NAD: PURPOSE & APPLICATIONS

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OBJECTIVES

1. What is NAD?
2. How does NAD function biochemically/in the body?
3. What issues stem from NAD decline?
4. How can NAD be used through injections or other healing modalities to help improve patient quality of life?

NICOTINAMIDE ADENINE DINUCLEOTIDE (NAD)

- Derived from nicotinic acid (Vitamin B).
- It normally carries a positive charge and can accept one hydrogen atom and two electrons to become the reduced form, NADH. NADH is generated during the oxidation of food, especially by the reactions of the Krebs cycle. It then gives up its two electrons (and single proton) to the electron transport chain, thereby reverting to NAD+ and generating three molecules of ATP per molecule of NADH. (*A Dictionary of Biology)*

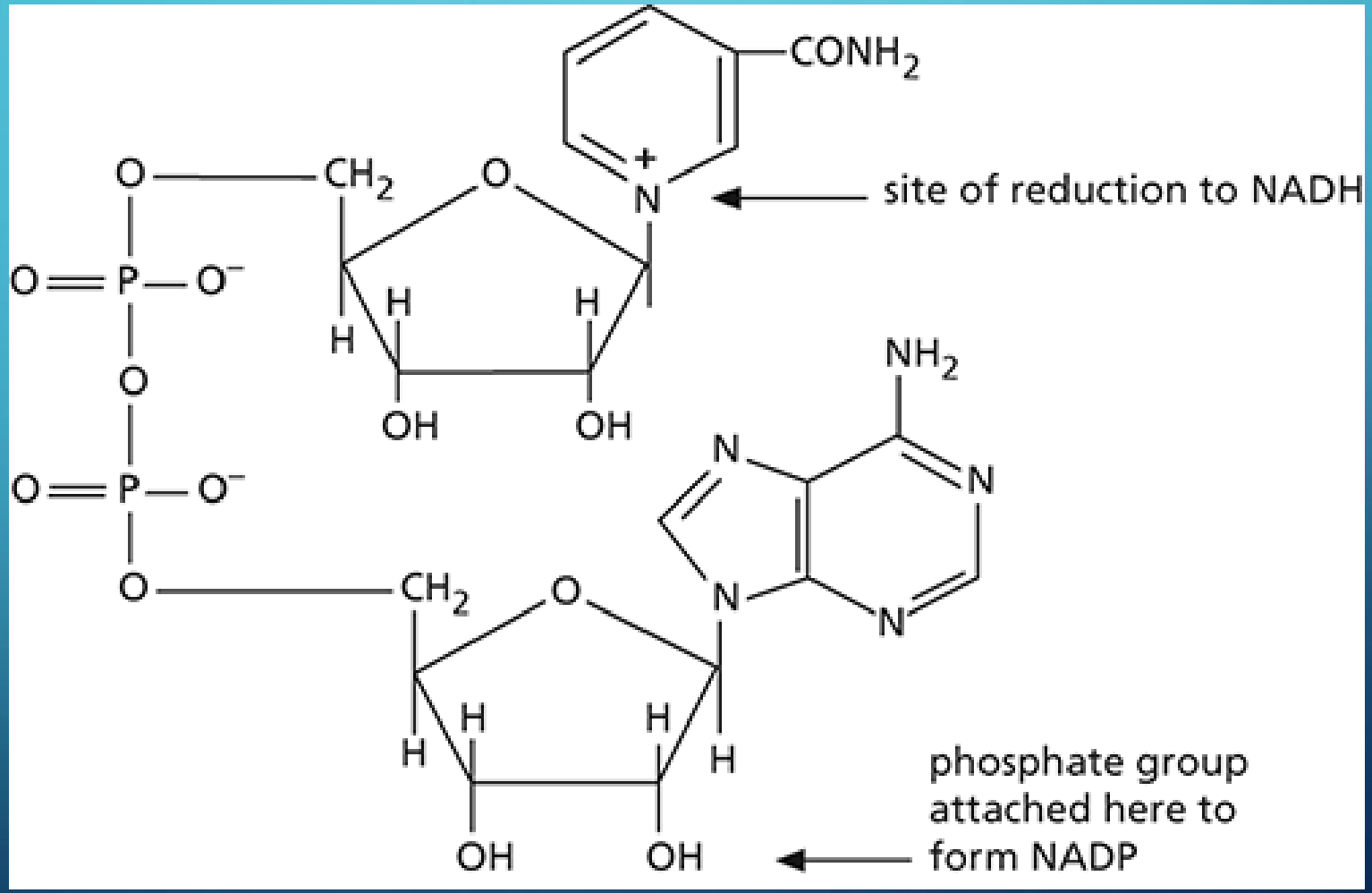
HISTORY OF NAD

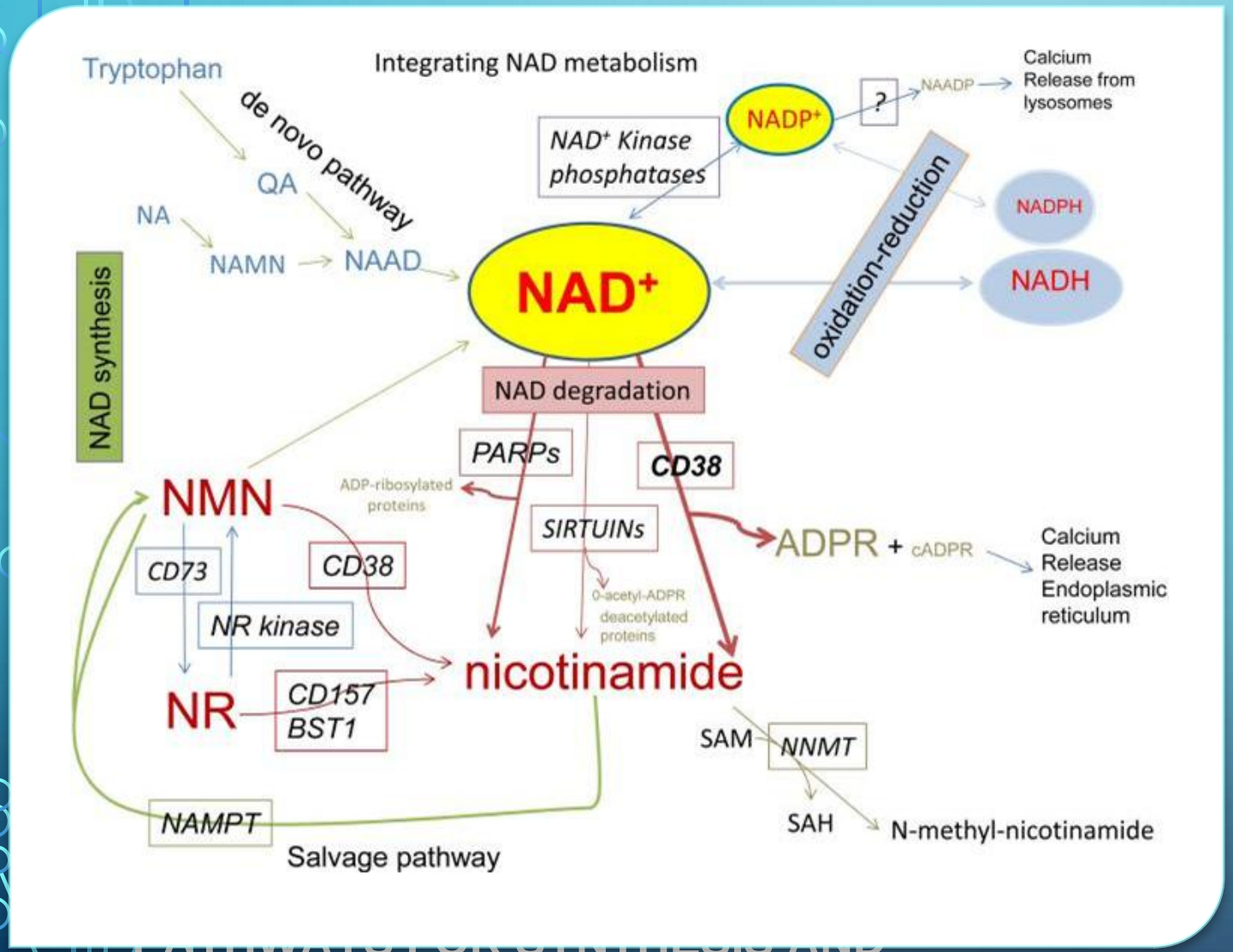
- The coenzyme NAD+ was first discovered by the British biochemists Arthur Harden and William John Young in 1906.
- In 1936, the German scientist Otto Heinrich Warburg showed the function of the nucleotide coenzyme in hydride transfer and identified the nicotinamide portion as the site of redox reactions.
- Vitamin precursors of NAD+ were first identified in 1938, when Conrad Elvehjem showed that liver has an "anti-black tongue" activity in the form of nicotinamide.

HISTORY OF NAD

- In 1939, he provided the first strong evidence that niacin is used to synthesize NAD+.
- In 1949, the American biochemists Morris Friedkin and Albert L. Lehninger proved that NADH linked metabolic pathways such as the citric acid cycle with the synthesis of ATP in oxidative phosphorylation.
- In 2004, Charles Brennerand co-workers uncovered the nicotinamide riboside kinase pathway to NAD+.

NAD Chemical Structure With Sites of Reductions and Attachments

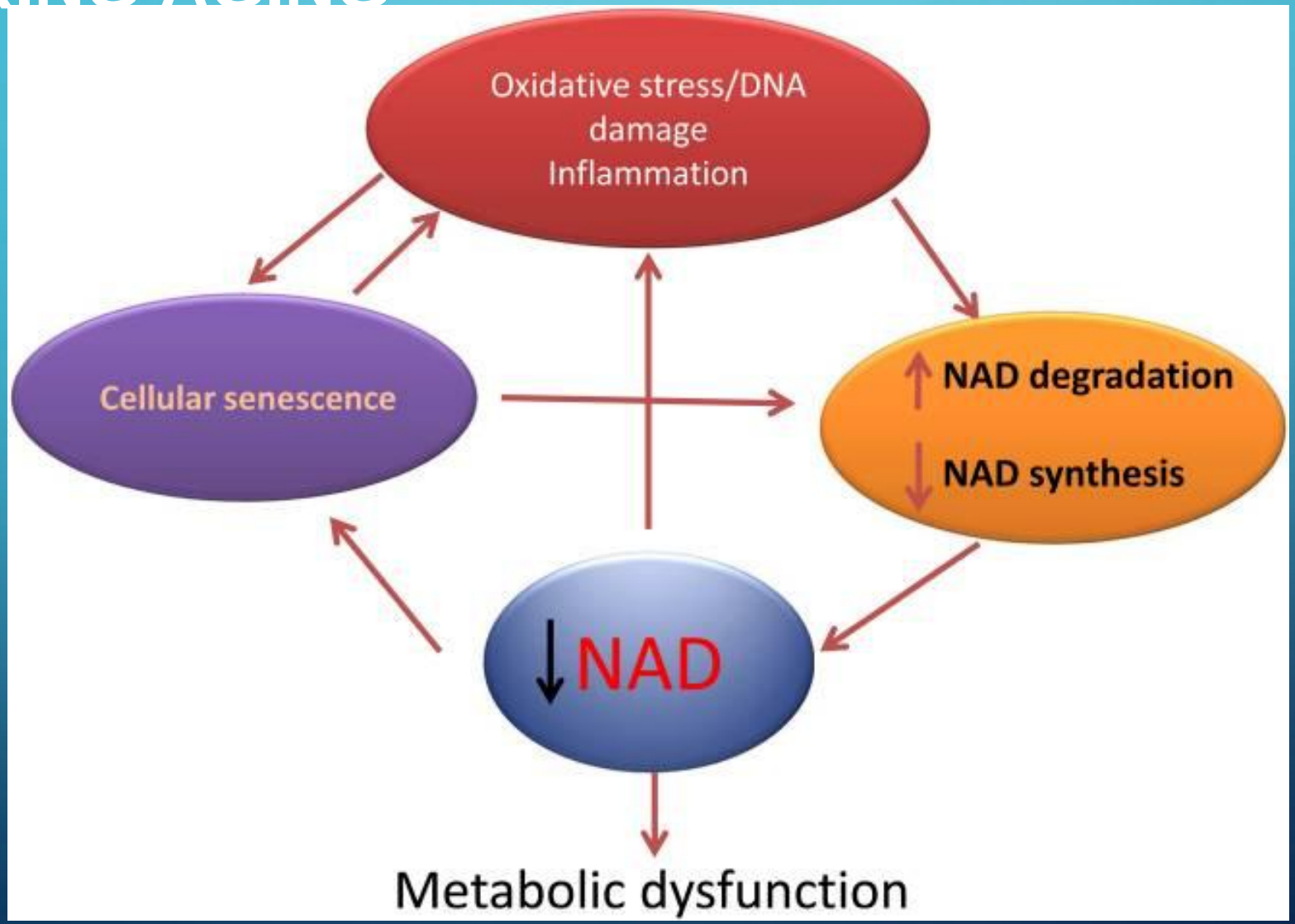




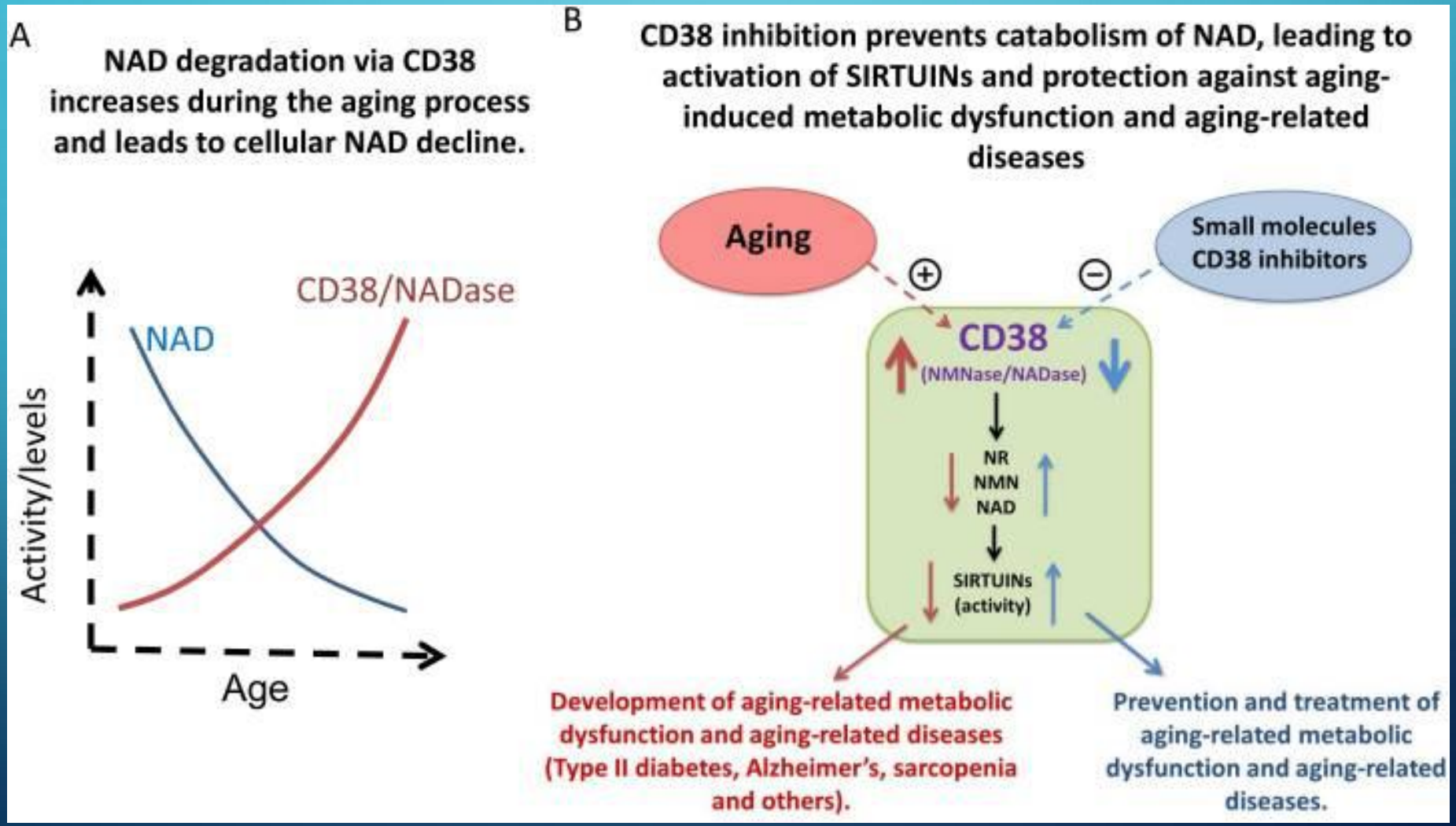
DEGRADATION OF NAD AND ITS METABOLITES

- De novo pathway: A biochemical pathway wher e a complex biomolecule is synthesized anew from simple precursor molecules.
- PARP: a critical enzyme involved in DNA repair and many other cellular processes including transcription and modulation of chromatin structure.
- Sirtuins: can only function in the presence of NAD, are responsible for regulating cellular health such as DNA expression.
- NMN: nicotinamide mononucleotide.

CYCLE THAT AMPLIFIES TISSUE NAD DECLINE, CELLULAR SENESCENCE, AND DAMAGE DURING AGING



CD38 PLAYS A KEY ROLE IN NAD DECLINE IN AGING



PURPOSE OF NAD

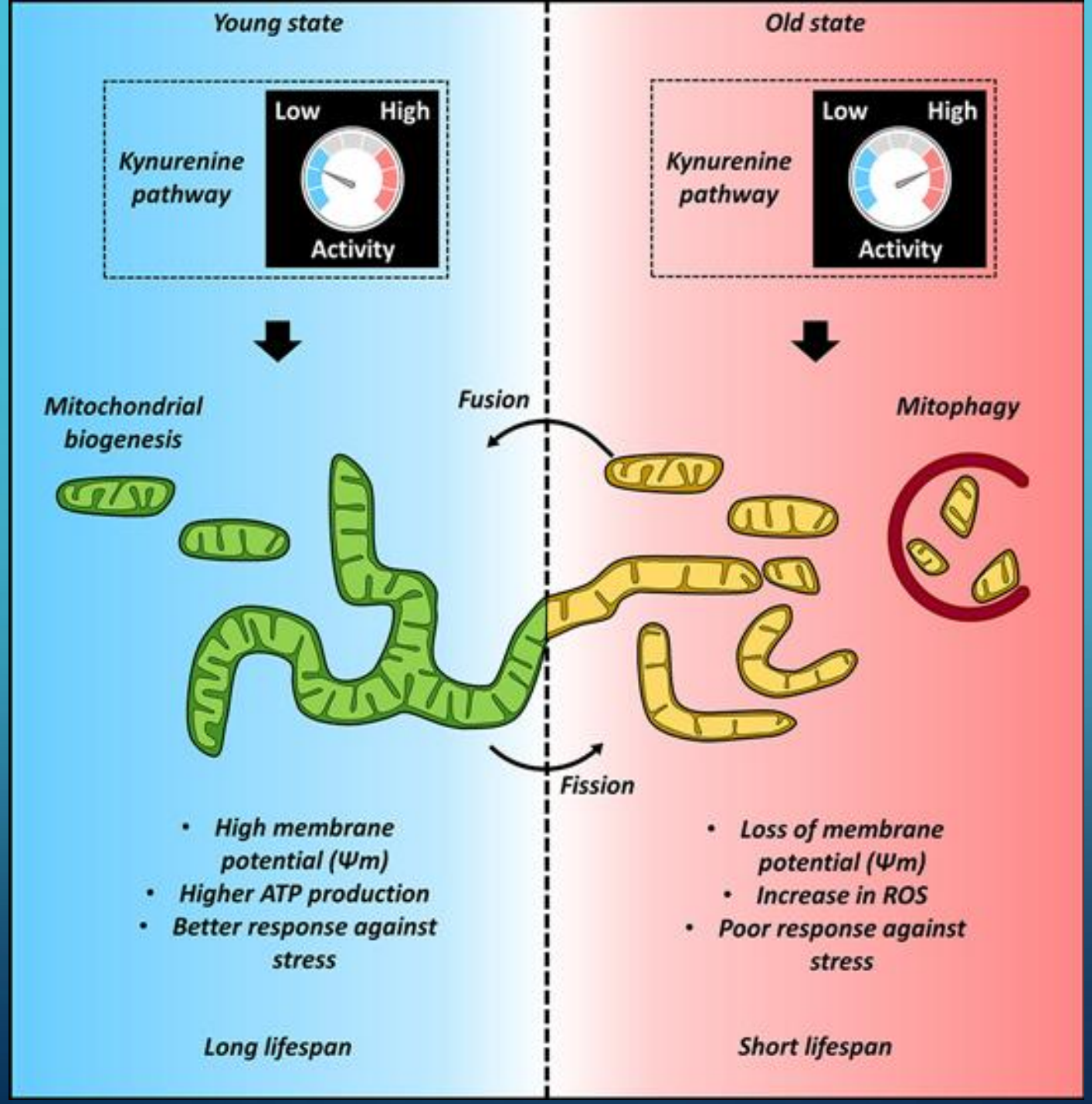
- One of its most significant roles within the body is in oxidation-reduction (redox) reactions.
- To regulate circadian rhythm and metabolic rate.
- Maintains DNA integrity and health.
- Functions as a quality control mechanism for new proteins.
- NAD increases the activity of SIRT1 and PARP 1 proteins, which are linked with a slower rate of aging and influencing DNA repair respectively.
- NAD works on mitochondria and increases the length of telomeres.

CONT'D PURPOSES OF NAD

- NAD has also been shown to play a key role in cell signaling, regulating several pathways from intracellular calcium transients to the epigenetic status of chromatin.
- Serves as a key molecule in cellular metabolic sensoring pathways.
- NAD affects longevity and transcriptional silencing through the regulation of the Sir2p family, which are NAD-dependent deacetylases.
- NAD helps the liver break down fats that are essential to provide energy for the body.

DECLINING FUNCTIONS OF NAD & ITS EFFECTS

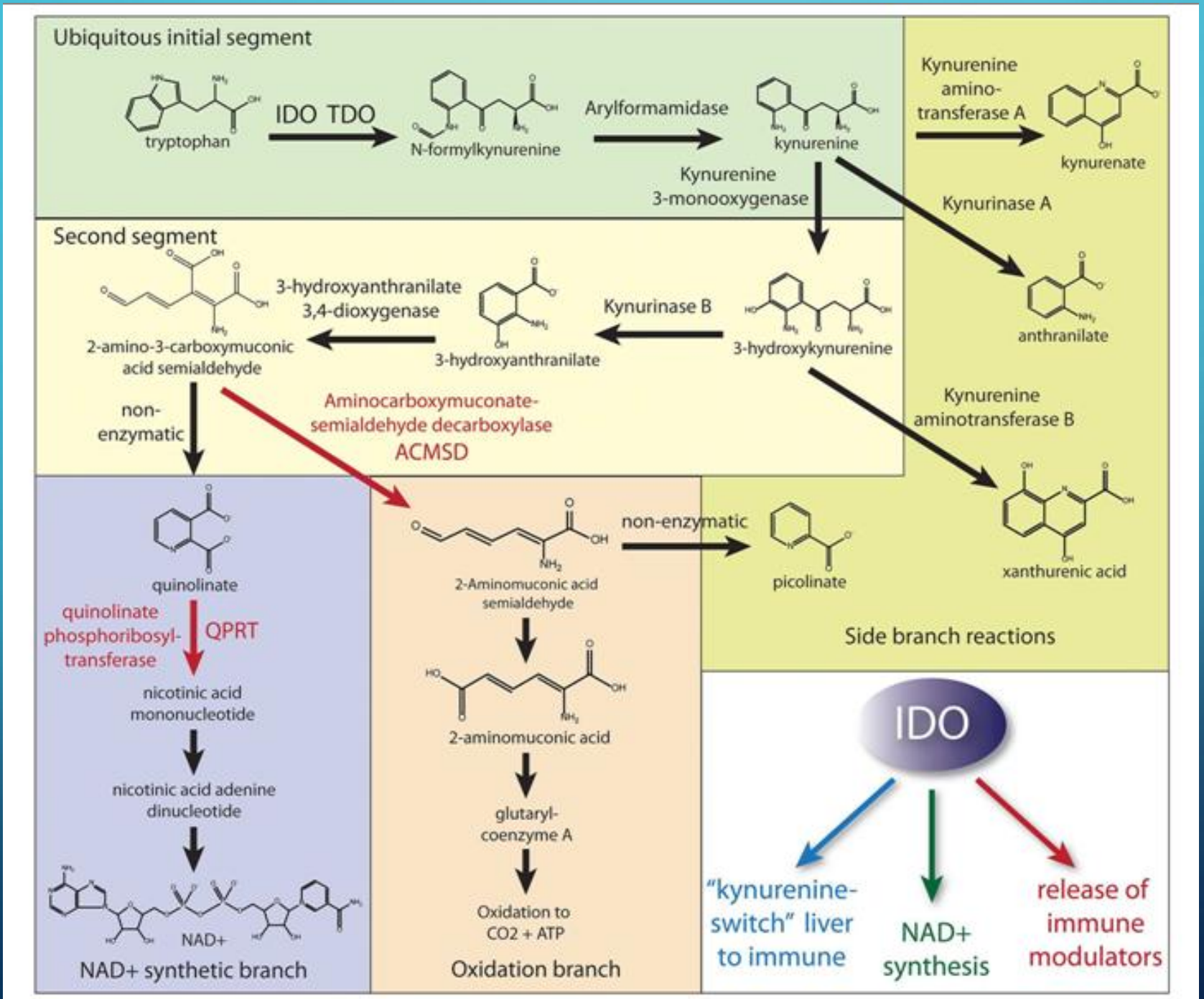
- NAD decline during aging leads to decrease in SIRTUINS activity, mitochondrial and metabolic dysfunction.
- NAD decline could be caused by increase in its catabolism or decrease in its synthesis.
- The enzyme CD38 is the main NADase in tissues and plays a key role on the age-related NAD decline.


Young state
Old state
Kynurenine pathway
Low
High
Activity
Kynurenine pathway
Low
High
Activity
Mitochondrial biogenesis
Fusion
Mitophagy
Fission
• High membrane potential (Ψm)
• Higher ATP production
• Better response against stress
Long lifespan
• Loss of membrane potential (Ψm)
• Increase in ROS
• Poor response against stress
Short lifespan

APPLICATION OF NAD FOR TREATMENT AND OTHER STRATEGIES

- NAD IV Therapy: though there are many different protocols and it has been found that NAD IV therapy is more effective with the addition of:

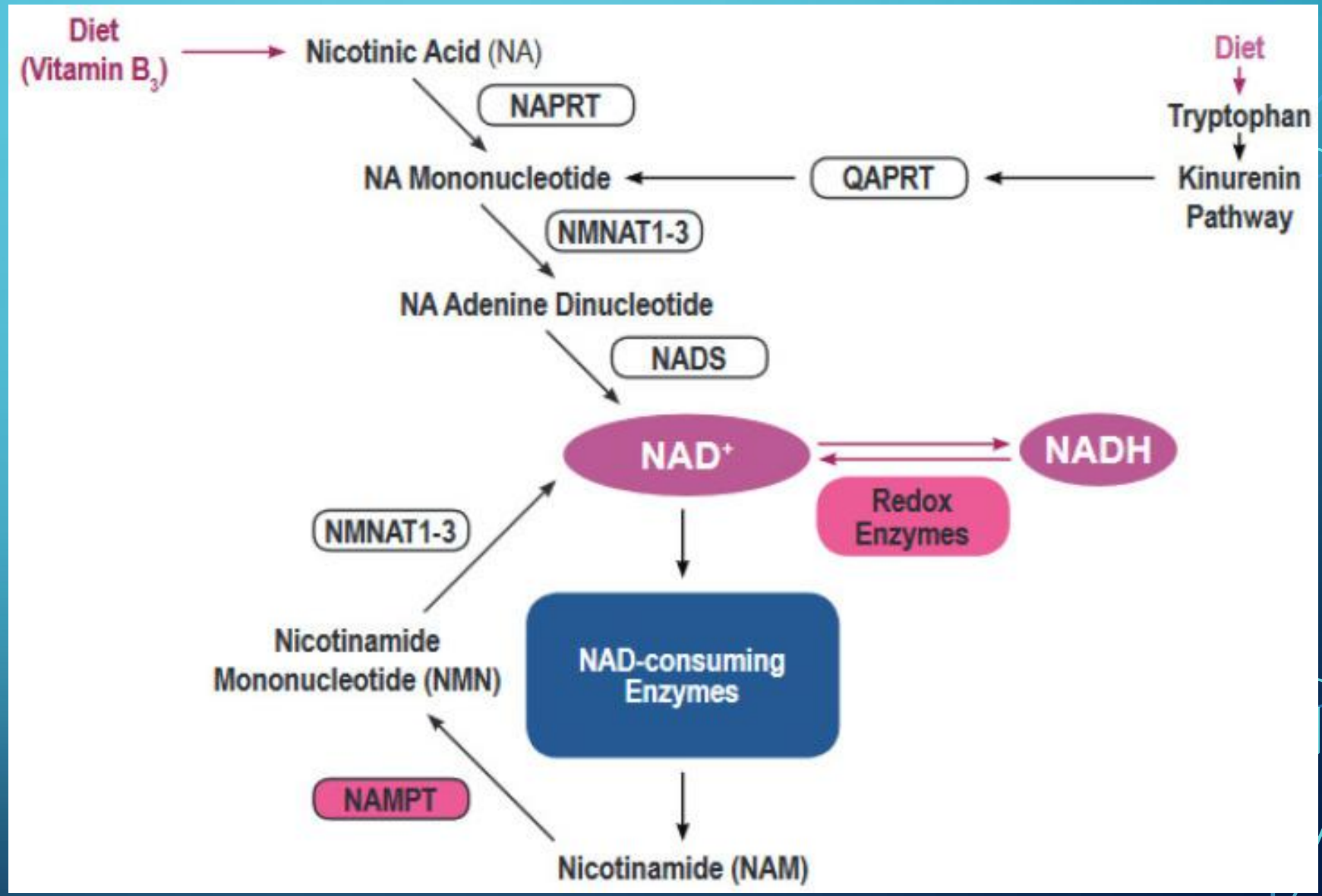
1. Amino acids
2. Glutathione and B-Complex
3. Cocarboxylase


Ubiquitous initial segment
tryptophan
IDO TDO
N-formylkynurenine
Arylformamidase
kynurenine
Kynurenine amino-transferase A
kynurenate
Kynurenine 3-monooxygenase
Kynurinase A
anthranilate
Second segment
2-amino-3-carboxymuconic acid semialdehyde
3-hydroxyanthranilate 3,4-dioxygenase
3-hydroxyanthranilate
Kynurinase B
3-hydroxykynurenine
non-enzymatic
Aminocarboxymuconate-semialdehyde decarboxylase
ACMSD
Kynurenine aminotransferase B
xanthurenic acid
quinolinate
quinolinate phosphoribosyl-transferase
QPRT
nicotinic acid mononucleotide
nicotinic acid adenine dinucleotide
NAD+
NAD+ synthetic branch
2-Aminomuconic acid semialdehyde
non-enzymatic
picolinate
Side branch reactions
2-aminomuconic acid
glutaryl-coenzyme A
Oxidation to CO2 + ATP
Oxidation branch
IDO
"kynurenine-switch" liver to immune
NAD+ synthesis
release of immune modulators

WHAT DOES NAD TREATMENT HELP?

- Chronic Fatigue Syndrome
- Memory Issues/Decline
- Metabolic and age-related issues
- Enhancement of the skeletal-muscular activity
- Faster rehabilitation after traumatic events
- Decrease oxidative stress
- Enhance anti-diabetic treatments
- Recovery from jet lag
- Parkinson’s Disease / Neurodegenerative diseases

Regulation of the nicotinamide adenine dinucleotide (NAD) metabolism. The figure shows the main synthesis pathways of NAD including the de novo synthesis via the kynurenine pathway or from nicotinic acid and the salvage pathways.



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