Characterization of HSP90 Complexes in Embryonic Stem Cells

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The noncanonical stable HSP90 complexes, initially discovered in tumors to account for the selectivity of HSP90 inhibitors towards cancer cells, have tremendous potential as biological targets for therapeutic interventions. These complexes are now shown to be upregulated under physiological and pathological conditions where robust proliferation and adaptability become essential for cell survival, such as in embryonic stem cells (ESCs) and cancer cells. Our recent studies further established a direct link between HSP90 phosphorylation ($HSP90^{P}$), HSP90 oligomeric complex formation, and robust cell proliferation. However, little is known about the molecular features and regulation of these complexes. We have developed a strategy to purify and separate ESC HSP90 oligomeric complexes in native states for MS-based proteomics characterization. Our results show the high heterogeneity of stable HSP90 multi-subunit complexes, corroborating its role in the function of diverse proteins and protein assemblies. Furthermore, our data elucidate novel insights on the relationship between the posttranslational modifications and chaperone, co-chaperone composition in these complexes.