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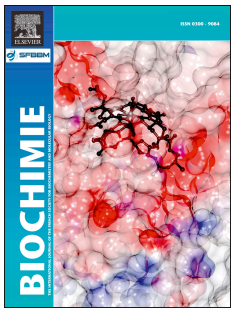

Peptides derived from transcription factor EB bind to calcineurin at a similar region as the NFAT-type motif

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ABSTRACT

Calcineurin (CN) is involved in many physiological processes and interacts with multiple substrates. Most of the substrates contain similar motifs recognized by CN. Recent studies revealed a new CN substrate, transcription factor EB (TFEB), which is involved in autophagy. We showed that a 15-mer QSYLENPTSYHLQQS peptide from TFEB (TFEB-YLENP) bound to CN. When the TFEB-YLENP peptide was changed to YLAVP, its affinity for CN increased and it had stronger CN inhibitory activity. Molecular dynamics simulations revealed that the TFEB-YLENP peptide has the same docking sites in CN as the 15-mer DQYLAVPQHPYQWAK motif of the nuclear factor of activated T cells, cytoplasmic 1 (NFATc1-YLAVP). Moreover expression of the NFATc1-YLAVP peptide suppressed the TFEB activation in starved Hela cells. Our studies first identified a CN binding site in TFEB and compared the inhibitory capability of various peptides derived from CN substrates. The data uncovered a diversity in recognition sequences that underlies the CN signaling within the cell. Studies of CN-substrate interactions should lay the groundwork for developing selective CN peptide inhibitors that target CN-substrate interaction *in vitro* experiments.

Keywords: calcineurin; transcription factor EB; nuclear factor of activated T cells; LxVP-type motif; TFEB-YLENP peptide