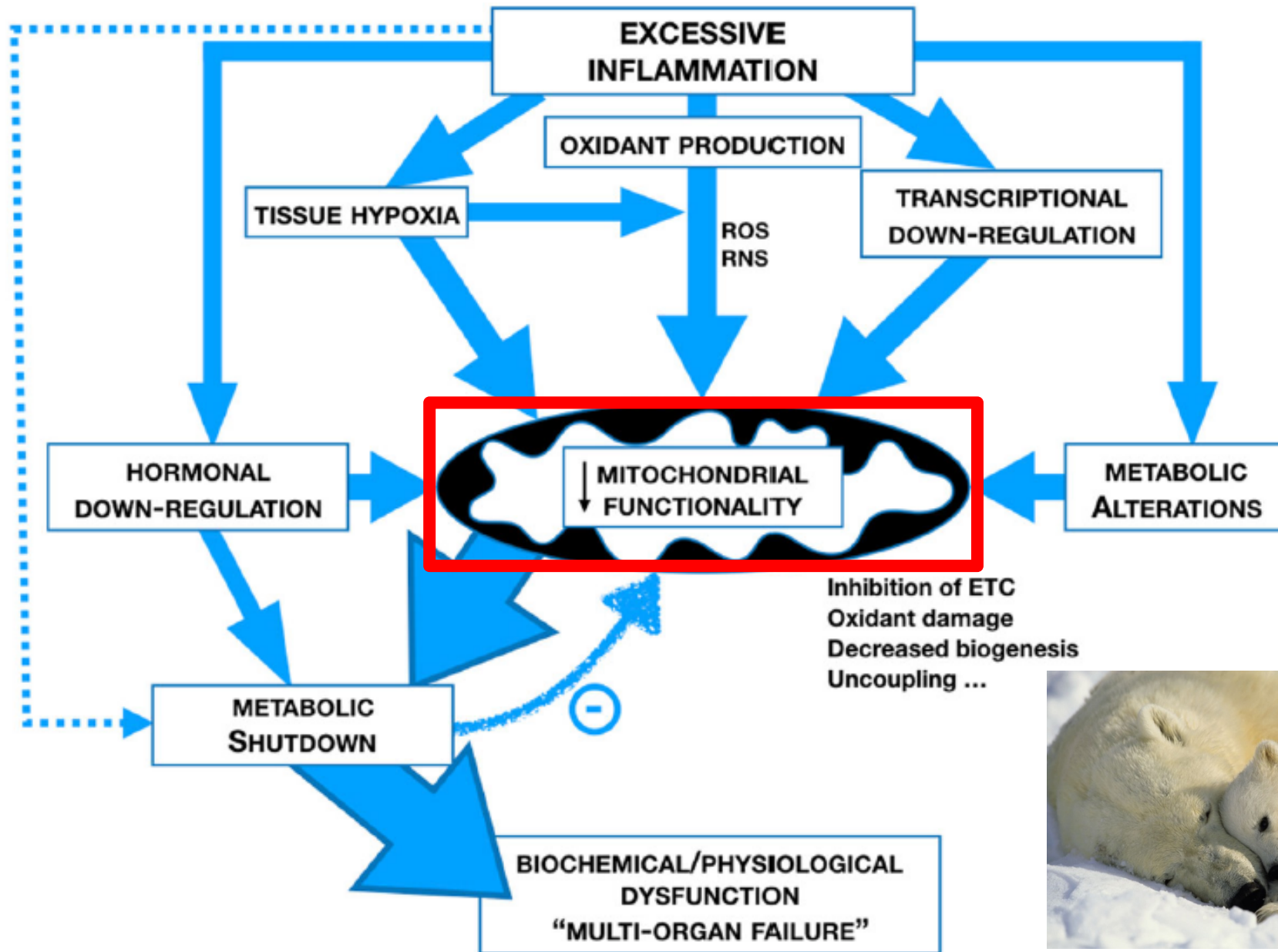
MITOCHONDRIAL DYSFUNCTION AND BIOENERGETIC FAILURE



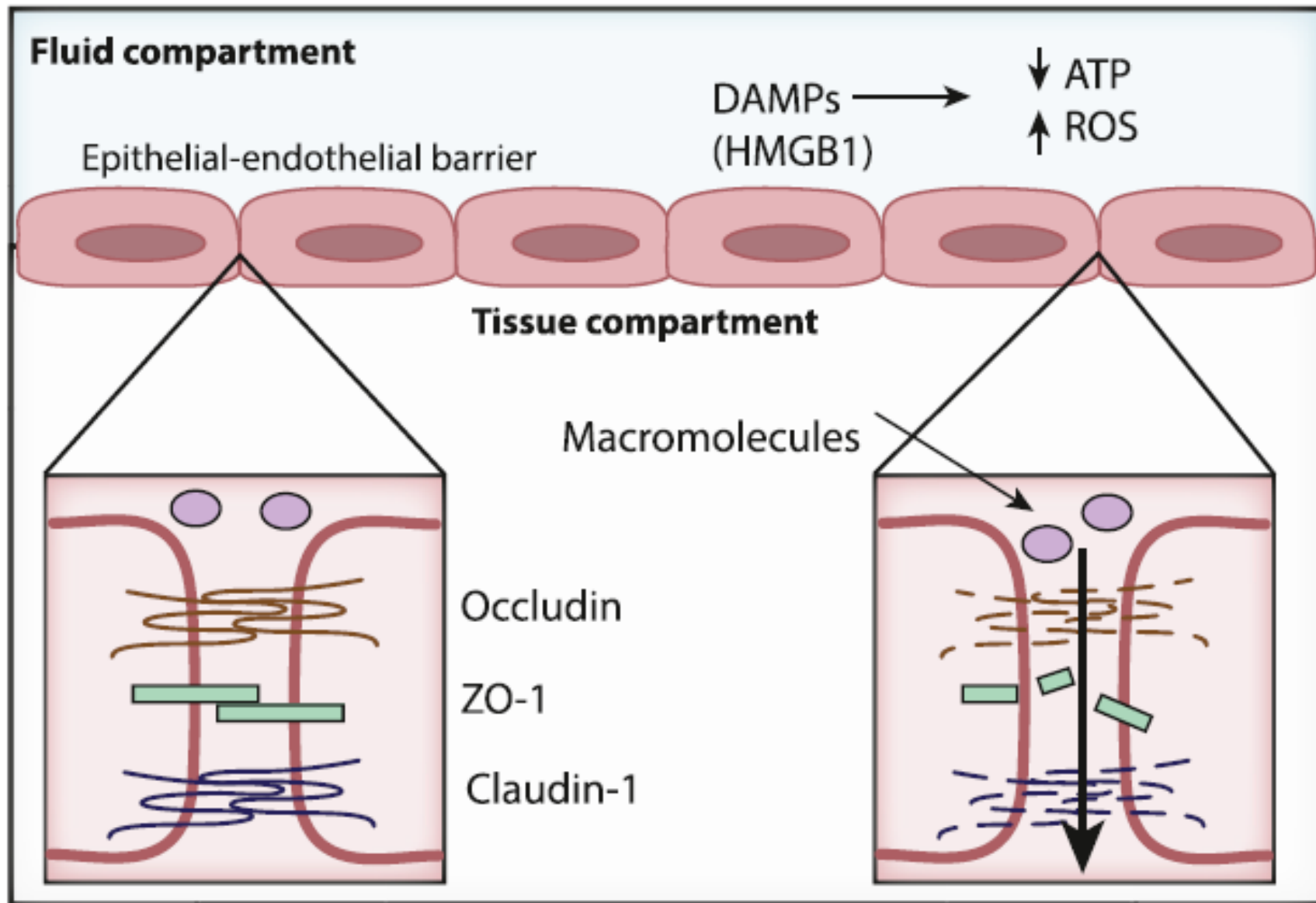
Mitophagy
Biogenesis



METABOLIC SHUTDOWN~HIBERNATION~ESTIVATION

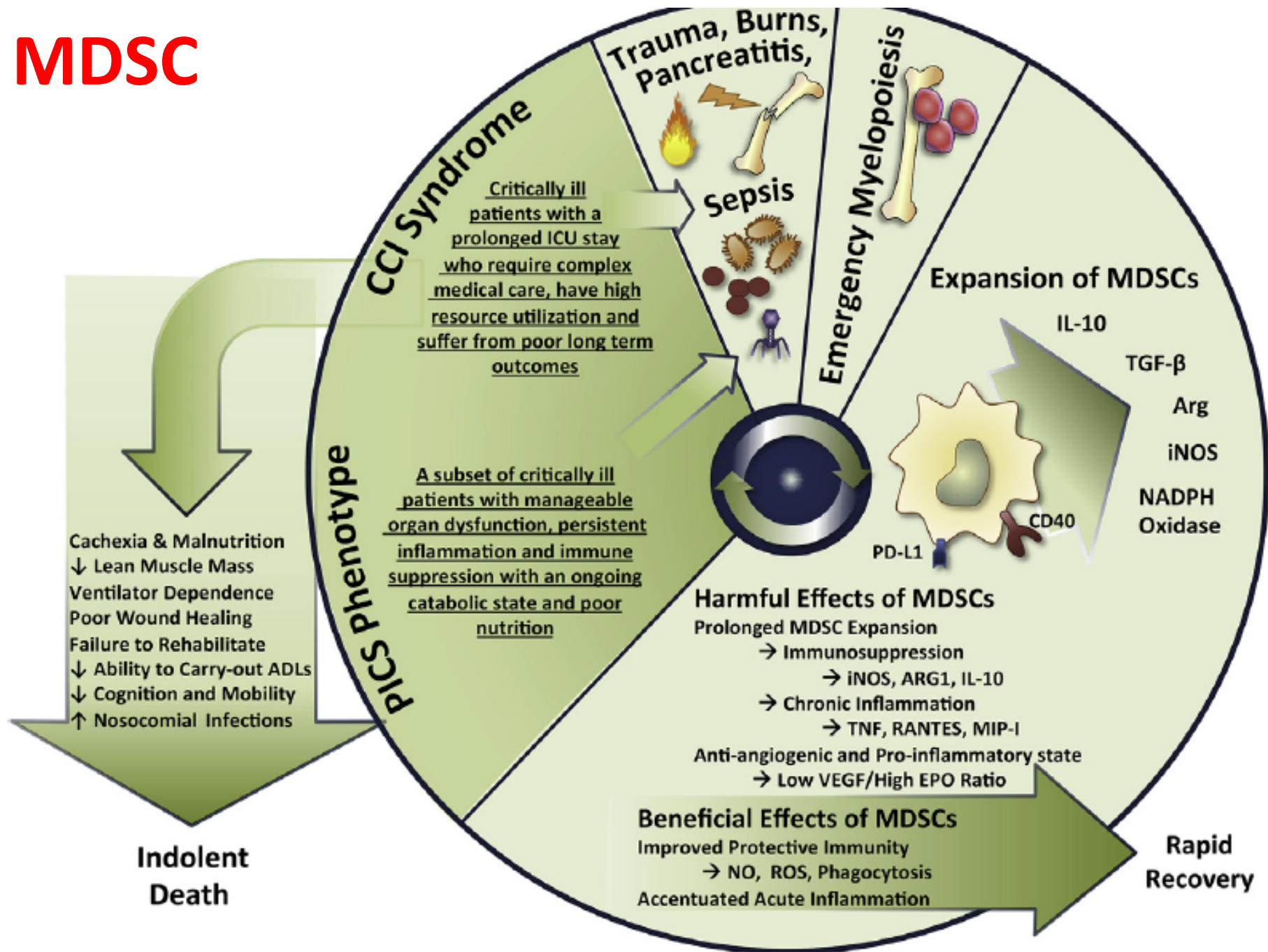


ENDOTHELIOPATHY: BARRIER FAILURE



Deutschman C. *Immunity* 40, April 17, 2014

MDSC



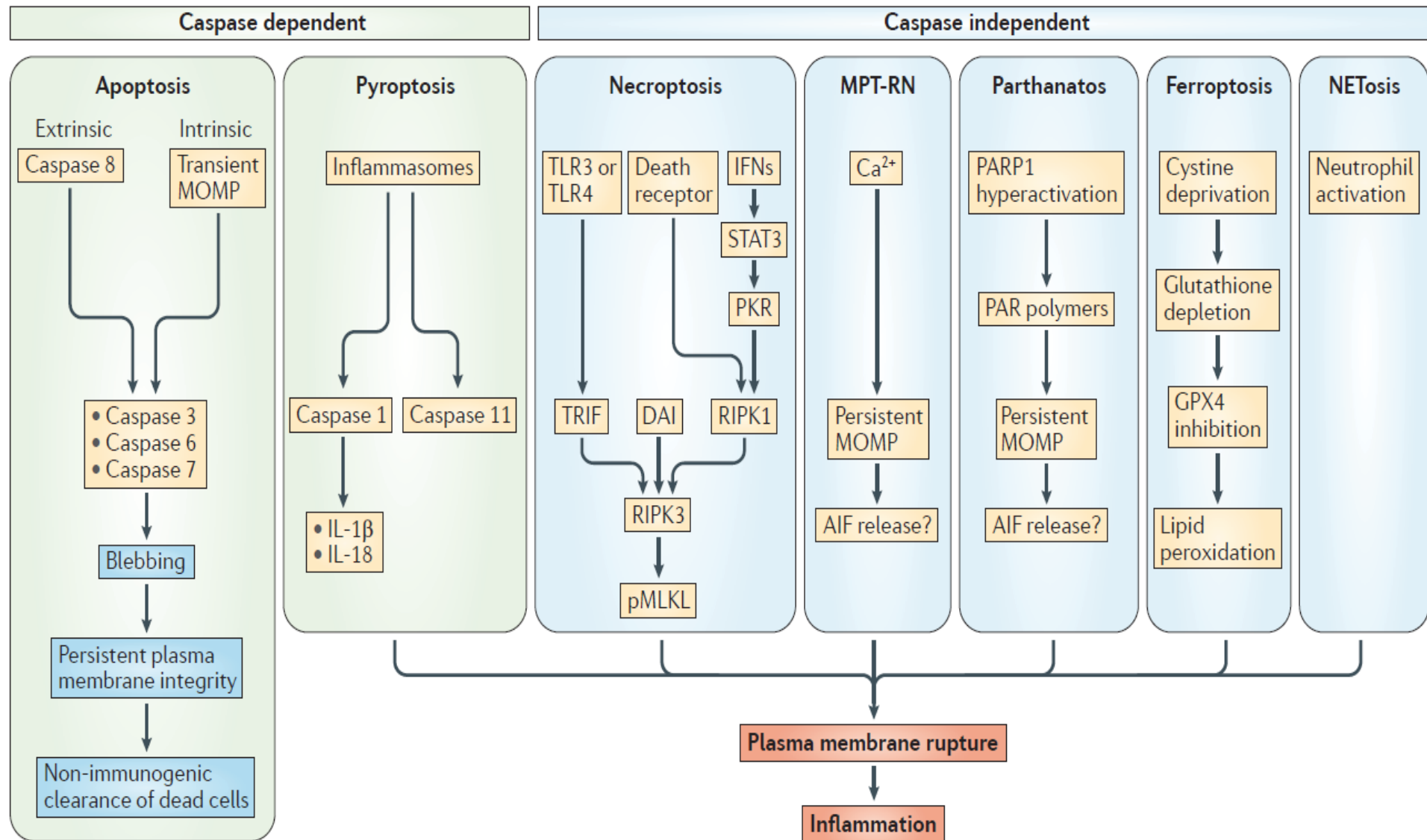
OVERVIEW OF SEPSIS IMMUNOPARALYSIS

1. Lymphocyte Apoptosis
2. mHLA-DR reduction
3. $Th_2 > Th_1$
4. T regulatory cells increase
5. $M_2 > M_1$
6. MDSC
7. TCR diversity reduction
8. Virome reactivation
9. PD_1 / $PD-L_1$ axis activation
10. Suppressive neutrophils

- *No clearance of primary infection*
- *Nosocomial infections with opportunistic germs*
- *Reactivation of dormant viruses*

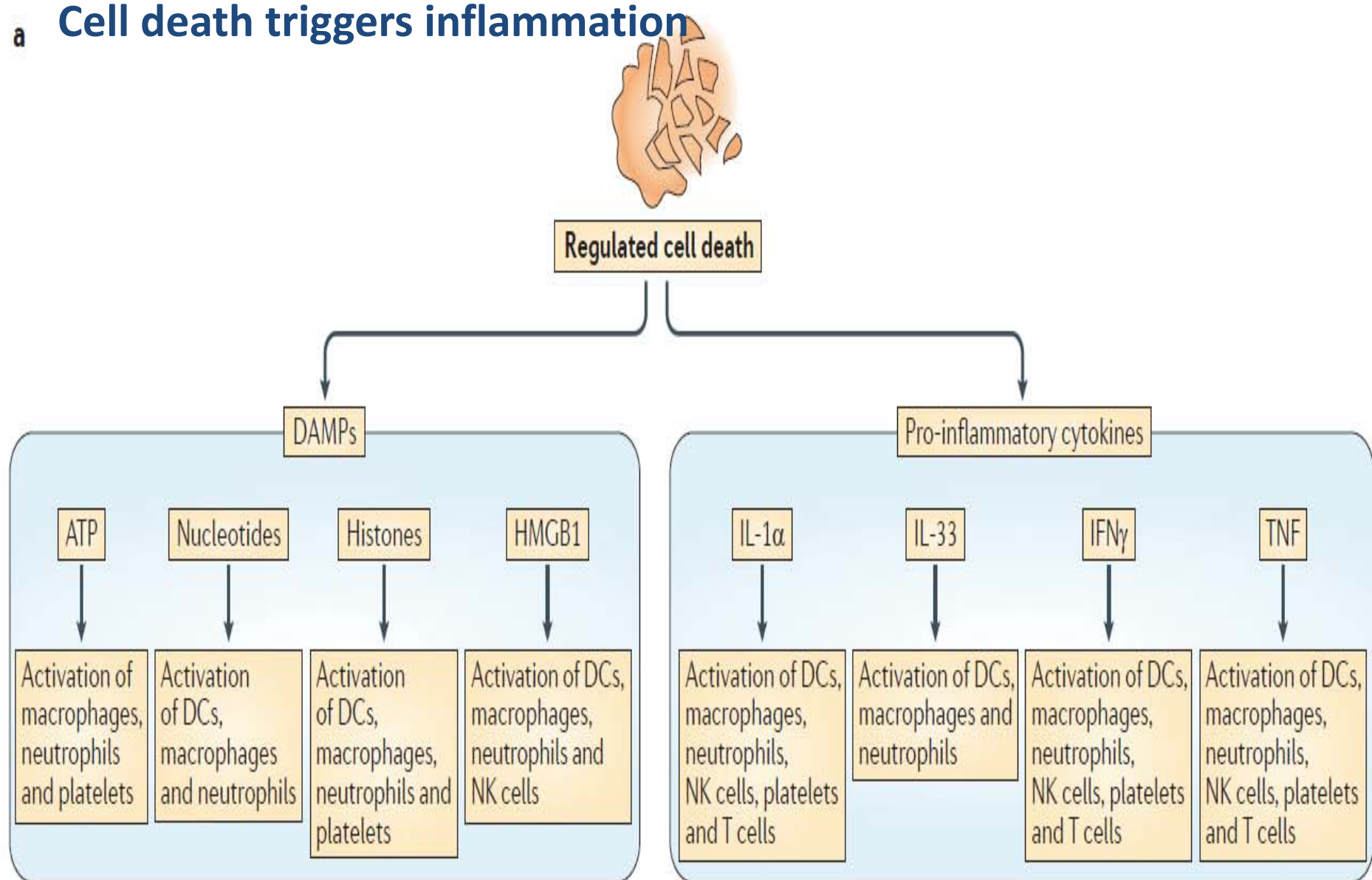


Regulated Cell Death



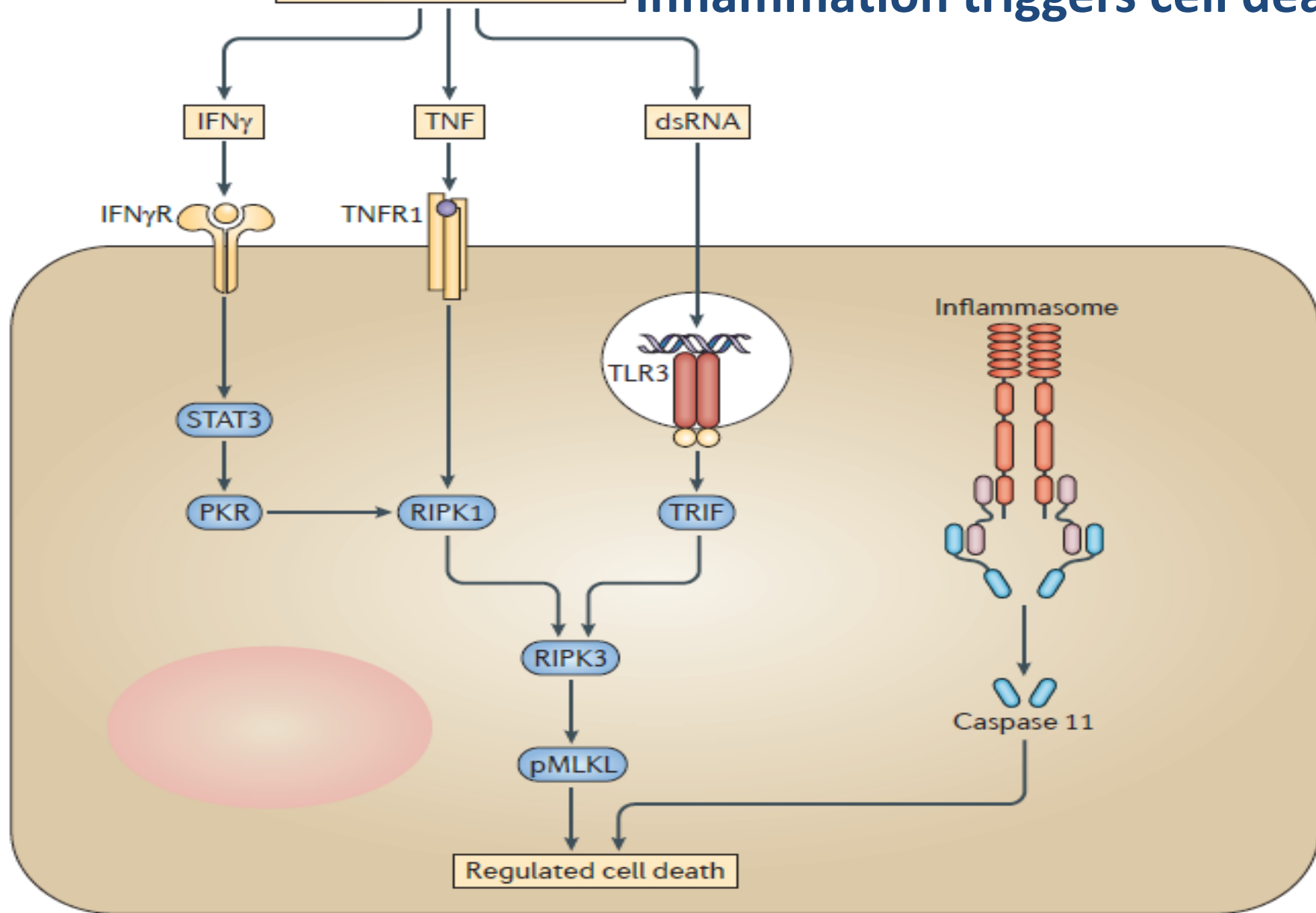
Linkermann A. Nat Rev Immun. 2014

a Cell death triggers inflammation



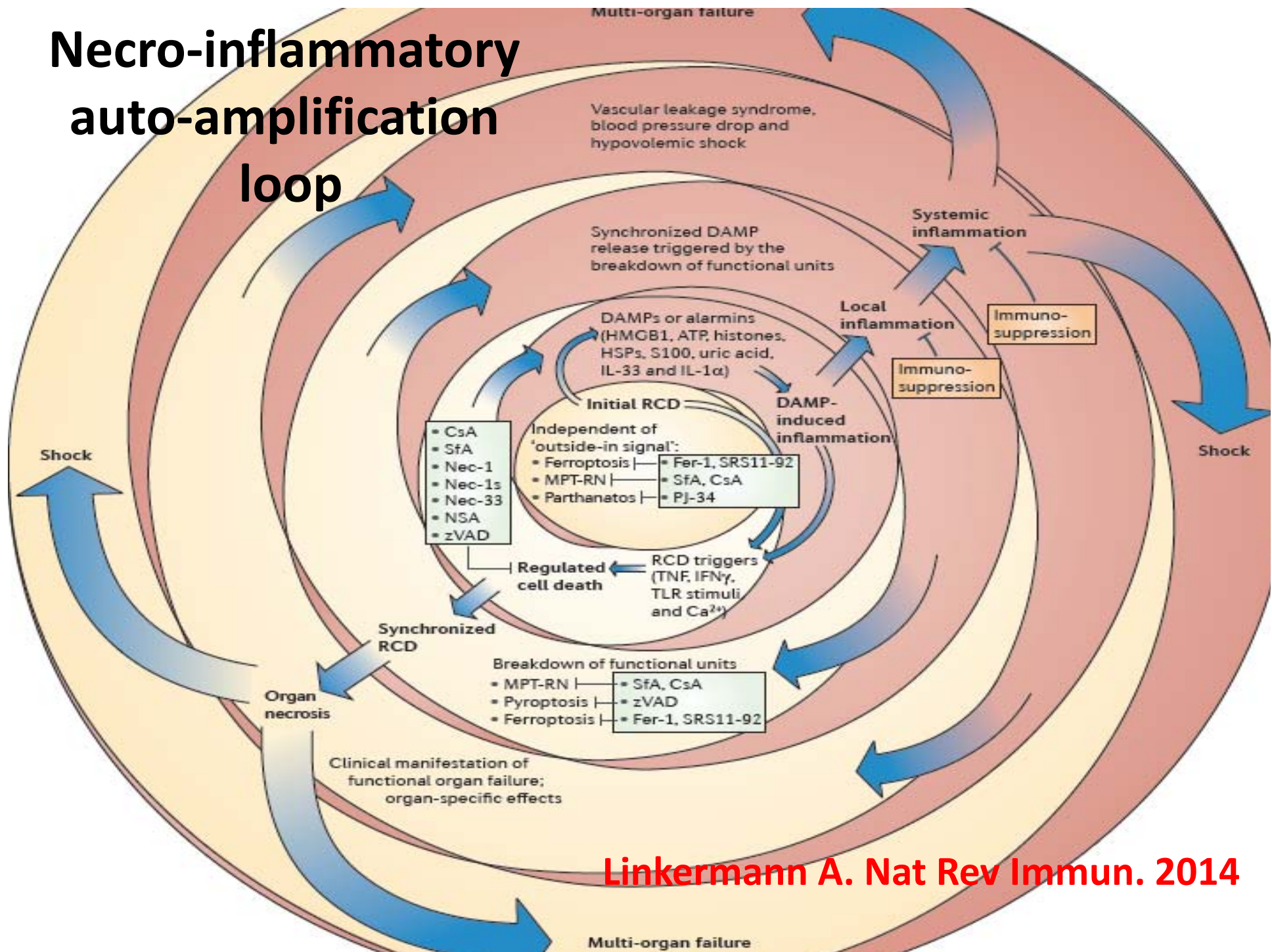
b**Infiltrating immune cells**

Inflammation triggers cell death



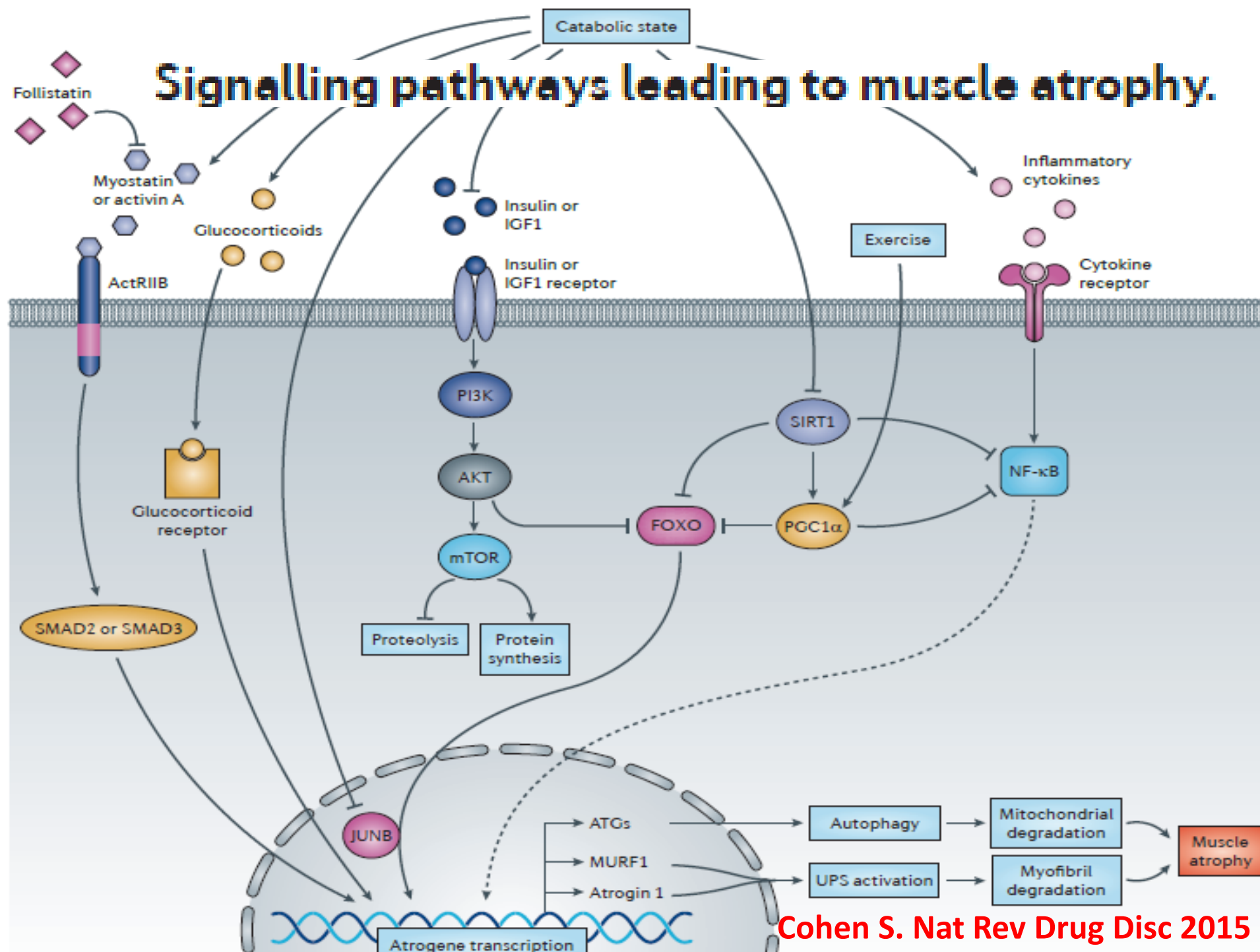
Linkermann A. Nat Rev Immun. 2014

Necro-inflammatory auto-amplification loop



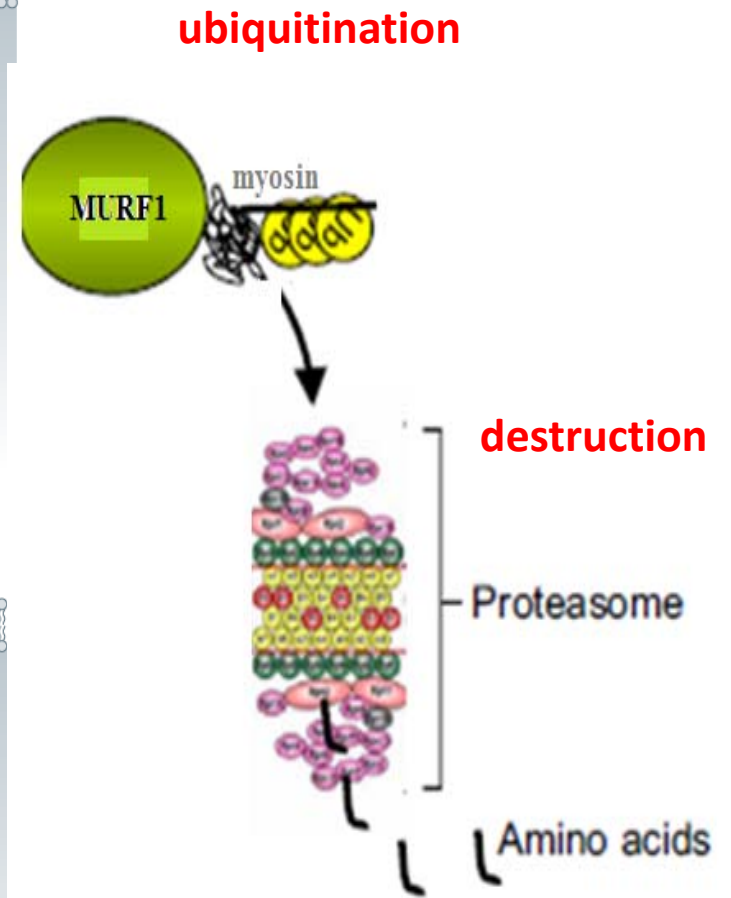
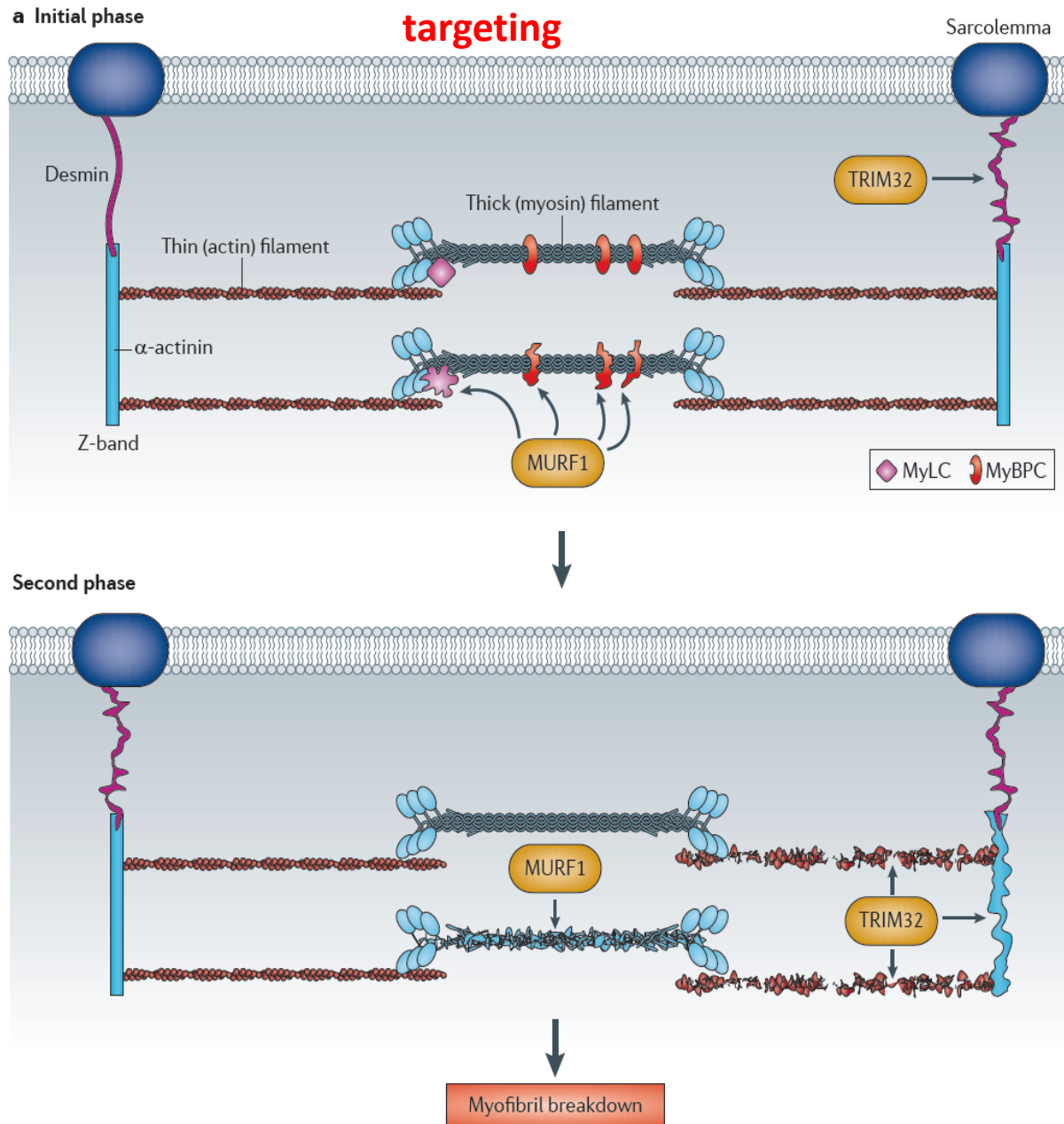
Linkermann A. Nat Rev Immun. 2014

Signalling pathways leading to muscle atrophy.



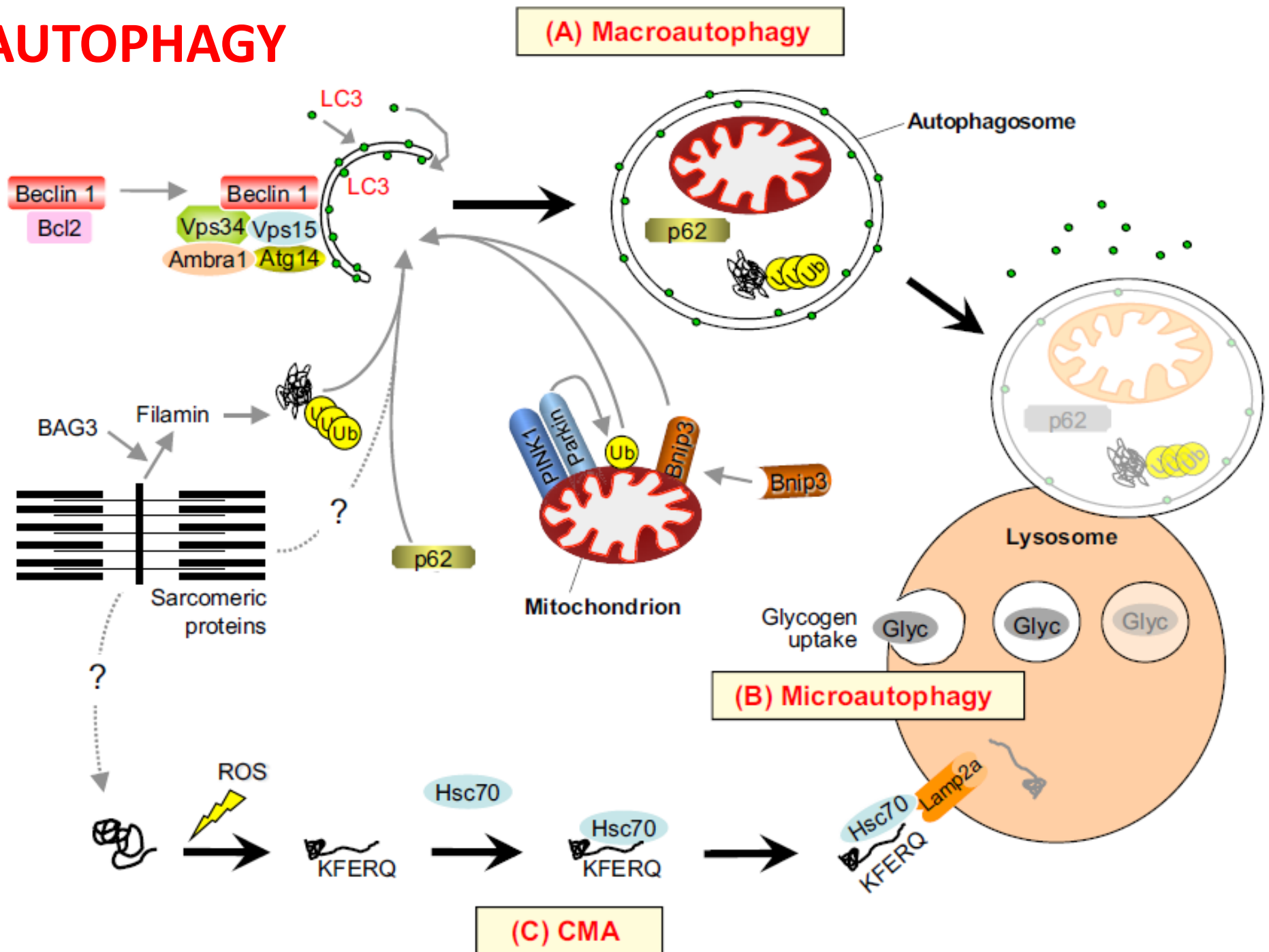
Cohen S. Nat Rev Drug Disc 2015

Mechanisms of myofibril breakdown and atrophy.

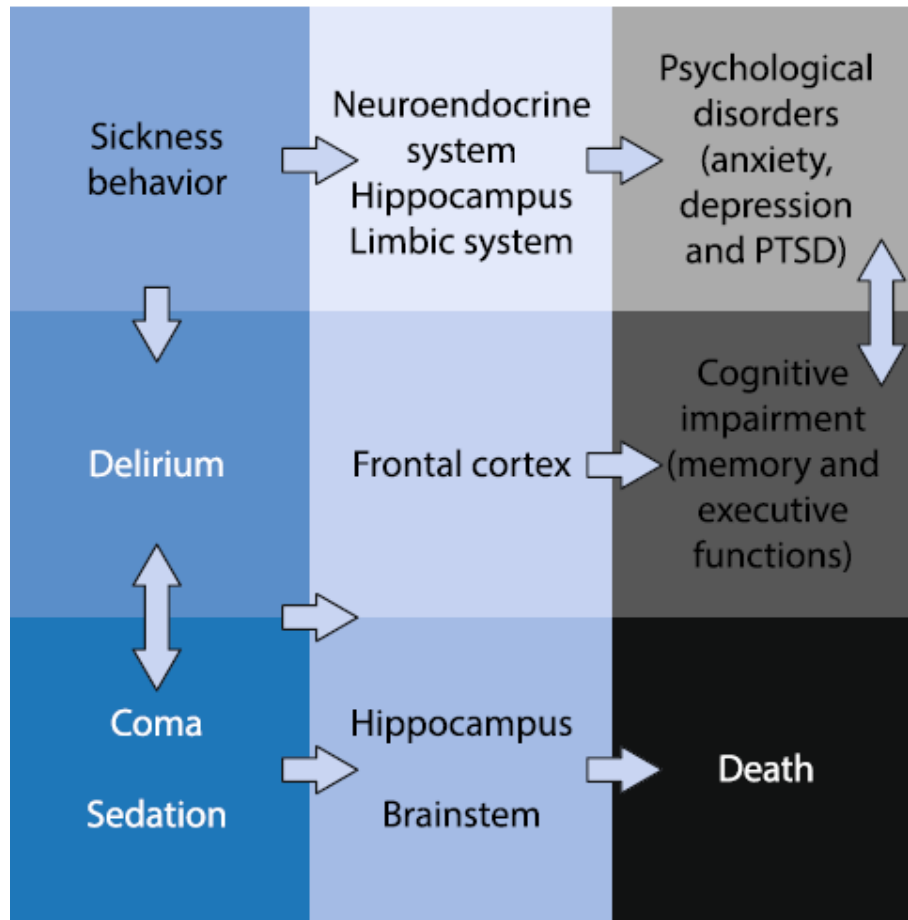


Disease Models & Mechanisms 6, 25-39 (2013)

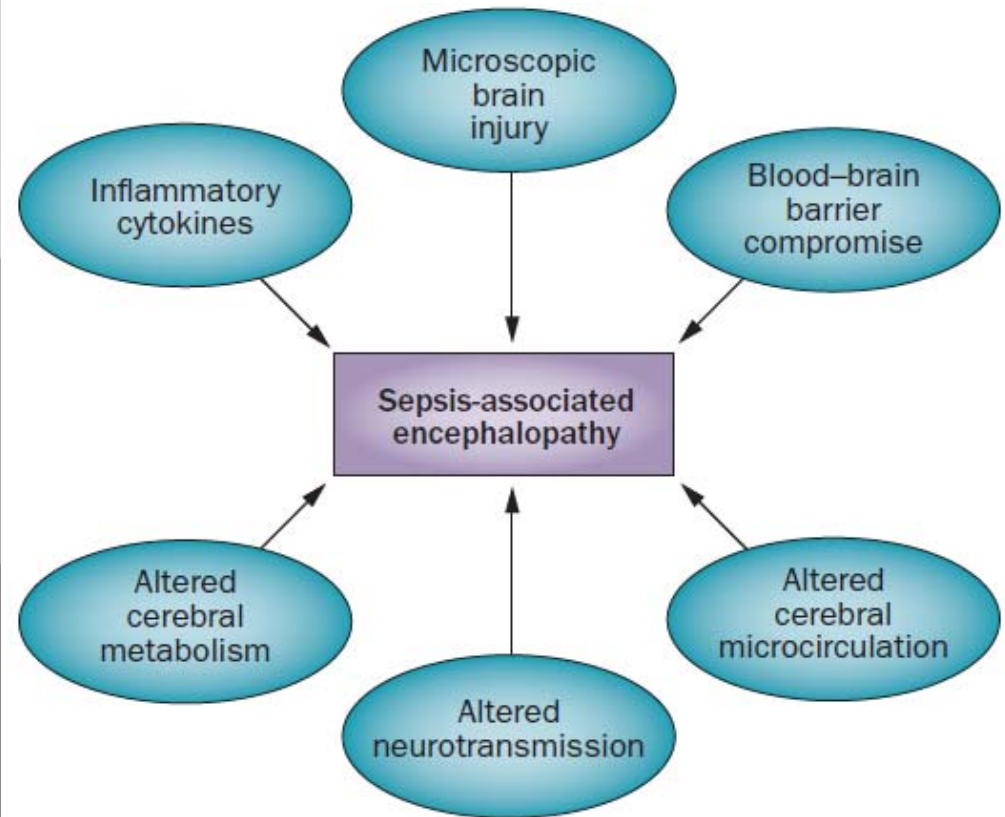
AUTOPHAGY



ENCEPHALOPATHY



Heming *et al. Critical Care* (2017)

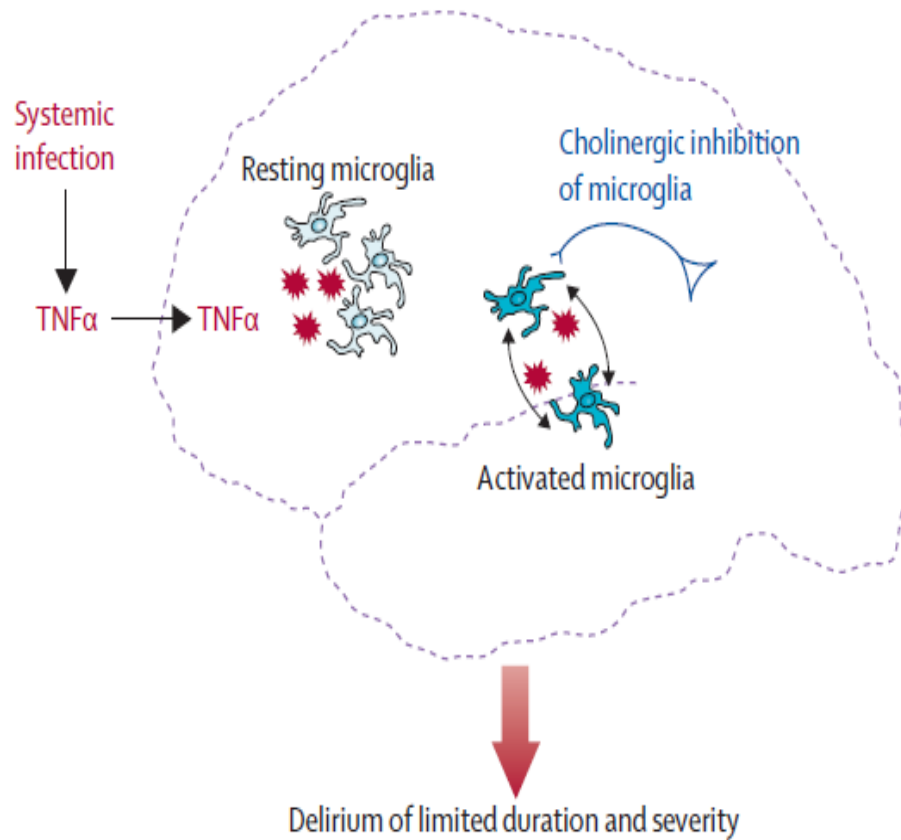


Gofton, T. E. & Young, G. B. *Nat. Rev. Neurol.* 8, 557–566 (2012)

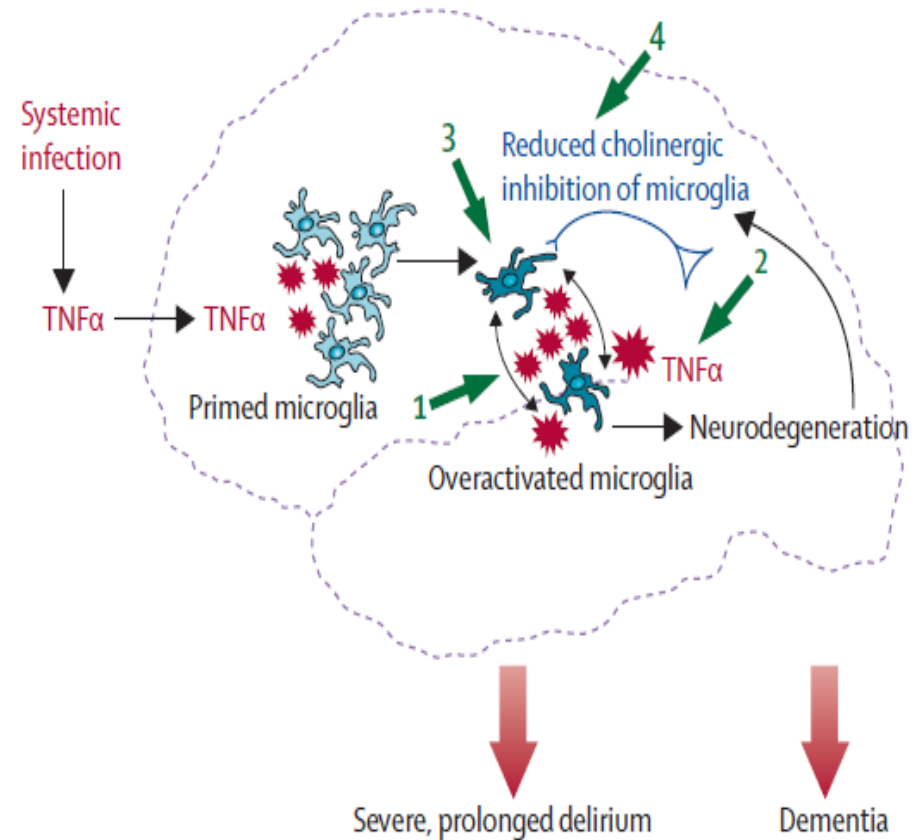
Systemic infection and delirium: when cytokines and acetylcholine collide

Willem A van Gool, Diederik van de Beek, Piet Eikelenboom

A Normal situation

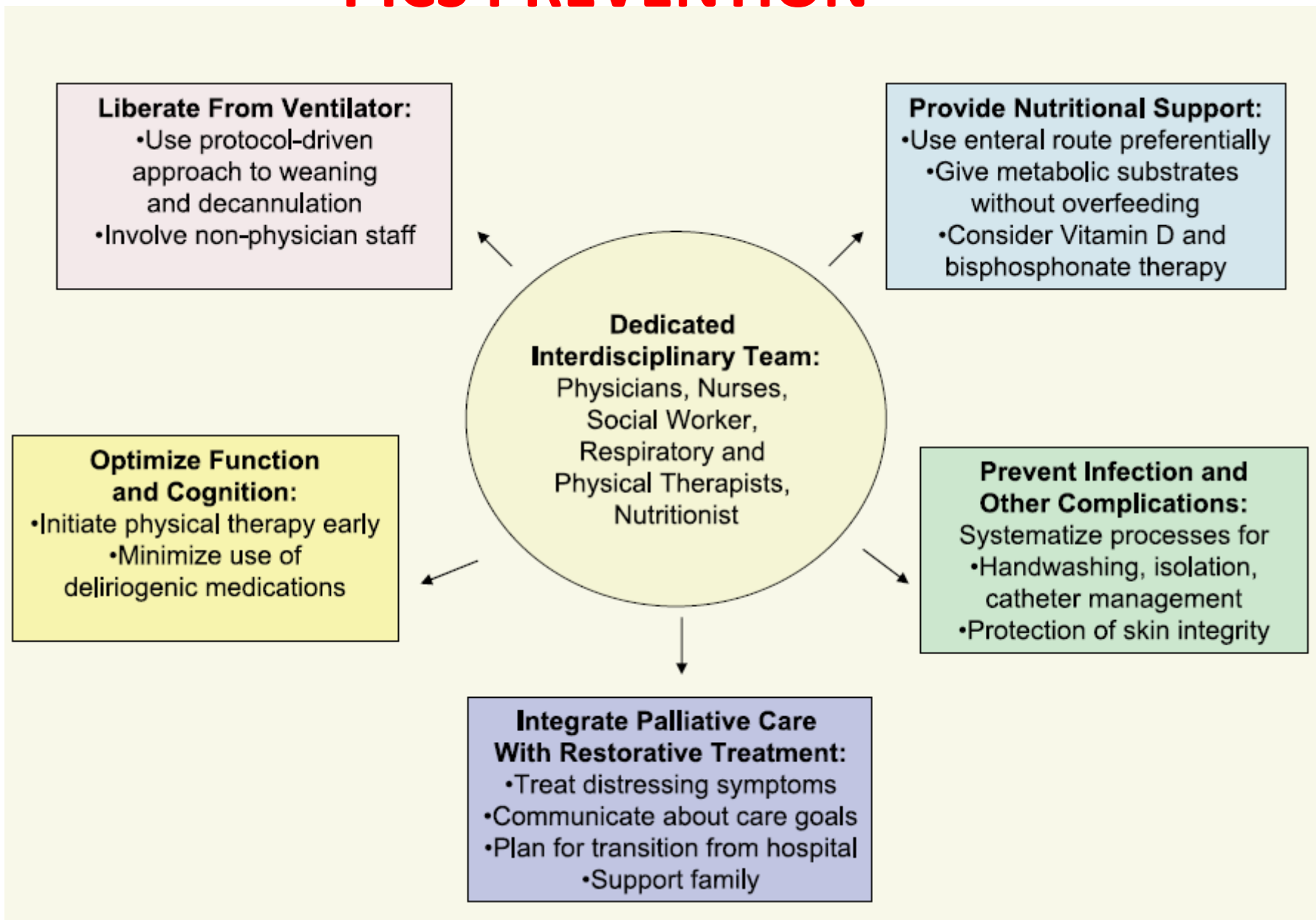


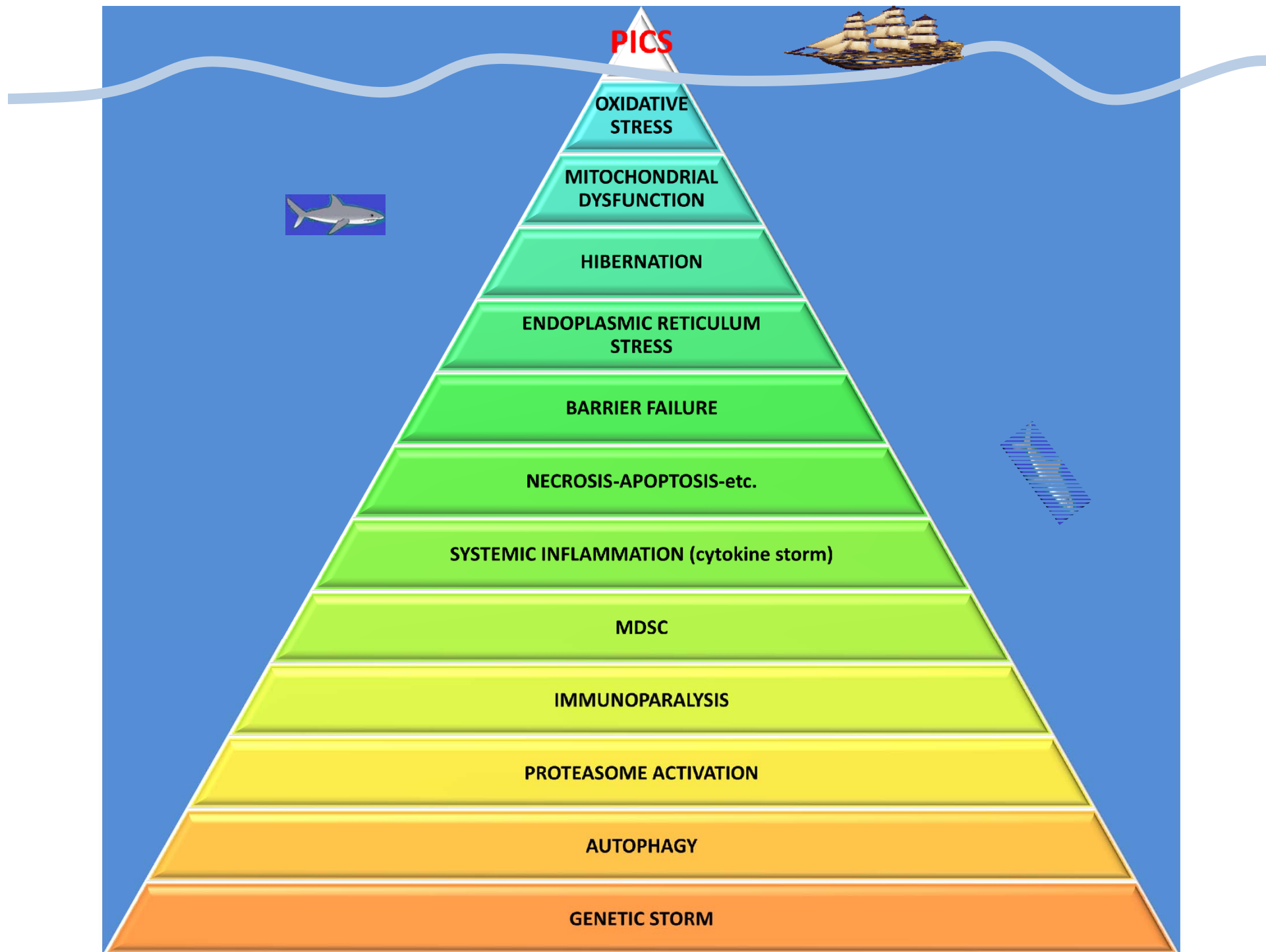
B Old age, incipient neurodegenerative disease, or anticholinergic drug treatment



Lancet 2010; 375: 773-75

PICS PREVENTION







ΕΥΧΑΡΙΣΤΩ