Title: **Androgen Receptor Expression Reduces Post-Hepatectomy Surgery Recurrence Risks of Hepatocellular Carcinoma**

**Introduction**: Androgen Receptor (AR) promotes hepatocarcinogenesis, yet, suppresses HCC (hepatocellular carcinoma) progression of HCC mouse models. Yet, the translational value of AR expression in HCC patients is not clear. The CD90 membrane protein is cancer stem/progenitor cells (CSPC) marker, which can be detected in Circulating Tumor Cells (CTC). It's recognized as post-surgery HCC recurrence confounder. In this report, we examined the roles of AR expressions in post- hepatectomy HCC recurrence, and provide cellular and molecular insight to AR effect in HCC recurrence. **Methods**: We detected AR vs. CD90 expressions in primary tumor and CTC of HCC patients whom subjected to hepatectomy surgery to associated with HCC recurrence. In addition, we delineated the cellular and molecular mechanisms in AR knockout (ARKO)-HCC model, as well as in human HCC cell lines. Furthermore, systems biological approach was also introduced to examine AR-mediated gene expression pathways enrichment. **Result**: We found opposite association power of AR vs. CD90 that higher CD90 was related to higher risk; yet, higher AR was refer to lower risks of HCC recurrence. The mechanisms are summarized as follow: 1). AR suppresses CD90 through Histone 3H2A (H3H2A) acetylation: The AR vs. CD90 is reversely expressed in the specimens. The CD90+ cells increases in ARKO compared to that in wildtype (WT) mouse HCC. AR abolishes CD90 expression in two HCC cell lines, in which H3H2A upregulation and acetylation also noted. Knockdown of H3H2A could recover CD90 expression under AR effect. 2). AR reprograms gene expression to inhibit cell migration: AR suppresses HCC cell migration in an AR-level dependent manner with shifted gene expression pattern. Systems biological analysis revealed that low AR is related to cell-cycle enrichment gene settings; yet, shift to cell migration suppression setting while AR level increased. 3). AR promotes cell anoikis through facilitating cellular stress produced by resolving cytoskeletons (amorphosis) in circulation: AR promotes cell anoikis through a non-classical AR function, by which to activate PI3K/AKT- and ROCK-related cytoskeletal rearrangement stress while the cells in anchorage independent condition. **Conclusion**: To sum up, this report demonstrated that AR expressions could serves as prognostic marker for HCC recurrence. And there are three mechanisms involved: AR reduces CD90 population through epigenetic modification, AR inhibits cell migration through gene expression shift, and AR promotes anoikis through increasing amorphosis stress.