WHITEPAPER

Meet the Marker: PCNA

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Cellular proliferation is an essential process in all organisms since it is key to tissue growth and maintenance.[1] However, its ubiquity may obscure the fact that this process is quite complex, with many points at risk for potential error. The fact that it proceeds so quickly and accurately despite its intricacies is due in large part to protein complexes that keep it tightly controlled. Proliferating cell nuclear antigen (PCNA) is one such complex.

In eukaryotic cells, cellular proliferation can be simplified into a four-phase cell cycle consisting of Gap phase (also known as Growth phase), Synthesis phase, Gap 2 phase, and the Mitosis phase.[3] During Gap or Growth (G1) phase, the cell grows in size and synthesizes mRNA and proteins in preparation for the DNA replication that will occur in Synthesis (S) phase. During S phase, the cell creates a duplicate copy of its genome, which prompts Gap 2 (G2) phase, where the cell rapidly grows once again in preparation for cellular division. Division occurs during the mitosis (M) phase, where the duplicate chromosomes are separated into two new nuclei. If the entire process is successful, it results in two genetically identical cells.

Although DNA replication during S phase is normally highly accurate, there is always the risk of error. DNA lesions and process errors can cause major problems which endanger cell genetic integrity and viability.[3] Therefore, certain protein complexes exist to mediate this process, catching and repairing damage and keeping all components tethered together and in their proper place.

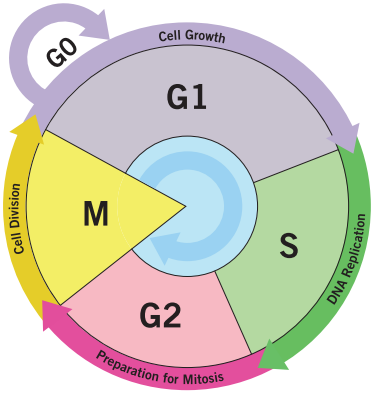
PCNA is a ring-shaped protein that encircles double-stranded DNA in the form of a "sliding clamp," which moves along during DNA synthesis, recruiting proteins involved in DNA replication, repair, and recombination.[2] Since it is active during DNA synthesis, PCNA levels spike just before S phase and remain elevated until M phase, when they begin to decrease.[5] As a result, PCNA serves as a cellular proliferation marker.[5]

As cancerous growths with high proliferation activity are more prone to metastasis, high expression of PCNA can be an indicator of potential malignancy and poor prognosis.[5] PCNA levels have been found to be significantly higher in various malignant tumors compared to normal tissues, such as in cases of breast cancer and duodenal cancer.[5]

PCNA overexpression is also correlated with cancer virulence, with studies showing that PCNA is directly related to the degree of tumor differentiation, cancer stage, and cancer prognosis.[6]

The vital role that PCNA plays in successful cellular replication and division also creates the potential for therapeutic applications. PCNA-targeting peptides have been shown to inhibit the growth or induce apoptosis in neuroblastoma, prostate cancer, breast cancer, bladder cancer, and multiple myeloma.[4,6]

Cell Cycle Phases

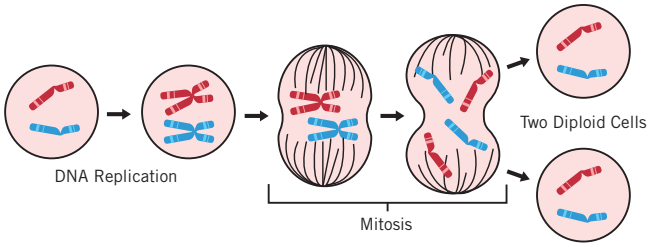


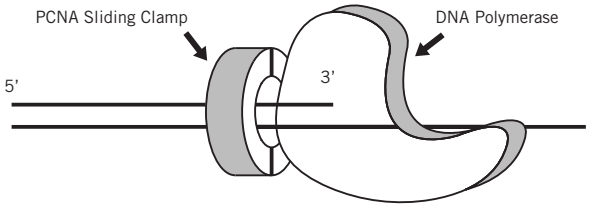
G1 – Gap 1 Phase - Cell Growth

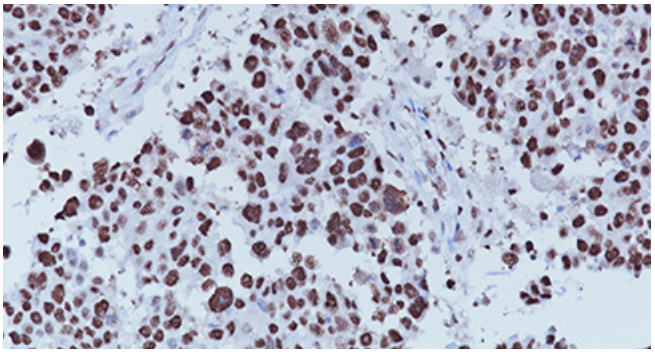
S – Synthesis Phase - Cell copies its DNA

G2 – Gap 2 Phase - Cell preparation for division

M – Mitosis Phase - Cell division







Breast carcinoma stained with PCNA [PC10] antibody

If you are interested in learning more about the potential for PCNA in your lab, please visit us at biocare.net or call 1-800-799-9499.

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