Impact of Boosting NAD on Immune Function: Results From NR Preclinical Studies

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Objectives: Immune responses to stress, inflammation, or infections utilize nicotinamide adenine dinucleotide (NAD) resources through upregulation of NAD-dependent cellular repair enzymes such as sirtuins and PARPs as well as other immune cell functions. Preclinical studies have demonstrated that disruptions in NAD metabolism are associated with impaired immune function and inflammation, while utilization of NAD precursors improves immune function and decreases expression of inflammatory markers. The objective of this analysis was to evaluate how supplementation with the NAD precursor, nicotinamide riboside (NR), influences immune cell function and markers of inflammation in preclinical models.

Methods: A systematic evaluation of peer-reviewed preclinical publications was conducted to identify the influence of NR supplementation on indicators of inflammation or immune function. Following study reviews, an assessment of gaps in the literature were determined.

Results: There were 7 primary studies that met the inclusion criteria of measuring NR supplementation alone with an outcome related to inflammatory markers or immune cell function. There was appreciable heterogeneity in the cell types and animal models evaluated, as well as the inflammatory or immune challenge. Of these studies, six measured TNF-α, three measured IL1ß, and four measured IL6; other markers were measured sporadically. NAD levels were shown to decline following an inflammatory or immune trigger in five studies. One study showed an increase in expression of NMRK1 which is integral in the utilization of NR and decreased viral infectivity with NR supplementation. A decrease in TNF-α, IL1ß, and IL6 was observed in most of the studies with one study showing no change. This study measured these markers in CD8 + tumor-infiltrating lymphocytes and mouse tumor cell lines as part of their overall outcome showing a beneficial effect of NR on tumor growth, unique among the studies included.

Conclusions: NR supplementation in preclinical models has shown some potential for supporting immune health and reducing inflammation. Future studies that incorporate markers inflammatory status and immune support as primary endpoints, as well as measurements of NAD metabolism are needed to fully assess NR as a modulator of inflammation and identify the mechanisms of action.

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