Cyclolinopeptide A (CLA) mediates its immunosuppressive activity through cyclophilin-dependent calcineurin inactivation.

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Streszczenie

The immunosuppressive cyclic nonapeptide cyclolinopeptide A inhibits calcium-dependent, but not calcium-independent, activation of T lymphocytes comparably to the actions of cyclosporin A and FK506. The concentration required for complete inhibition, however, is 10 times higher than that of cyclosporin A. In addition, we demonstrate that calcineurin, a phosphatase which plays an important role in T lymphocyte signalling, is inhibited in vitro by cyclolinopeptide A by a mechanism dependent on the peptidyl-prolyl *cis-trans* isomerase (PPIase) cyclophilin A but not FKBP12. Direct binding of cyclolinopeptide A to cyclophilin A was confirmed using tryptophan fluorescence studies and PPIase assays. These results represent a third example of the production of a natural product that neutralises calcineurin by a mechanism dependent on the primary binding to a PPIase.

Słowa kluczowe

Cyclolinopeptide A, Cyclophilin A, Calcineurin, T lymphocyte activation, Peptidyl-prolyl cis-trans isomerase

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