

Heat-shock protein 90 (HSP90) is a molecular chaperone that represents one of the most important proteins for cellular homeostasis in all life domains. Chaperones are proteins that assist other proteins in proper folding and refolding. First discovered as a protein of a heat-shock response, HSP90 eventually emerged as a hub connecting multiple cellular functions, such as transcription, translation, DNA repair, immune response, cell signaling, etc. Unsurprisingly, HSP90 also plays a role in the pathogenesis of human diseases: various cancers, and neurodegenerative and respiratory diseases. For that reason, it became a target of medical research. HSP90 is a homodimer consisting of two protomers, each of which is composed of three domains: N-terminal domain, middle domain, and C-terminal domain. To fulfill its functions, HSP90 goes through an ATP-dependent conformational cycle, tightly regulated by a large group of assisting proteins—co-chaperones, and several post-translational modifications, such as phosphorylation and acetylation. Acetylation is known to affect HSP90 binding to nucleotides, clients, and co-chaperones, and thus it is suggested as a control mechanism of HSP90 function. Potentially, HSP90 acetylation can be utilized in the treatment of hormone-dependent cancers. Therefore, regulators of HSP90 acetylation are currently under intensive investigation. Histone deacetylase 6 (HDAC6) is proposed to be the major deacetylase of HSP90, however, available data about HSP90—HDAC6 interaction are very limited up to date. This thesis summarizes current knowledge about the structure and function of HSP90 with a focus on the regulation of HSP90 acetylation status.