1. Overview

CGGBP1 is a transcription regulator which binds to repeat sequences in the genome. It is involved in various cytoprotective functions and maintains cellular homeostasis. CGGBP1 is essential for cell cycle progression and is known to be involved in inhibiting intrinsic DNA damage. CGGBP1, similar to most proteins involved in the cell cycle, also undergoes Post-translational modifications (PTMs) to exert its functions. S164 phosphorylation by ATR in CGGBP1 protects telomere integrity. The other serine phosphorylation sites in CGGBP1 are S56 and S59, as reported in the PhosphoSitePlus database. These serine residues are predicted to be present in the sequence motif for Casein kinase 1 (CK1) phosphorylation by ELM tool. Casein kinase 1 is a serine/threonine kinase with well-characterised role in cell growth and DNA damage response (DDR). DDR signalling involves a multitude of proteins functioning together to maintain genomic stability.

In this study, phospho-deficient and phospho-mimetic forms of CGGBP1 are used to investigate the functional relevance of these predicted casein kinase 1 phosphorylation sites. Previous studies revealed that the overexpression of phospho-site mutants in HEK293T cells exhibited a dominant negative effect. It was observed that the absence of this phosphorylation affects p53BP1 foci formation upon DNA damage by exogenous factors. The endogenous DNA damage response in cells overexpressing the phospho-deficient or phospho-mimicking forms of CGGBP1 is understood using p53BP1 as a DNA damage response marker. The dominant negative effects of these mutants in endogenous DNA damage response and genomic stability is investigated.