

Activity of α -aminoadipate reductase depends on the N-terminally extending domain.

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Abstract

L- α -aminoadipic acid reductases catalyze the ATP- and NADPH-dependent reduction of L- α -aminoadipic acid into the corresponding 6-semialdehyde during fungal L-lysine biosynthesis. These reductases resemble peptide synthetases with regards to their multi-domain composition but feature a unique domain of unknown function, now referred to as adenylation activating (ADA) domain, that extends the reductase N-terminally and whose function was elusive. Based on NPS3, the L- α -aminoadipic acid reductase of the basidiomycete *Ceriporiopsis subvermispora*, truncated enzymes lacking the ADA domain partially or entirely as well as an ADA-adenylation di-domain and the ADA domainless adenylation domain were tested for activity in vitro. We provide evidence that the ADA domain is required for substrate adenylation, i.e., the initial step of the catalytic turnover. Our biochemical data is supported by in silico modeling which identified the ADA domain as a partial peptide synthetase condensation domain.

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