

The longevity gene mammalian Indy (mINDY) is involved in blood pressure regulation

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Authors from the German Center for Diabetes Research (DZD) presented data showing that the longevity gene mammalian Indy

(mINDY) is involved in blood pressure regulation in the *Journal of Clinical Investigation (JCI) insight*. Reduced expression of mINDY, which is known to extend life span in lower organisms and to prevent diet induced obesity, fatty liver and insulin resistance in mice, has now been shown to lower blood pressure and heart rate in rodents.

The authors provided mechanistic insights for the underlying physiological mechanism based on in vivo data in a genetic knock out model as well as microarray and in vitro studies. Furthermore, the hypothesis is supported by confirming critical effects in vitro using a small molecule inhibitor of mINDY. The authors conclude that deletion of mINDY recapitulates beneficial cardiovascular and metabolic responses to caloric restriction, making it an attractive therapeutic target.

Andreas Birkenfeld and colleagues provide a comprehensive study showing that mIndy deletion attenuates sympathoadrenal support of blood pressure and reduced arterial blood pressure and heart rate in a murine knockout model. Blood pressure was assessed invasively using intra-arterial pressure probes over several days. Urinary analysis for catecholamines and metanephrines as well as unbiased transcriptomic analysis of adrenal glands identified the affected biosynthetic pathways. Indeed, catecholamine biosynthesis was attenuated in mINDY-KO adrenals, whereas plasma steroids and steroid hormone synthesis were unaffected.

In vitro studies on an adrenal cell line supported this hypothesis. mIndy codes for a is a carboxylic acid transporter protein expressed in plasma membrane. Citrate, the main substrate of the mINDY transporter, increased catecholamine content, while pharmacological inhibition of mINDY by a small molecule inhibitor blunted the effect.

The study provided further insights into the physiological mechanisms of the beneficial effects of reducing mINDY activity which is known to

protect from diet and aging induced metabolic diseases by mechanisms akin to caloric restriction. Therefore, the data showed a novel mechanism contributing to a cardiometabolic cross talk and further supporting mINDY as a promising target for the whole spectrum of metabolic syndrome components, including increased blood pressure.

More information: Diana M. Willmes et al, The longevity gene mIndy (I'm Not Dead, Yet) affects blood pressure through sympathoadrenal mechanisms, *JCI Insight* (2021). [DOI: 10.1172/jci.insight.136083](https://doi.org/10.1172/jci.insight.136083)

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