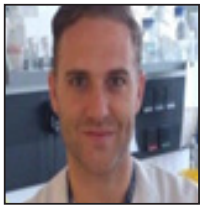
Insight Medical Publishing

JOURNAL OF INFECTIOUS DISEASES AND TREATMENT

Therapeutic potential of NAD+ Boosters in Rheumatoid Arthritis



Carlos Pérez-Sánchez

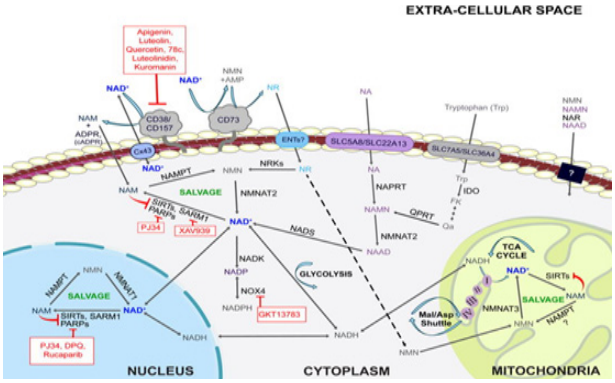
University of Cordoba, Spain

Abstract

NAD+ is an important cofactor/second messenger for key cellular processes whose modulation might have a therapeutic role in Rheumatoid Arthritis (RA).

Aims: 1- To study the NAD+ metabolism in RA patients. 2- To analyze the effect of NAD+ boosters in leukocytes from active RA patients. Plasma and PBMCs were purified from 100 RA patients and 50 healthy donors (HDs). NAD+ levels were determined by using the NAD/NADH-Glo Assay. NAD+-consuming genes expression were analyzed by RT-PCR. In parallel, PBMCs from six HDs and six active RA patients were treated ex vivo with 1 mM of NAD+ boosters including nicotinamide (NAM), nicotinamide riboside (NR), and nicotinamide mononucleotide (NMN). After 24 hours, intracellular reactive oxygen species (ROS) levels (DFCHDA) and the percentage of apoptotic PBMCs (annnexin V/PI) were assessed by flow cytometry. Finally, a panel of pro-inflammatory genes were evaluated by RT-PCR. NAD+ levels were significantly reduced in plasma of RA patients compared with HDs and directly related to disease activity. Accordingly, the expression levels of genes involved in the consumption of NAD+ such as SIRT-1, CD38 and PARP-1 were found up-regulated in RA PBMCs. PBMCs isolated from RA patients showed an increased oxidative, apoptotic and proinflammatory status compared with HDs. The in vitro treatments with NAD+ boosters significantly increased the NAD+ levels and promoted a deep reduction of intracellular ROS, the percentage of apoptotic cells and the expression levels of key inflammatory mediators, such as IL-6, IL-8, IL-1b, TNF-α, CCL2, IL-23, and STAT-3.

Conclusions: 1. NAD+ metabolism is altered in RA, involving both, reduced NAD+ levels and increased expression of NAD+-consuming genes. 2. NAD+ boosters reduced the oxidative, apoptotic and inflammatory profile of RA leukocytes through the parallel increase of intracellular NAD+ levels. Thus, NAD+ boosters might be considered novel therapeutic tools for RA patients.



Biography

Dr Pérez Sánchez has a PhD in biomedicine at the University of Cordoba (UCO), Spainand has two Masters. Currently, hehold a post-dococtoral position at IMIBIC and is the co-director and CSOof the Start-up Shortcut Scientific based in Cambridge. He has an H-index of 14, 618 cites and35 peer-reviewed publications in the highest impact journals in the field. He is the main or last author in 22of these publications.Hecolaborate with national and international groups as a result of different research stages during his PhD and postdoc training in centres such as Lupus Unit Research of London (UK, 6 months), and Department of Medicine at the Univ. of Cambridge, Smith Lab (UK, 24 months).He hasauthored 5 patents related to genomic biomarkers of autoimmune diseases and has participated asmember of several Scientific Societies, Evaluator panels and Reviewer boards.

Publications

1. Perez Sanchez C et al. Antioxidants 2021. Therapeutic Potential and Immunomodulatory Role of Coenzyme Q10 and Its Analogues in Systemic Autoimmune Diseases.
2. Perez Sanchez C et al. Front Immunol 2021. Integrative Clinical, Molecular, and Computational Analysis Identify Novel Biomarkers and Differential Profiles of Anti-TNF Response in Rheumatoid Arthritis.
3. Perez Sanchez C et al. J Pers Med 2021. Clinical Utility of microRNAs in Exhaled Breath Condensate as Biomarkers for Lung Cancer.
4. Perez Sanchez C et al. Int J Mol Sci. 2020. Effects of Biological Therapies on Molecular Features of Rheumatoid Arthritis.
5. De la Rosa IA, Perez-Sanchez C, et al. Haematologica. 2020. mpaired microRNA processing in neutrophils from rheumatoid arthritis patients confers their pathogenic profile. Modulation by biological therapies