

Role of NAD metabolism in maintaining intestinal homeostasis

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Nicotinamide adenine dinucleotide (NAD) is an essential cofactor associated with numerous redox reactions including energy production. NAD also serves as a substrate for ADP-ribosylation by poly(ADP-ribose) polymerase and protein deacetylation by sirtuins. Interventions using NAD precursors have been reported to have various beneficial effects on aging-associated diseases, such as obesity, diabetes, and Alzheimer disease. In mammals, NAD is synthesized from niacin (nicotinamide and nicotinic acid) and tryptophan. It is known that deficiency of niacin causes Pellagra featured by diarrhea, inflamed skin, and dementia. However, it is not fully understood why niacin deficiency causes Pellagra. Here we found that deficiency of NAD synthetase (NASD) caused the shortening of villi length in small intestine in mice. This photocopies the colitis observed in Pellagra patients. Furthermore, these mice are more sensitive to colitis induced by 5-fluorouracil treatment. These results suggest that NADS is involved in mechanism of Pellagra onset and is important for maintaining intestinal homeostasis.