AhR plays a key role on epigenetic regulation within HDAC inhibitor treatment

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Background: Tumor resistance of late-stage treatment resulting the poor prognosis and malignant metastasis, which is also a leading cause of cancer mortality. Elucidating the mechanism and finding early molecular targets may be an effective way on therapy improvement. However, circumventing this drug-resistance for treatment is still an intractable issue. In this study, we found Aryl hydrocarbon receptor (AhR), which is a transcription factor involved in histone acetylation by regulating histone deacetylases (HDACs). This epigenetic regulation may reveal if AhR is a potential target for cancer therapy. Methods: Three lung cancer cell lines were used for observing protein expression by Western blot with HDAC inhibitor (LBH589) treatment. Luciferase/colorimetric assay were used for detecting HDAC/HAT activity within LBH589 treatment. LBH589-changed cell motility associated with AhR expression has been assayed by Boyden chamber assay (migration assay). To prove the interaction between AhR and HDACs was assayed by Co-IP and IF staining. Results: We have found that inhibition of HDACs activity can increase acetylation of histone, the results demonstrated that AhR and histone protein expression was up-regulation with LBH589 treatment in time and dose manner. Besides, we found that the higher histone acetylation with higher AhR expression level, contributing to lower cell motility. Moreover, we also discovered that activity of HDACs was up-regulated in shAhR cells, but not HATs. LBH589-induced AhR expression also increased AhR/HDACs complex formation. Conclusion: These results suggested that HDACs activity was suppressed by upregulated-AhR in LBH589 treatment, which plays an important role in histone acetylation in cancer epigenetic. The novel insight for this study might provide an innovative therapeutic strategy based on using epigenetic drugs to control AhR-related epigenetic regulation, and improve the tumor resistance on cancer therapy.