Marta Dzimkova, J Blood Disord Transfus 2018,Volume:9
DOI: 10.4172/2155-9864-C3-038

Marta Dzimkova
Veterinary Research Institute,
Czech Republic

CDK12 regulates gene expression of *DNMT1* and *ERBB3* by altering transcription of *MIR152*

The DNA-damage-response (DDR) pathway is a cellular mechanism which has evolved to protect cellular integrity by detection and repair of DNA lesions. Previously, our group and others demonstrated that the cyclin-dependent kinase 12 (*CDK12*) maintains genome stability via regulation of transcription of DDR genes, specifically, *BRCA1, RAD51* and others. Importantly, down-regulation of the *CDK12* caused induction of the 53BP1 and γH2AX foci and accumulation of cells in the G2-M phase of the cell cycle. Since various microRNA (miRNA) are situated within coding genes, such as DDR, we hypothesize that expression of some of them might be also affected by *CDK12* depletion. Therefore, we conducted a pilot study focused on identification of candidate miRNAs that might be significantly altered in *CDK12* deficient cells. Indeed, downregulation of *CDK12* protein level led to aberrant expression of several miRNAs. Among studied miRNAs, the level of miR-152 was significantly elevated. By using predictive algorithm, several proteins that might be targeted by miR-152 were examined. We confirmed that upregulated expression of miR-152 leads to decreased expression of *DNMT1* (DNA methyl transferase 1), RICTOR and MET proteins, which are often found deregulated in wide spectrum of oncogenic diseases. Defects in methylation of *MIR152* has been observed in several cancers and studies have been proven an on/of loop between expressions of *DNMT1* and *MIR152*. In addition to *DNMT1*, the protein level of *ERBB3* (erb-b2 receptor tyrosine kinase 3) was also affected by down-regulation of *CDK12* in various ovarian cancer cells, such as PEO1, COV362 and OVCAR5. We speculate that *CDK12* participates in DDR machinery by two distinct mechanisms, either by orchestrating transcription of DDR genes or by stabilization of *DNMT1* protein by blocking expression of miR-152 targeting *DNMT1*.

Biography

Marta Dzimkova has a Graduate degree in Molecular Biology and Genetics. She is currently working on her PhD in Biochemistry focusing on transcription kinase CDK12 and its role in cancer development and potential therapeutic and prognostic significances.

dzimkova@vri.cz

Notes: