The essentiality of PKCα and PKCβI translocation for CD14+monocyte differentiation towards macrophages and dendritic cells;respectively

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摘要

Abstract

Human peripheral cD14+monocytes have been known to differentiate into monocyte-derived macrophages (MDMs) or dendritic cells (MoDCs) upon suitable stimulation. However, the key intracellular molecule(s) associated with their differentiation towards specific cell types was(were) not fully understood. This study was designated to determine the association of PKC isoenzymes with the differentiation of CD14+monocytes into MDMs or MoDCs. Purified human peripheral CD14+monocytes were cultured with GM-CSF, or GM-CSF plus IL-4 for 7 days to induce cell differentiation. The phenotypic changes were analyzed by Flow-Cytometry using various specific antibodies to cell type-specific surface markers. The immunological functions of these differentiated cells were determined by measuring the amounts of TNF-a secretion for MDMs, and the capacities of antigen-capturing and bacterial phagocytosis for MoDCs. The translocations of PKC isoenzymes in these cells from cytosol to plasma membrane were examined by Western Blot analysis and Confocal Microscopic observation. The treatment of CD14+monocytes with either GM-CSF or PMA elicited PKCa translocation and consequently induced their differentiation into MDMs. The inclusion of PKC α / β 1 specific inhibitor, Go6976, greatly inhibited the GM-CSF-induced PKCa translocation and dose-dependently reduced the GM-CSF- induced MDM differentiation. On the other hand, the simultaneous pretreatment of CD14+monocytes with Go6976 and PKC β -specific inhibitor predominantly suppressed the GM-CSF/IL-4-induced generation of MoDCs. Further study demonstrated that GM-CSF/IL-4 selectively induced the translocation of PKC β l, not PKC α or PKC β ll, in cDl4+ monocytes. In conclusion, the cell fate commitment of cDl 4+monocytes towards MDMs or MoDCs appears to be steered by the selective activation of PKCa or PKC β l, respectively