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Enzyme Engineering

Editorial

Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9): A Promising Therapeutic Target for Cardiovascular Diseases

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INTRODUCTION

Determination PCSK9 is a secretory serine proteinase; belong to Pro-Protein Convertase (PCs) family [1]. It was initially discovered by a French group investing a rare genetic disorder of autosomal dominant hypercholesterolemia [2]. PCSK9 has a wide spectrum of mutations in human population. PCSK9 gain-of-function variations are associated with hypercholesterolaemia, whereas loss-of-function variations are associated with hypo cholesterolaemia [3]. Due to its direct binding to and degradation of LDLR[1], PCSK9 isregarded as a valid and novel target for the treatment of hypercholesterolemia. Indeed, PCSK9- knock-out mice exhibit higher levels of liver LDLR and reduced serum cholesterol [4], while over expression of PCSK9 reduces LDLR and increases serum cholesterol [5]. Interestingly, those individualswithloss offunctionmutations of PCSK9 have lower levels of LDL cholesterol and are protected from cardiovascular diseases [6]. sensitivity of these methods was not satisfactory for the rigorous experiment. Although many of the modified PCR based mutation screening methods have been produced, none of these become popular due to the low sensitivity and/or inconvenience. PCSK9 is emerging as one of the best genetically validated targets for treatment of heart disease. Pro-PCSK9 is a 73 kDa zymogen, which is undergoes autocatalytic cleavage in the endoplasmic reticulum and then secreted as a 63 kDa mature protein which forms a complex with the N-terminal predomain. If enough samples are gathered at once, NGS is a hopeful and fascinating strategy, because pooling of samples lowers the running cost per sample. But if you are intended to examine 1050 kb of DNA sequence by single experiment, you require an efficient and convenient screening method. He secreted PCSK9 binds spiccato\ to the epidermal growth factor (EGF)-like repeatAof the LDLRat the cellsurface [1]. PCSK9 posttranslationally regulates the number of the cell-surface LDLR, although the exact mechanism by which PCSK9 chaperones LDLR to the lysosomes degradation remains unknown. Recently, we have used shotgun proteomic approach and that a Cellular Inhibitor of Apoptosis 1 (C-IAP1) protein binds and processes PCSK9 [7]. We found that there is a dramatic decrease in secreted mature PCSK9 protein accompanied bycan't increase in LDLRprotein levelsin CIAP1 null Mouse Embryonic Browbeats (MEFs), in comparison with matched wild-type MEF cells [7].

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