脳卒中易発症ラット肝臓中の メバロン酸ニリン酸脱炭酸酵素 mRNA レベル低下における 転写調節とマイクロ RNA214 の関与

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Involvement of microRNA214 and Transcriptional Regulation in Reductions in Mevalonate Pyrophosphate Decarboxylase mRNA Levels in Stroke-Prone Spontaneously Hypertensive Rat Livers

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ABSTRACT: Hypocholesterolemia has been epidemiologically identified as one of the causes of stroke (cerebral hemorrhage). We previously reported that lower protein levels of mevalonate pyrophosphate decarboxylase (MPD), which is responsible for reducing serum cholesterol levels in stroke-prone spontaneously hypertensive rats (SHRSP), in the liver were caused by a reduction in mRNA levels. However, the mechanism responsible for reducing MPD expression levels in the SHRSP liver remains unclear. Thus, we compared microRNA (miR)-214 combined with the 3'-untranslated region of MPD mRNA and heterogeneous nuclear RNA (hnRNA) between SHRSP and normotensive Wistar Kyoto rats (WKY). miR-214 levels in the liver were markedly higher in SHRSP than in WKY, whereas hnRNA levels were significantly lower. These results indicate that the upregulation of miR-214 and downregulation of MPD transcription in the liver both play a role in the development of hypocholesterolemia in SHRSP.

抄録 本研究において我々は、肝臓中のマイクロ RNA214 アップレギュレーションと メバロン酸二リン酸脱炭酸酵素転写レベルにおけるダウンレギュレーションの両方が、 脳卒中易発症ラットにおける低コレステロール血症の発症に働いていることを示した。