The BARD1/CDK13 Interaction in DNA Damage Repair

Fernandes, V.C.¹, Nepomuceno, T.C.¹, Carvalho, R.S.¹, Monteiro, A.N.², Carvalho, M.A.¹,³

¹Instituto Federal do Rio de Janeiro, Campus Maracanã, Rio de Janeiro, Brazil. ²H. Lee Moffitt Cancer Center, Tampa, USA. ³Instituto Nacional de Câncer, Rio de Janeiro Brazil.

Introduction. DNA damage repair (DDR) pathway is extremely important for the maintenance of genomic stability, thus, proteins involved in this pathway are main keys in the cell survivor. Mutations in these genes may lead to diseases, such as cancer. It is well characterized, that some mutations in the BRCA1 gene can increase the risk of breast and ovarian cancer development up to 80%. The BRCA1 protein has two major domains: RING finger and two tandem BRCT (tBRCT). The major interaction partner of BRCA1 is BARD1, which has a similar domain structure. The tBRCT is commonly found in DDR-associated proteins. Recently our group reported the tBRCT interactome for 7 different proteins, using tandem affinity purification followed by mass spectrometry and yeast two hybrid screening approaches. CDK13 (Cyclin-Dependent Kinase 13) was identified as a putative tBRCT BARD1 interactant. This protein is described to be involved in several processes, such as chromatin remodeling, transcription regulation and splicing coordination, however the biological role of CDK13 remains unclear.

Material and Methods. Fragments encoding the HA-tagged regions 1-706aa (N-terminal), 706-982aa (Kinase domain) and 1006-1452aa (C-terminal) of CDK13 were ectopically co-expressed with Flag-tagged full-length BARD1 or GFP-tagged BARD1 tBRCT. Whole cellular extracts were used in immunoprecipitation assays. Results and Discussion: We confirmed the interaction between ectopically expressed CDK13 full length, N-terminal and BARD1 full-length and BARD1 tBRCT. We intend to fine-map this interaction and generate CDK13 silenced cells to assess its role in DDR. Conclusions. Our data suggests the formation of BARD1/CDK13 complex and that BARD1 tBRCT, as well as, CDK13 N-terminal region are critical for this interaction. The role of CDK13 in DDR pathway is still under evaluation.

Keyword: CDK13, DNA damage, BARD1, BRCA1.
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