ANTI-AGING VACCINE

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Aging

- complex biological phenomenon result in gradual decline of physiological function and increased risk of age-related diseases
- Cellular damage caused by ROS and other oxidative stress one of the contributing factor

Aging

- The damage can accumulate over time and lead to age-related diseases including
- CVS ,
- Neurodegenerative disorders
- cancer

Recent anti-aging strategies

- Metformin
- dietary NAD+ precursor supplements

Benefits of vaccination

- requiring few doses
- eliciting longer efficacy through autologous immune responses
- demonstrated protective effects against HFD-induced aging and age-related metabolic diseases

Previous anti-aging vaccines

- CD153 &GPNMB vaccines
- GPNMB (glycoprotein nonmetastatic melanoma protein B :marker on senescent cell
- focused primarily on targeting senescent T cells and vascular endothelial cells

CD38 cell expression

- Initially discovered as a T-cell surface marker
- erythrocytes
- macrophages
- dendritic cells
- neutrophils
- lymphocytes
- endothelial cells
- precursor immune cells

CD38

- Structurally, the majority of CD38 molecules function as type II transmembrane proteins with an extracellular catalytic site
- Intracellular localization to organelles such as
- the endoplasmic reticulum,
- mitochondria
- nuclear membrane

CD38 overexpression

- CD38 overexpression in cells reduced the total respiratory capacity,
- increased dependence on glycolysis
- abnormal mitochondrial morphology due to the leakage of NAD+ and NADH from dysfunctional mitochondria

CD38

- in addition to cellular senescence and chronic inflammation, CD38 may play an important role in
- genomic instability
- mitochondrial dysfunction
- macroscopic autophagy dysfunction

CD38

- CD38 directs age-related NAD+ decline
- CD38 accumulates in the macrophages of aged mice
- high CD38 expression causes cells to undergo an epithelial–mesenchymal transition process,

Cellular stressor

- Cellular stressors, such as DNA damage, lead to the accumulation of senescent cells over time and induce the release of essential SASP (senescence-associated secretory phenotype).

Cellular stressor

- Increased intestinal permeability during senescence increases the serum levels of endotoxin and other PAMP (pathogen-associated molecular pattern)s, which activate innate immune cells.

Cellular stressor

- SASP and PAMP promote macrophage M1-like polarization, thereby increasing CD38 expression in macrophages up to 600-fold in tissues

Mitochondrial Function

- declined mitochondrial function is a hallmark of aging
- Significant increases in mitochondrial oxygen consumption and activity were found in the liver tissue and spleen mitochondria from CD38-deficient mice
- One study reported that CD38 enzymatic activity in cancer patients was two to three times higher than that in healthy controls

CD38 as a mediator of aging and age-related diseases

- Declining NAD levels are now recognized as a major driver of physiological deterioration during aging and the development of age-related diseases
- Elevated CD38 activity has been correlated with age and pathological conditions.

NAD+

- NAD+ is a coenzyme that plays a vital role in many biological processes.
- It facilitates the transfer of electron and effectively converts NAD+ into reduced NADH in redox reactions, i.e.
- β-oxidation
- glycolysis
- tricarboxylic acid cycle (TCA)
- oxidative phosphorylation

NAD+

- NAD+ is critical in the cellular and tissue aging process
- Antiaging approaches aimed at NAD+ pool maintenance, including
- NAD+ precursor boosting
- NAD+ synthesizing activation
- NAD+ consumption deceleration

NAD+

- involved in several biological functions,
- cellular bioenergetics,
- DNA repairing,
- metabolic homeostasis,
- genomic stability,
- mitochondrial biogenesis
- cell survival

NAD+

- CD38 is the main consumer of NAD+ and is associated with age-related NAD+ decline
- CD38 acts as a NAD glycohydrolase, cleaving NAD to generate nicotinamide (NAM) and adenosine diphosphate ribose (ADPR).

NAD+ precursors

- NAD+ is synthesized from dietary NAD+ precursors
- nicotinic acid NA,
- nicotinamide (NAM),
- nicotinamide riboside (NR),
- nicotinamide mononucleotide (NMN)
- tryptophan

Therapeutic target

- CD38 has emerged as a promising therapeutic target for various diseases, with strategies including
- cytotoxic antibodies,
- enzymatic inhibitors
- small-molecule antagonists showing therapeutic potential

CD38 antibodies

- have demonstrated efficacy against multiple age-related syndromes, including
- fibrosis
- systemic sclerosis
- NAD+ deficiency
- Cardio-toxicity

Small molecules targeting CD38

- Small molecules targeting CD38 can alleviate
- glucose intolerance
- physical dysfunction
- Neuro-inflammation

CD38 Peptide Vaccine

- Prevents Physical and Cognitive Decline in Aged Mice
- Ameliorates Metabolic Dysfunction-Associated Features in Aged Mice
- Reduces Cellular Senescence and Maintains NAD+/NADH Levels
- Ameliorates Abnormal Metabolic-Related Proteome Changes in the Liver