

## **Supplementary Information**

***De novo* deoxyribonucleotide biosynthesis regulates cell growth and tumor progression in small-cell lung carcinoma**

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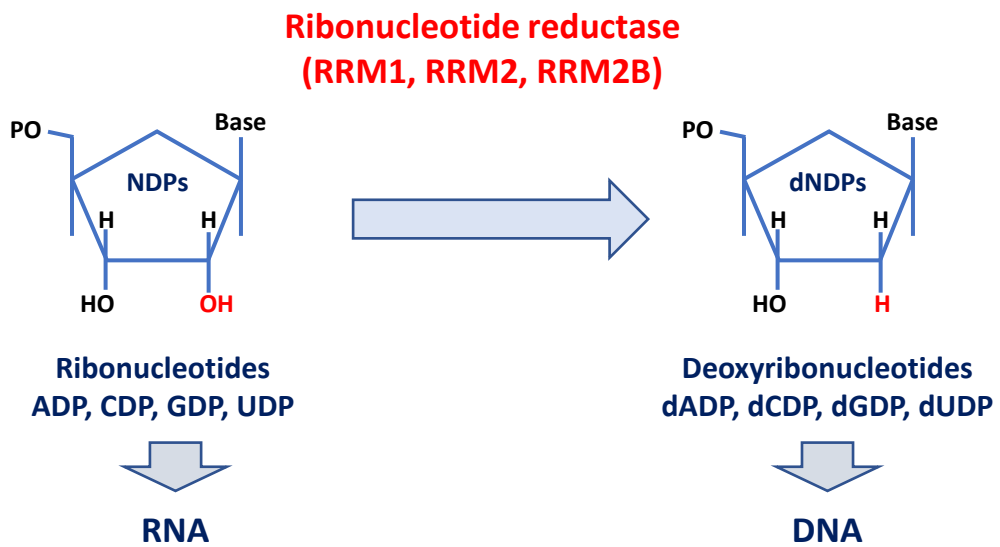
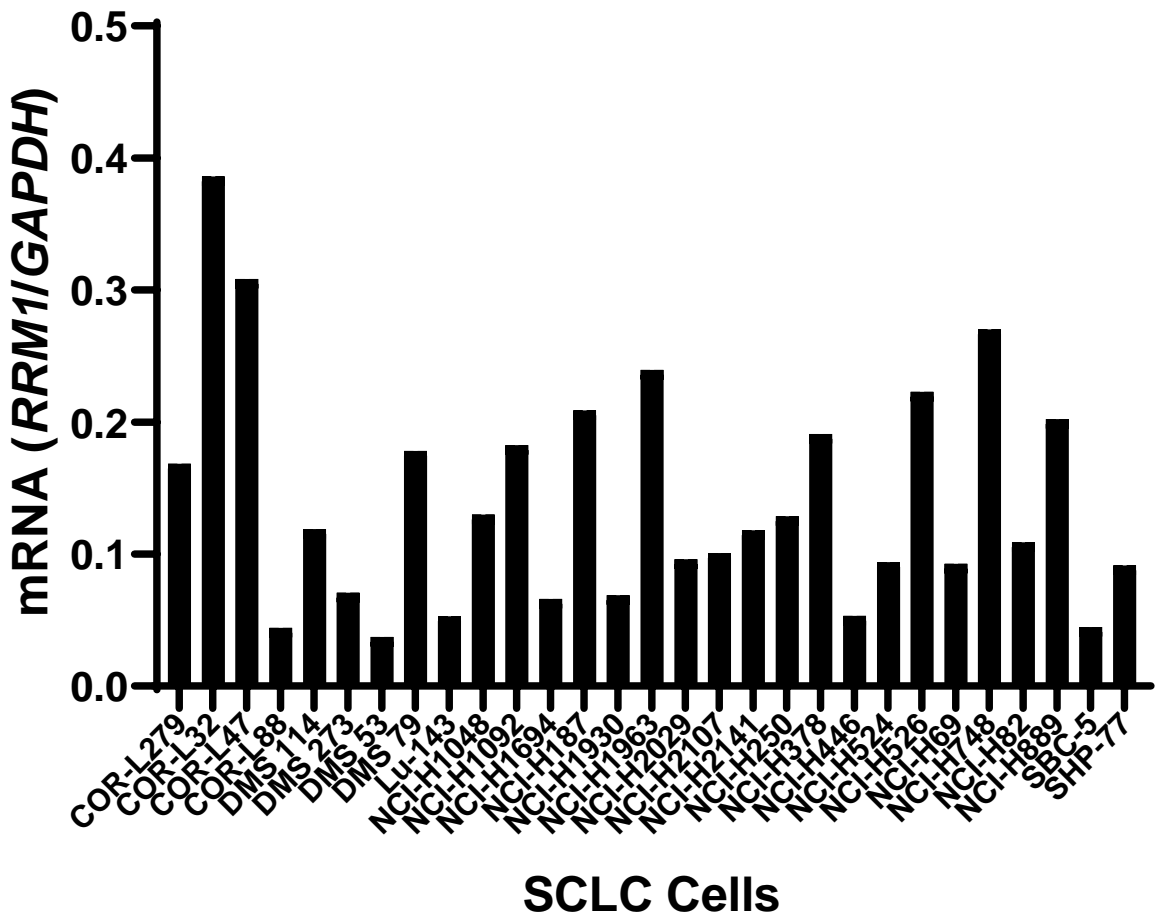
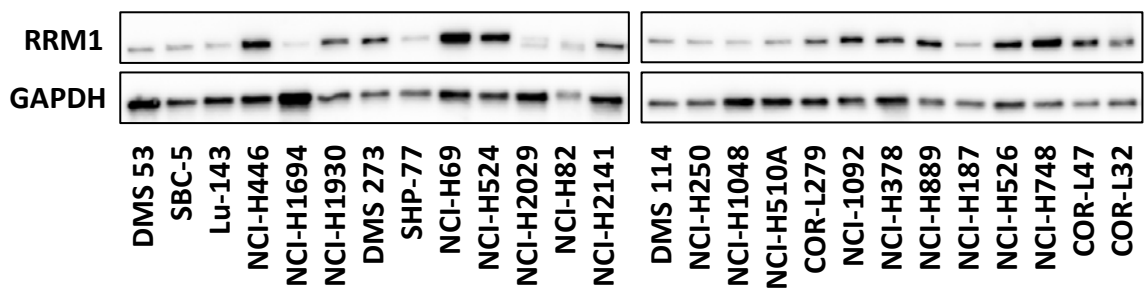


Figure. S1 Schematic diagram of reaction catalyzed by ribonucleotide reductase.



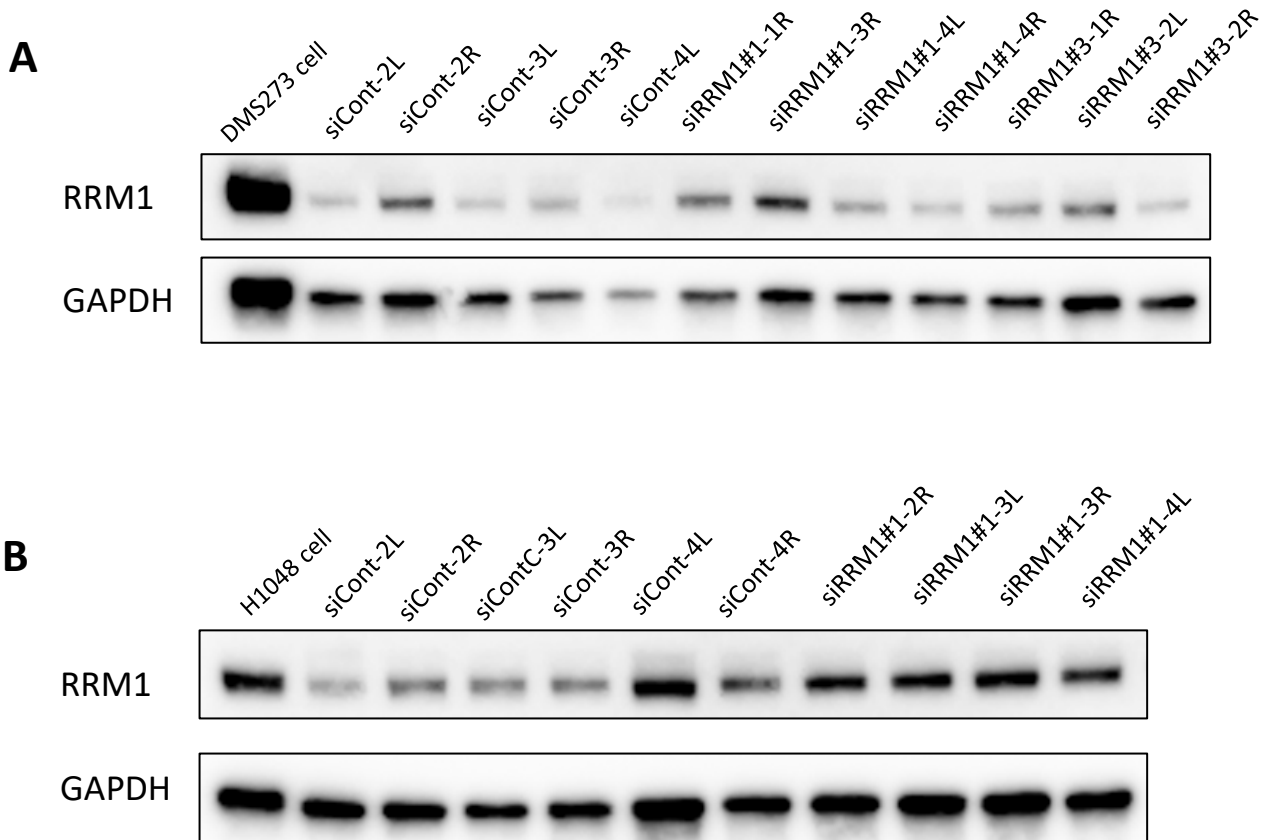
**Figure. S2** Relative level of *RRM1* mRNAs in SCLC cells.

Total RNA was isolated from SCLC cells. Relative mRNA level of *RRM1* to *GAPDH* was shown. Data are shown as the mean  $\pm$  SD. ( $n = 3$ ).



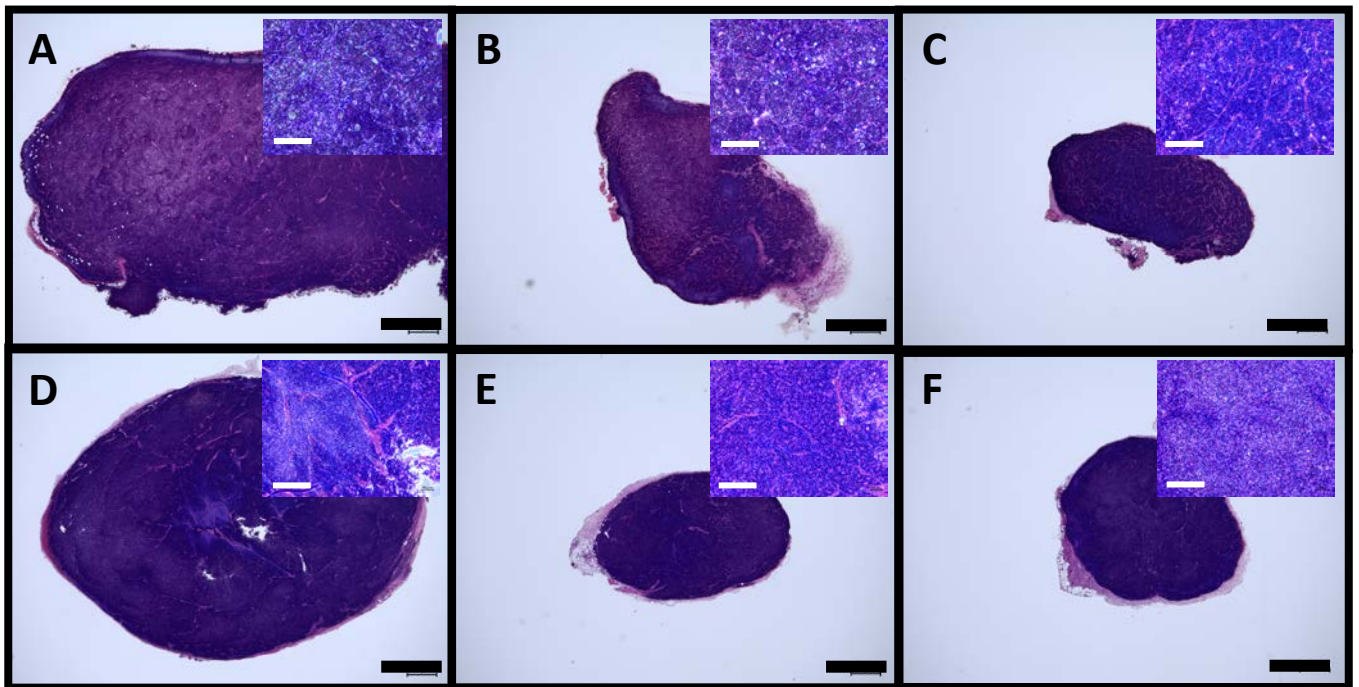
**Supplementary Fig. S3 RRM1 Protein level in SCLC cells.**

Western blot analysis of RRM1 expression in 26 SCLC cell lines. GAPDH was loading control. The blots were cropped and full-length blots are included in a Supplementary Information file.



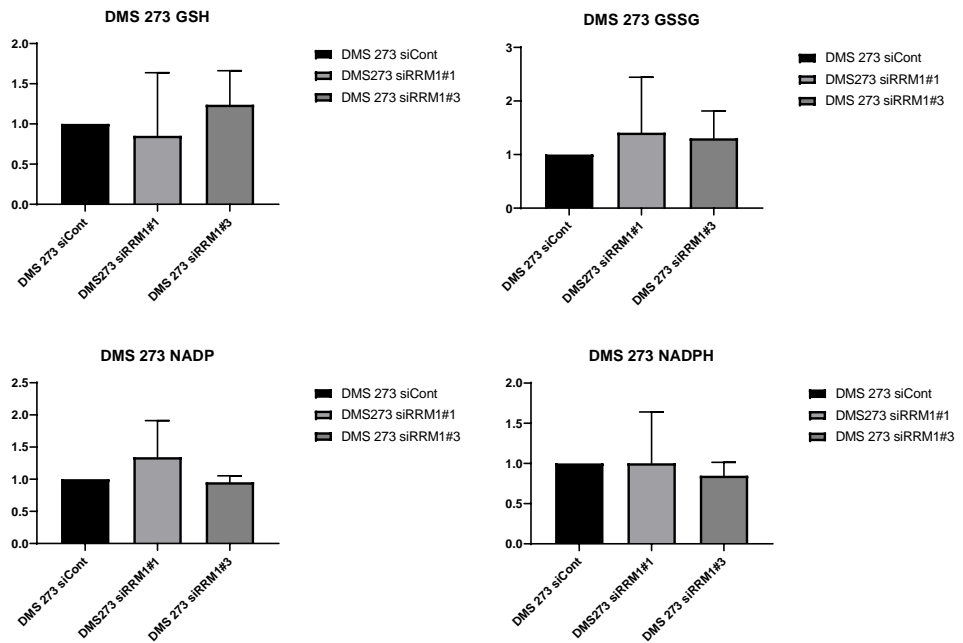
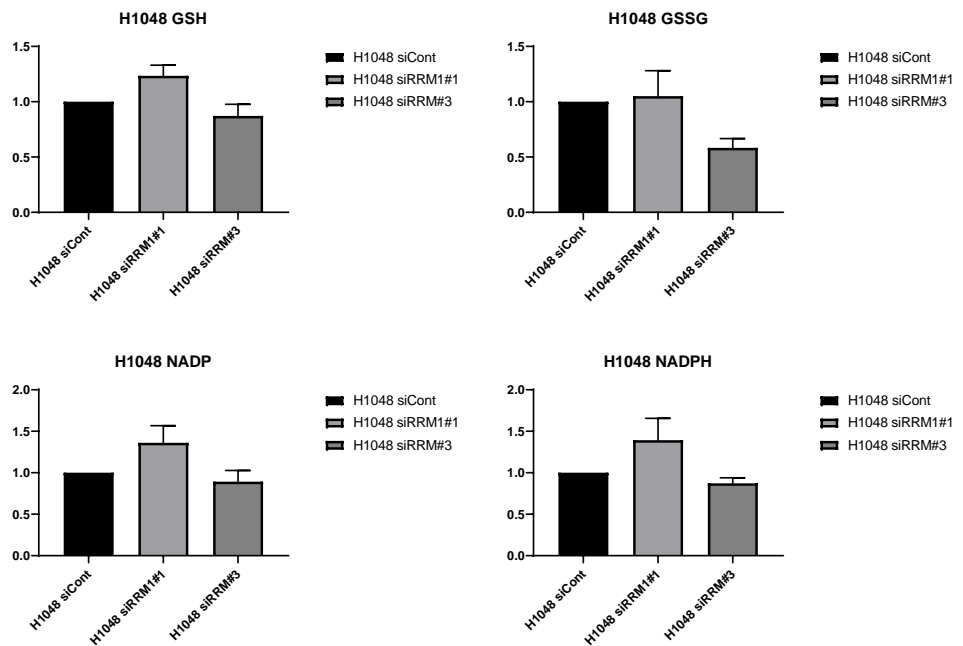
**Supplementary Fig. S4 Western blot analysis of RRM1 expression in mouse-xenografted tumours.**

DMS 273 tumours (A) and H1048 tumours (B) were shown. GAPDH was loading control. The blots were cropped and full-length blots are included in a Supplementary Information file.



**Supplementary Fig. S5 Histological characterization of the SCLC xenografts.**

Histological features of the xenograft. For viewing cellular and tissue structure detail, hematoxylin and eosin staining were used. DMS 273 tumors (A-C) and H1048 tumors (D-F) were shown. Images were acquired with BZ-X710 All-in-One Fluorescence Microscope (Keyence, Osaka, Japan). Black scale bars were 1,000  $\mu\text{m}$  and white scale bars were 100  $\mu\text{m}$ .

**A****B****Supplementary Fig. S6 Metabolome analysis oxidative stress marker.**

Relative intracellular levels of key metabolites in the nucleotide biosynthesis pathway after RRM1 inhibition in DMS 273 (A) and H1048 (B) cells. Other metabolites are listed in Supplementary Table 1. Data represent the mean  $\pm$  SD ( $n = 3$ ).

# Original images of gross pathology

Figure 3E

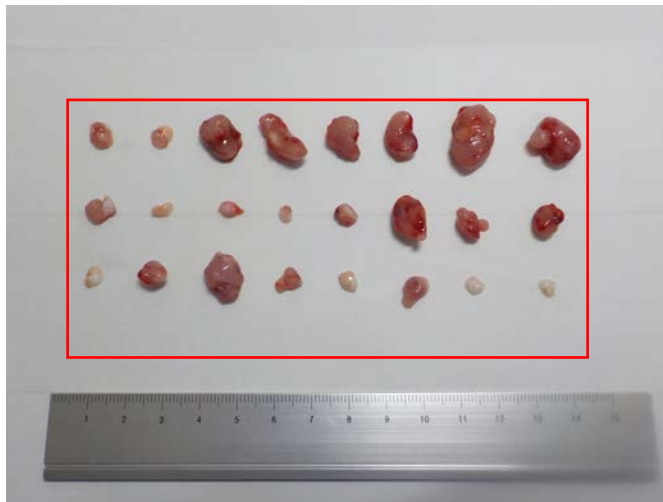


Figure 3F





# Original images of blots



# Membrane edges of blots

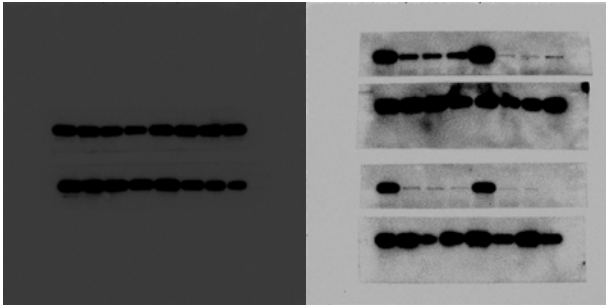


Figure 2  
GAPDH

Figure 2  
RRM1

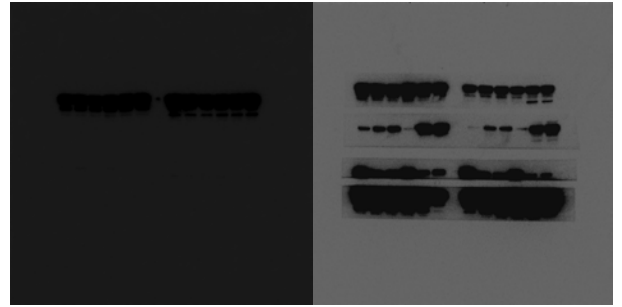


Figure 5  
GAPDH

Figure 5  
RRM1

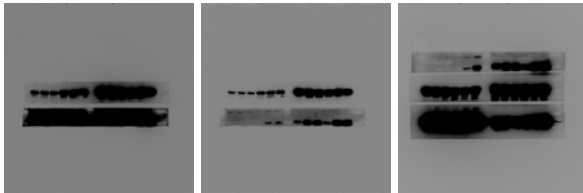


Figure 5  
P53 & p-p53

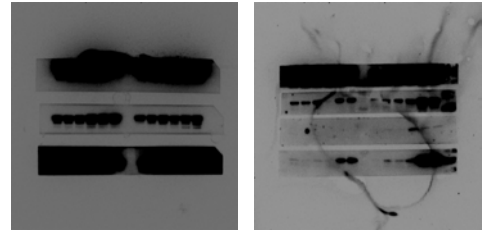


Figure 5  
CHK2 & p-CHK2

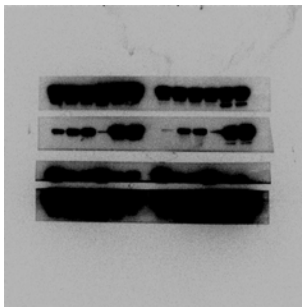


Figure 5  
CHK1 & p-CHK1

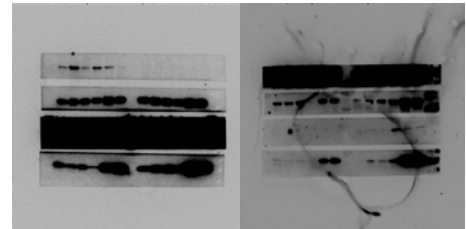
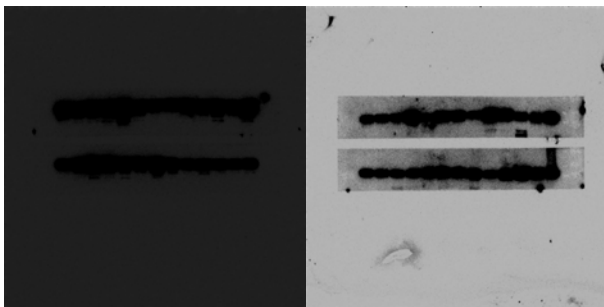
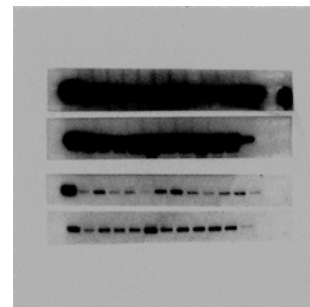


Figure 5  
H2AX &  $\gamma$ H2AX



Supplementary Fig S3  
GAPDH

Supplementary Fig S3  
RRM1



Supplementary Fig S4  
GAPDH & RRM1