Boosting Immunity by Targeting Post-translational Prenylation of Small GTPases.

**Summary**

Diseases leading to immune activation and autoinflammatory phenotypes may provide a reservoir of potentially druggable pathways for optimizing immune adjuvants or boosting antitumor immune responses. Now, Xia et al. report that lipophilic statins or bisphosphonates, targeting the mevalonate pathway, act as efficient vaccine adjuvants and synergize with anti-PD1 against cancer.

Translational control of tumor immune escape via the eIF4F-STAT1-PD-L1 axis in melanoma.

**Summary**

Preventing the immune escape of tumor cells by blocking inhibitory checkpoints, such as the interaction between programmed death ligand-1 (PD-L1) and programmed death-1 (PD-1) receptor, is a powerful anticancer approach. However, many patients do not respond to checkpoint blockade. Tumor PD-L1 expression is a potential efficacy biomarker, but the complex mechanisms underlying its regulation are not completely understood. Here, we show that the eukaryotic translation initiation complex, eIF4F, which binds the 5’ cap of mRNAs, regulates the surface expression of interferon-γ-induced PD-L1 on cancer cells by regulating translation of the mRNA encoding the signal transducer and activator of transcription 1 (STAT1) transcription factor. eIF4F complex formation correlates with response to immunotherapy in human melanoma. Pharmacological inhibition of eIF4A, the RNA helicase component of eIF4F, elicits powerful antitumor immune-mediated effects via PD-L1 downregulation. Thus, eIF4A inhibitors, in development as anticancer drugs, may also act as cancer immunotherapies.
Regulation of eIF4F translation initiation complex by the peptidyl prolyl isomerase FKBP7 in taxane-resistant prostate cancer.  
*Clinical cancer research : an official journal of the American Association for Cancer Research* :  
DOI : clincanres.0704.2018

**Summary**

Targeted therapies that use the signaling pathways involved in prostate cancer are required to overcome chemoresistance and improve treatment outcomes for men. Molecular chaperones play a key role in the regulation of protein homeostasis and are potential targets for overcoming chemoresistance.

Regulation of RNA polymerase III transcription during transformation of human IMR90 fibroblasts with defined genetic elements.  
*Cell cycle (Georgetown, Tex.)* : 1-11 : DOI : 10.1080/15384101.2017.1405881

**Summary**

RNA polymerase (Pol) III transcribes small untranslated RNAs that are essential for cellular homeostasis and growth. Its activity is regulated by inactivation of tumor suppressor proteins and overexpression of the oncogene c-MYC, but the concerted action of these tumor-promoting factors on Pol III transcription has not yet been assessed. In order to comprehensively analyse the regulation of Pol III transcription during tumorigenesis we employ a model system that relies on the expression of five genetic elements to achieve cellular transformation. Expression of these elements in six distinct transformation intermediate cell lines leads to the inactivation of TP53, RB1, and protein phosphatase 2A, as well as the activation of RAS and the protection of telomeress by TERT, thereby conducting to full tumoral transformation of IMR90 fibroblasts. Transformation is accompanied by moderately enhanced levels of a subset of Pol III-transcribed RNAs (7SK; MRP; H1). In addition, mRNA and/or protein levels of several Pol III subunits and transcription factors are upregulated, including increased protein levels of TFIIIB and TFIIIC subunits, of SNAPC1 and of Pol III subunits. Strikingly, the expression of POLR3G and of SNAPC1 is strongly enhanced during transformation in this cellular transformation model. Collectively, our data indicate that increased expression of several components of the Pol III transcription system accompanied by a 2-fold increase in steady state levels of a subset of Pol III RNAs is sufficient for sustaining tumor formation.
Team Publications
RNA Biology linked to DNA damage