

# Acquisition of hypoxia inducibility by oxygen sensing N-terminal cysteine oxidase in spermatophytes

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## Abstract

N-terminal cysteine oxidases (NCOs) use molecular oxygen to oxidize the amino-terminal cysteine of specific proteins, thereby initiating the proteolytic N-degron pathway. To expand the characterization of the plant family of NCOs (PCOs), we performed a phylogenetic analysis across different taxa in terms of sequence similarity and transcriptional regulation. Based on this survey, we propose a distinction of PCOs into two main groups. A-type PCOs are conserved across all plant species and are generally unaffected at the mRNA level by oxygen availability. Instead, B-type PCOs differentiated in spermatophytes to acquire transcriptional regulation in response to hypoxia. The inactivation of two A-type PCOs in *Arabidopsis thaliana*, PCO4 and PCO5, is sufficient to activate the anaerobic response in young seedlings, whereas the additional removal of B-type PCOs leads to a stronger induction of anaerobic genes and impairs plant growth and development. Our results show that both PCO types are required to regulate the anaerobic response in angiosperms. Therefore, while it is possible to distinguish two clades within the PCO family, we conclude that they all contribute to restrain the anaerobic transcriptional program in normoxic conditions and together generate a molecular switch to toggle the hypoxic response.

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