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2. **Title**

   Mechanisms of PD-L1 Upregulation in Renal Cell Carcinoma

3. **Period**

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4. **Summary**

Immunotherapy based on blockade of the programmed death-1 (PD-1)/programmed death-ligand 1 (PD-L1) axis has shown promising clinical activity for renal cell carcinoma (RCC) patients; however, the most effective use of these agents in combination with conventional targeted therapy remains to be resolved. The results of the present study demonstrated that anti-PD-L1 treatment enhanced the antitumor effect of everolimus (EVE) in a mouse model, supporting a direct translation of this combination strategy to the clinic for the treatment of RCC. We also showed that PI3K/mTOR dual inhibition might overcome the resistance to EVE in renal cell carcinoma and IFN-γsignaling might be related to PD-L1 upregulation by EVE. Moreover, we established successfully a novel rat RCC model for lung metastasis evaluation, and established two high metastatic cell lines that PD-L1 mRNA expression was upregulated compared to control cell line. These models are useful for evaluation of immunity of metastatic RCC and the antitumor effects of immune checkpoint inhibitors.