Abstract

Genome integrity maintenance is crucial for proper functioning and survival of all organisms, especially if the cell is constantly exposed to various genotoxic agents. For that reason, there are specific mechanisms that detect DNA damage, facilitate signalling and promote repair of the damaged region. These processes are referred to as DNA damage response (DDR). Necessary part of the DDR is also the MRE11-RAD50-NBS1 complex (MRN), comprised of the nuclease MRE11, ATPase RAD50 and regulatory docking protein NBS1. The MRN complex has an indispensable role in the detection and immediate resection of double-strand breaks (DSBs), signal transduction and activation of ataxia telangiectasia mutated (ATM) kinase with its downstream effectors necessary for the DDR. The compounds of the MRN complex are involved in processes crucial for efficient DNA repair, cell survival and maintenance of genomic stability.

The main aim of this work is to elucidate less known functions of the MRN complex in the nucleoli, nuclear membrane-less organelles formed around the copies of genes coding rRNA. This work discusses how the MRN complex is involved in the repair of rDNA double-strand breaks, transient inhibition of rRNA transcription or nucleolar segregation. Thereafter, this work puts into context the latest knowledge in the field of the nucleolar DNA damage response (n-DDR) and emphasises the importance of the entire MRN complex in response to nucleolar DNA damage. These findings are in contrast with the previous opinion that upon rDNA damage, the nuclear MRN complex falls apart and only NBS1 operates in the nucleolus while other components, MRE11 and RAD50, remain in the nucleoplasm.

Based on the recent research, the MRN complex makes a significant contribution in the nucleolar DNA damage response and maintains the stability of the genetic information of the cell. Current knowledge, reviewed in this work, raises new questions about transport of DDR factors into the nucleolus, modifications of nucleolar chromatin or possible role of phosphatases in the n-DDR, and opens new possibilities for the research of the n-DDR and also nucleolus in general.

Keywords: n-DDR, MRN complex, rDNA damage, TCOF1, nucleolar segregation