Characterization of cytosolic proliferating cell nuclear antigen (PCNA) in neutrophils: antiapoptotic role of the monomer.

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Résumé en anglais	We have shown previously that PCNA, a nuclear factor involved in DNA replication and repair in proliferating cells, is localized exclusively in the cytoplasm of neutrophils, where it regulates their survival. Nuclear PCNA functions are tightly linked to its ring-shaped structure, which allows PCNA to bind to numerous partner proteins to orchestrate DNA-related processes. We have shown that only monomeric PCNA can expose its NES to be relocalized from nucleus to cytosol during granulocyte differentiation. This study tested the hypothesis that monomeric PCNA could have a biological role in neutrophils. With the use of a combination of cross-linking and gel-filtration experiments, trimeric and monomeric PCNAs were detected in neutrophil cytosol. The promyelocytic cell line PLB985 was next stably transfected to express the monomeric PCNAY114A mutant to examine its function compared with the WT trimeric PCNA. Monomeric PCNAY114A mutant potentiated DMF-induced differentiation, as evidenced by an increased percentage of CD11b- and gp91phox-positive PLB985PCNAY114A cells and by an increased, opsonized zymosan-triggered NADPH oxidase activity compared with PLB985PCNA or PLB985 cells overexpressing WT PCNA or the empty plasmid, respectively. Regarding antiapoptotic activity, DMF-differentiated PLB985 cells overexpressing WT or the monomeric PCNAY114A mutant displayed a similar antiapoptotic activity following treatment with gliotoxin or TRAIL compared with PLB985. The molecular basis through which cytoplasmic PCNA exerts its antiapoptotic activity in mature neutrophils may, at least in part, be independent of the trimeric conformation.
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