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### Geldanamycin suppresses angiotensin II-induced cardiac hypertrophy through regulation of NF-κB pathway

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Angiotensin II (AngII), vasoactive octapeptide, has a modulatory role on hypertrophic effect in cardiac cells. In hypertrophic process by cardiac overload, it was found that heat shock proteins (Hsp) were induced. Heat shock proteins are a group of chaperone proteins that helps to maintain protein stability and to refold or target for degradation unfolded proteins when cells are subjected to heat shock or other stresses. Numerous studies have evidenced that AngII induced NF-κB activation in cultured cardiac cells, and reported that activation of NF-κB is required for hypertrophic growth of primary rat neonatal ventricular cardiomyocytes. Interestingly, recent studies showed that disruption of Hsp90 function resulted in blockage of the NF-κB activation. In this study, we investigated whether Hsp90 regulates NF-κB activation in AngII-induced cardiac hypertrophy. Geldanamycin (GA), a specific inhibitor of Hsp90, inhibited AngII-induced NF-κB activation and [3H]leucine incorporation in cardiac myoblast H9c2 cells. GA also inhibited AngII-induced phosphorylation of IκBα and phospho-IKKα/β. In addition, IKKα/β expression level was significantly decreased by GA. Theses results suggest that Hsp90 sustains NF-κB activity by IKKα/β stabilization, following transduction of hypertrophic signal in cardiac cells.

## D-38

### Heme oxygenase-1 mediates the anti-inflammatory effect of mushroom Phellinus linteus in LPS-stimulated RAW264.7 macrophages

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This work aimed to elucidate the anti-inflammatory mechanism of the n-BuOH subfraction (PL) prepared from fruiting bodies of Phellinus linteus. PL induced heme oxygenase-1 (HO-1) of the RAW264.7 macrophages in concentration- and time-dependent manner. It suppressed induction of inducible nitric oxide synthase (iNOS) and subsequent production of nitric oxide (NO) through down-regulation of iNOS promoter activity in lipopolysaccharide (LPS)-stimulated macrophages. Zn(II) protoporphyrin IX (ZnPP), a specific inhibitor of HO-1, partly blocked suppression by PL on iNOS promoter activity and NO production, which were elevated in LPS-stimulated macrophages. LPS was able to enhance NO production via reactive oxygen species (ROS) generation, c-Jun NH2-terminal kinase (JNK) and c-Jun induction. ZnPP prevented PL from down-regulating ROS generation and JNK activation in LPS-stimulated macrophages. Taken together, PL shows its anti-inflammatory activity via mediation of HO-1 in an in vitro inflammation model.

## D-39

### How fibroin enhances glucose uptake in 3T3-L1 adipocytes?

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It has been known that fibroin enhances glucose uptake in 3T3-L1 adipocytes. In this study, we explored the mechanism underlying the fibroin effect in more detail. It was found that fibroin increased tyrosine phosphorylation of insulin receptor β-subunit. Fibroin also augmented the phosphorylation of PKC-ζ both in the presence and absence of acute insulin stimulation. PKC-ζ is known to be related to GLUT4 translocation. From the result, it is concluded that fibroin increases GLUT4 translocation to the plasma membrane via PI3-kinase pathway, especially through a mechanism of PKC-ζ dependent GLUT4 translocation. In addition, fibroin increased the GLUT4 protein level in whole cell lysates, indicating that the chronic exposure to fibroin seems to enhance GLUT4 expression in 3T3-L1 adipocytes. When the cells were treated with several hydrolysates obtained by hydrolysis with proteolytic enzymes including trypsin, pepsin, and chymotrypsin, the glucose uptake increases were higher than that of whole fibroin treatment, and the peptic hydrolysate was most effective in enhancing glucose uptake. The peptic hydrolysate increased both of basal and insulin-stimulated glucose uptake in time-dependent pattern.These results indicates that the effect of fibroin is strongly related to some special peptide sequence(s) and/or amino acid residue(s).

## D-40

### Hsp9 protein which regulated by the stress-activated MAP kinase, is potentially involved in 14-3-3 binding to cdc25 in Schizosaccharomyces pombe

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A small heat shock protein, Hsp9, was isolated as a multicopy suppressor of a ras1 synthetic lethal mutant of fission yeast. The three repeats of the stress-responsive CCCCT motif(STRE) and consensus sequence of the heat shock element were founded in the Hsp9 promoter region. The disruption of hsp9 gene itself shown the retarded cell growth at low temperatures, but did not show any observable effect on the cell growth and thermo-tolerance at high temperature. The hsp9 gene increased in the cells exposed to heat shock, osmostress, oxidative stress, and nitrogen starvation as well as in the cells at stationary phase. However, it did not show in the cells of Δwis1 and Δsty1 and slightly increased in Δras1. Furthermore, Pka1-disrupted and Ras1Val19 mutants exhibit high basal levels of hsp9. The Δhsp9 cell slightly short in morphologically and it may be deduced from high Cdc2 activity followed by the association of 14-3-3 with cdc25 get weaken, and the Δwis1Δhsp9 mutant is less sensitive in the stressed conditions. These results suggested that stress-induced expression of hsp9 should be regulated by the ras1 and sty1-MAP kinase pathway. Hsp9 protein which regulated by the stress-activated MAP kinase is potentially involved in 14-3-3 binding to cdc25