HSP-90 and vasoregulation in portal hypertension

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A research team from Germany investigated the role of heat shock protein-90 (HSP-90) in neuronal NO-synthase (nNOS)-function and vasoregulation in the mesenteric vasculature. Their results showed that interaction and co-localization of nNOS and HSP-90 are evidenced. The inhibition of HSP-90 largely ameliorates enhanced nNOS-mediated vasodilation in portal hypertension making HSP-90 a potential therapeutic target during portal hypertension.

Neural vasoregulation represents a rapid and potent mode of altering vascular tone but has not been investigated thoroughly during portal hypertension. Heat shock protein-90 (HSP-90) is well-known to act as a molecular chaperone optimizing endothelial and neural NO-synthase (eNOS, nNOS) enzyme activity and thus, NO production. Although HSP-90 has been shown to mediate in large parts the enhanced eNOS-dependent NO overproduction in the splanchnic circulation during portal hypertension, it is not clear what role HSP-90 plays in nNOS-mediated vasorelaxation in this scenario.

A research article to be published on April 21, 2010 in the World Journal of Gastroenterology addresses this question. This research relates to the utilization of the McGregor preparation enabling physiological and pharmacological testing of the whole mesenteric vasculature in its original anatomy and innervations. In contrast to arterial strips, this ensures testing of neural vasoregulation at close to in vivo conditions.

The investigators for the first time demonstrate a critical role of HSP-90

for nNOS-mediated vasorelaxation and furthermore, can provide evidence for this interaction being responsible in large parts for the well-accepted pronounced nNOS-dependent vasodilatation in portal hypertension. In addition, the authors visualize the localization of nNOS and HSP-90 in mesenteric nerves which can be appreciated as co-localized within the nerve axon. Finally, co-immunoprecipiatation reveals a close protein-protein-interaction explaining the functional hemodynamic results presented. Therefore, HSP-90 may well have great potential to be identified as a future target in clinical trials focusing on amelioration of portal hypertension and associated hemodynamic disturbances.

More information: Moleda L, Jurzik L, Froh M, Gäbele E, Hellerbrand C, Straub RH, Schölmerich J, Wiest R. Role of HSP-90 for increased nNOS-mediated vasodilation in mesenteric arteries in portal hypertension. World J Gastroenterol 2010; 16(15): 1837-1844
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