Biochemistry Conference 2018- Transcriptional regulation of cyclin D1 expression by YB-1 and NKX2-1 in human non-small cell lung cancers- Masatoshi Kitagawa, Masanori Harada and Yojiro Kotake- Hamamatsu University School of Medicine, Japan

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Abstract

The known oncogene cyclin D1 (CCND1) participates in progression of the cell cycle from G1 to S phase. Expression of cyclin D1 is frequently promoted in multiple human cancers including non-small cell lung cancer (NSCLC). Transcription factors YB-1 and NKX2-1 (also called TTF-1) are frequently expressed in NSCLCs. We found Y-box and NKX2-1 binding sequence in the cyclin D1 promoter. However, the functional association of cyclin D1 with YB-1 and NKX2-1 has not been fully elucidated. In the presence study, we demonstrated that not only YB-1 but also NKX2-1 promoted transcription of cyclin D1. Moreover, ChIP assay indicated that they bound to their binding sequence in the cyclin D1 promoter. Interestingly, additional expression of YB-1 enhanced NKX2-1-mediated promoter activity of cyclin D1. Therefore, YB-1 and NKX2-1 may collaboratively promote transcription of cyclin D1. Furthermore, we found that expression of cyclin D1 was significantly correlated with YB-1 as well as NKX2-1 in human NSCLC clinical specimens. These results strongly suggest that YB-1 and NKX2-1 are the transcription factor for cyclin D1 expression in human NSCLC. Overexpression of cyclin D1 has been found in NSCLC. It has been reported that overexpression of cyclin D1 is not only positively, but also negatively correlated with poor prognoses. Therefore, the association between cyclin D1 expression and prognosis is controversial. Here, we found that cyclin D1 expression was significantly correlated with NKX2-1 in human adenocarcinomas but not squamous cell carcinomas. NKX2-1 was a good prognosis factor in cyclin D1-positive adenocarcinomas. Expression of NKX2-1 but not cyclin D1 was inversely associated with metastatic incidence as an independent good prognostic factor of adenocarcinoma. Altogether, NKX2-1-expressing adenocarcinomas, whereas NKX2-1 promoted cyclin D1 expression, may show good prognosis features by the metastasis inhibition potency of NKX2-1 regardless cyclin D1 expression.

This work is partly presented at International Conference on Biochemistry, Proteomics & Bioinformatics- May 16-17, 2018 Singapore