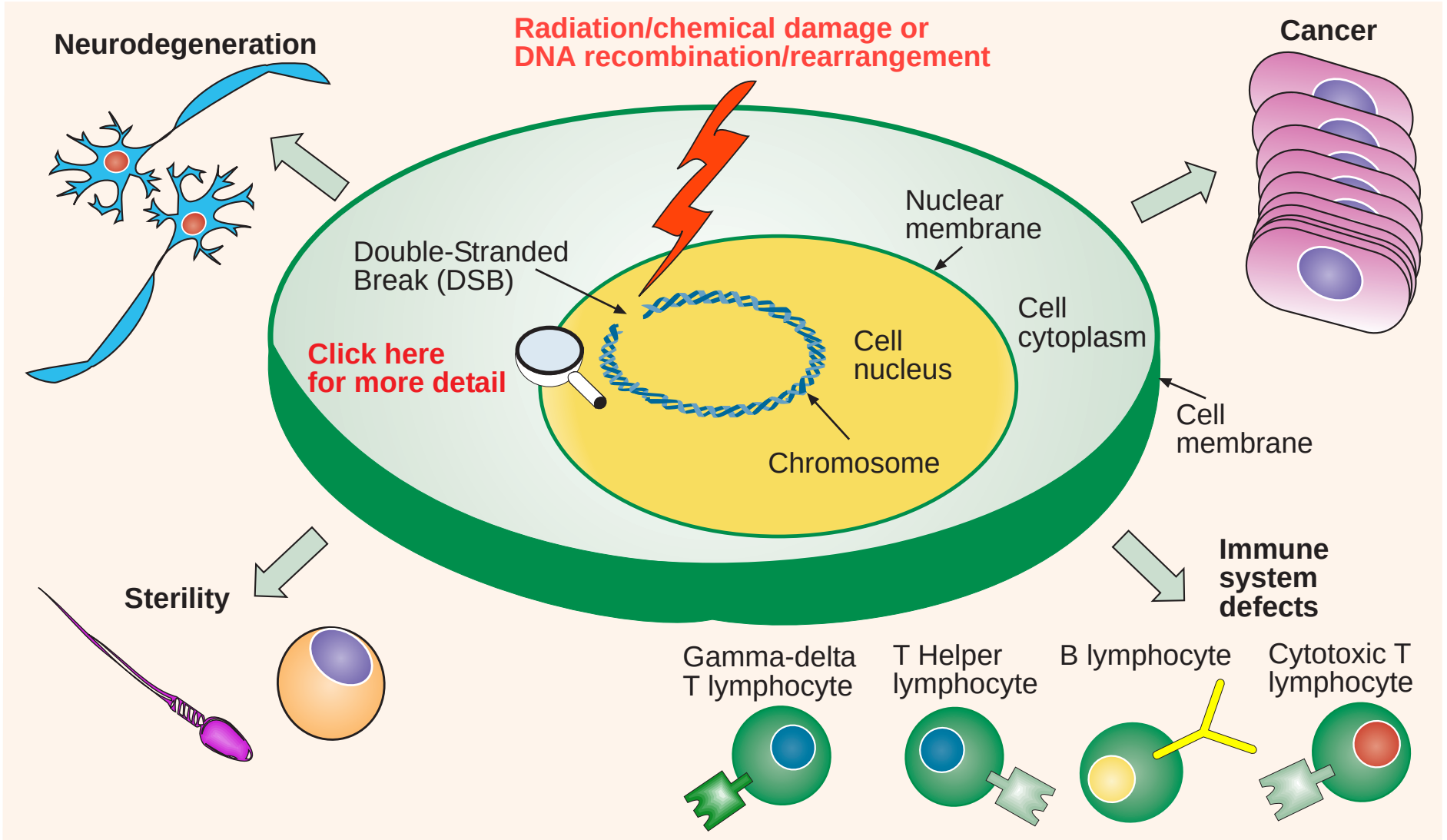
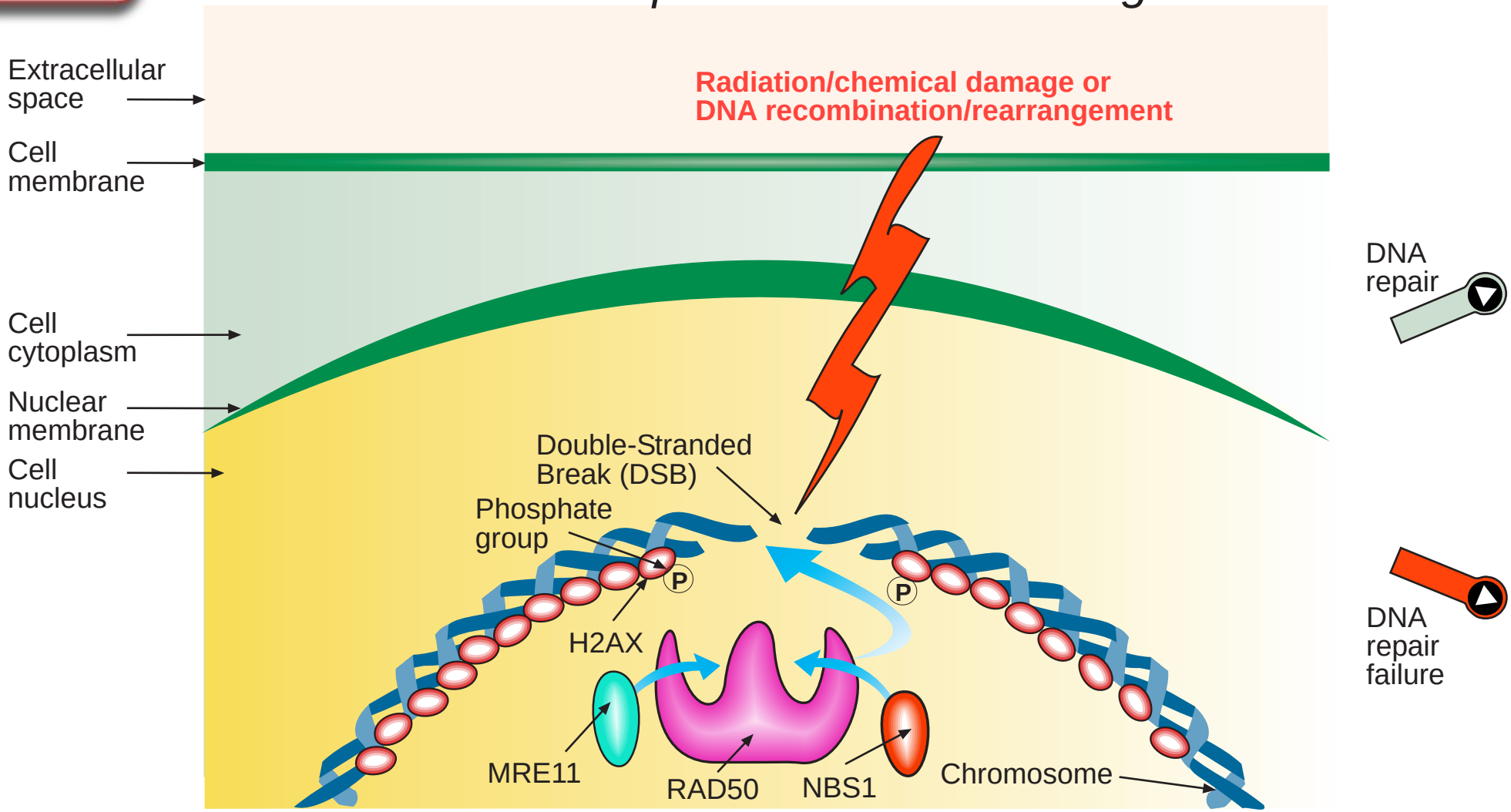
Ataxia -Telangiectasia



In Ataxia-Telangiectasia, failure to repair double-stranded breaks (DSB) in chromosomal DNA results in abnormalities in the regulation of cell growth. DSB can be caused by radiation/chemical damage or as a result of meiotic recombination and genetic rearrangements of immunoglobulin and T cell receptor genes. Mutations in the Ataxia-Telangiectasia Mutated (ATM) gene underlie the cause of the disease. ATM is essential for the repair of DSB in DNA and is also involved in the activation of tumour-suppressor proteins, cell-cycle regulatory proteins and telomere maintenance proteins.

PREVIOUS

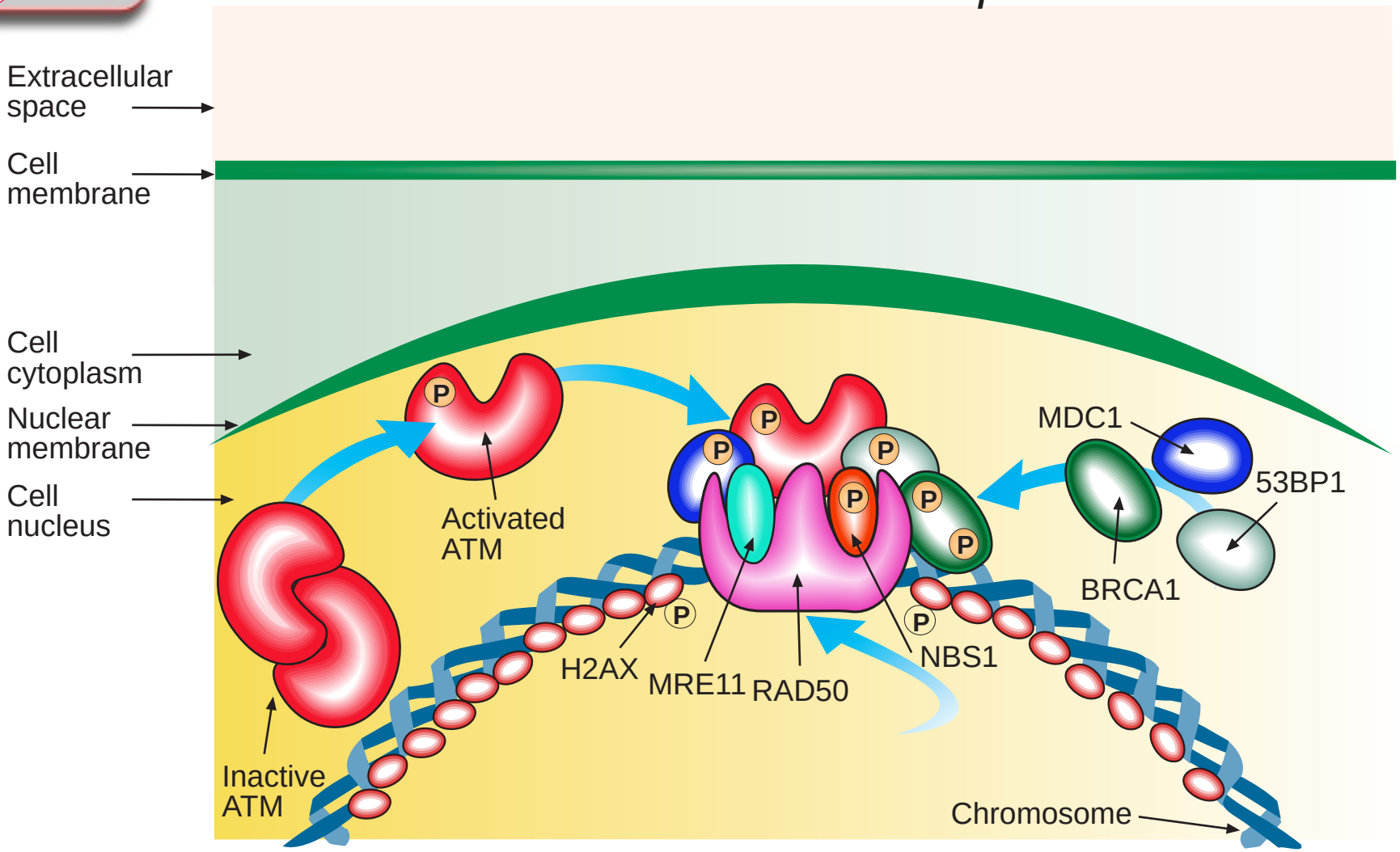
Inside the cell - response to DNA damage



A response to double-stranded breaks (DSB) in DNA caused by radiation/chemical damage or as a result of meiotic recombination and genetic rearrangements is initiated by H2AX histone proteins that become activated (by phosphorylation) and recruit RAD50, MRE11 and NBS1 proteins (known as the MRN complex) to the damaged area.

PREVIOUS

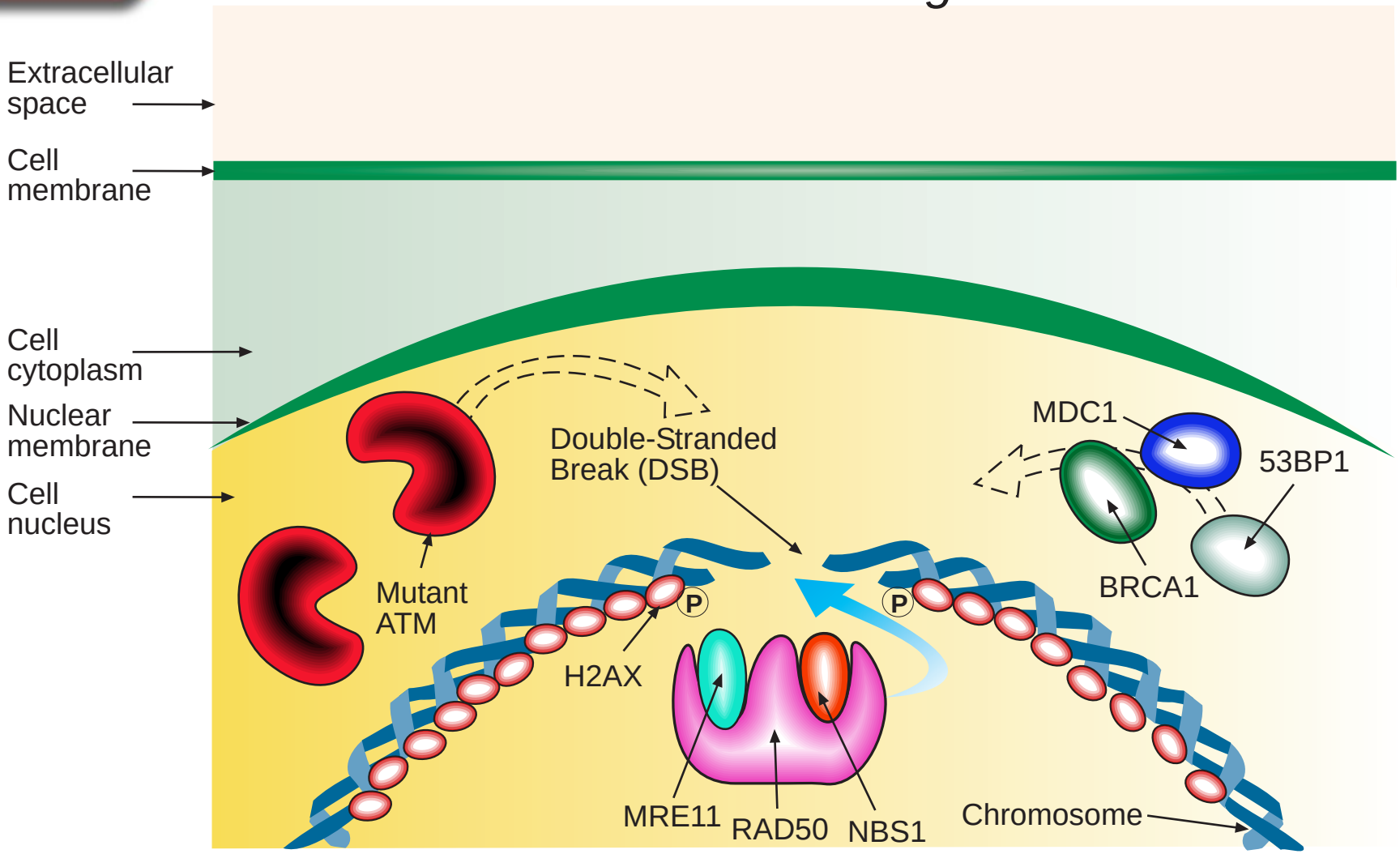
Inside the cell - normal DNA repair



In the nucleus ATM proteins are present in an inactive dimeric form and become activated by autophosphorylation when the DNA repair mechanism is engaged. Active ATM monomers are recruited to the MRN complex along with BRCA1, MDC1 and 53BP1. ATM is a protein kinase and activates BRCA1, MDC1, 53BP1 and NBS1 by phosphorylation. ATM also activates other cellular proteins such as tumour-suppressor proteins, cell-cycle checkpoint regulatory proteins and also proteins involved in telomere maintenance.

PREVIOUS

Inside the cell - Ataxia -Telangiectasia



In Ataxia-Telangiectasia, due to mutations in the ATM gene, reduced levels or dysfunctional ATM proteins are produced. This affects the repair mechanism of DNA double-stranded breaks (DSB) caused by ionising radiation or DNA damaging agents. DSB caused by natural mechanisms such as during meiotic recombination or gene rearrangements are also affected. In addition, ATM may fail to activate (by phosphorylation) other cellular proteins such as tumour-suppressor proteins, cell-cycle checkpoint regulatory proteins and also proteins involved in telomere maintenance.