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Non-enzymatic Functions of Aldolase A Induce Oct4 Activation to Promote Lung Cancer Stemness

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ALDOA is involved in glycolysis process. The enzyme can exert its function to catalyze Fructose 1, 6-bisphosphate to glyceraldehyde 3-phosphate and dihydroxyacetone phosphate. In recent year, several reports focusing on exploring the non-enzymatic role of ALDOA to control proliferation and/or enhance metastasis ability in cancer. However, its roles in cancer stemness remain unclear. Therefore, we established the ALDOA-based transcriptomics and proteomics database to explore its functional roles in lung cancer. Through Genespring software to normalization, we have selected candidate targets for prediction potential upstream regulator and pathway by Ingenuity Pathway Analysis (IPA) that may be mediated the induction of lung cancer stemness. Our preliminary results showed that stemness-related transcription factor Oct4 was activated in ALDOA overexpressed cell. Furthermore, we designed several specific mutant forms of ALDOA to block its enzymatic activity or wild-type ALDOA expression. We observed ALDOA still induced significant *in vitro* sphere formations and *in vivo* tumorigenicity. Knockdown of these molecules of Oct4 downstream could significantly decrease stemness ability in lung cancer. In addition, the established ALDOA transcriptomics database in our study identified the candidate drug that significantly suppressed Oct4 activation-induced axis signaling and suppressed ALDOA induced invasion *in vitro* and metastasis *in vivo*. Combined All evidences, our study reveals novel ALDOA functional roles in inducing cancer stemness through activating Oct4 transcriptomic responses. These findings provided a new therapeutic strategy to modulate the Oct4 activation and downstream signalling to combat lung cancers stemness.