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Unveiling the functional diversity of the alpha/beta hydrolase superfamily in the plant kingdom

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The alpha/beta hydrolase (ABH) superfamily is a widespread and functionally malleable protein fold recognized for its diverse biochemical activities across all three domains of life. ABH enzymes possess unexpected catalytic activity in the green plant lineage through selective alterations in active site architecture and chemistry. Furthermore, the ABH fold serves as the core structure for phytohormone and ligand receptors in the gibberellin, strigolactone, and karrikin signaling pathways in plants. Despite recent discoveries, the ABH family is sparsely characterized in plants, a sessile kingdom known to evolve complex and specialized chemical adaptations as survival responses to widely varying biotic and abiotic ecologies. This review calls attention to the ABH superfamily in the plant kingdom to highlight the functional adaptability of the ABH fold.

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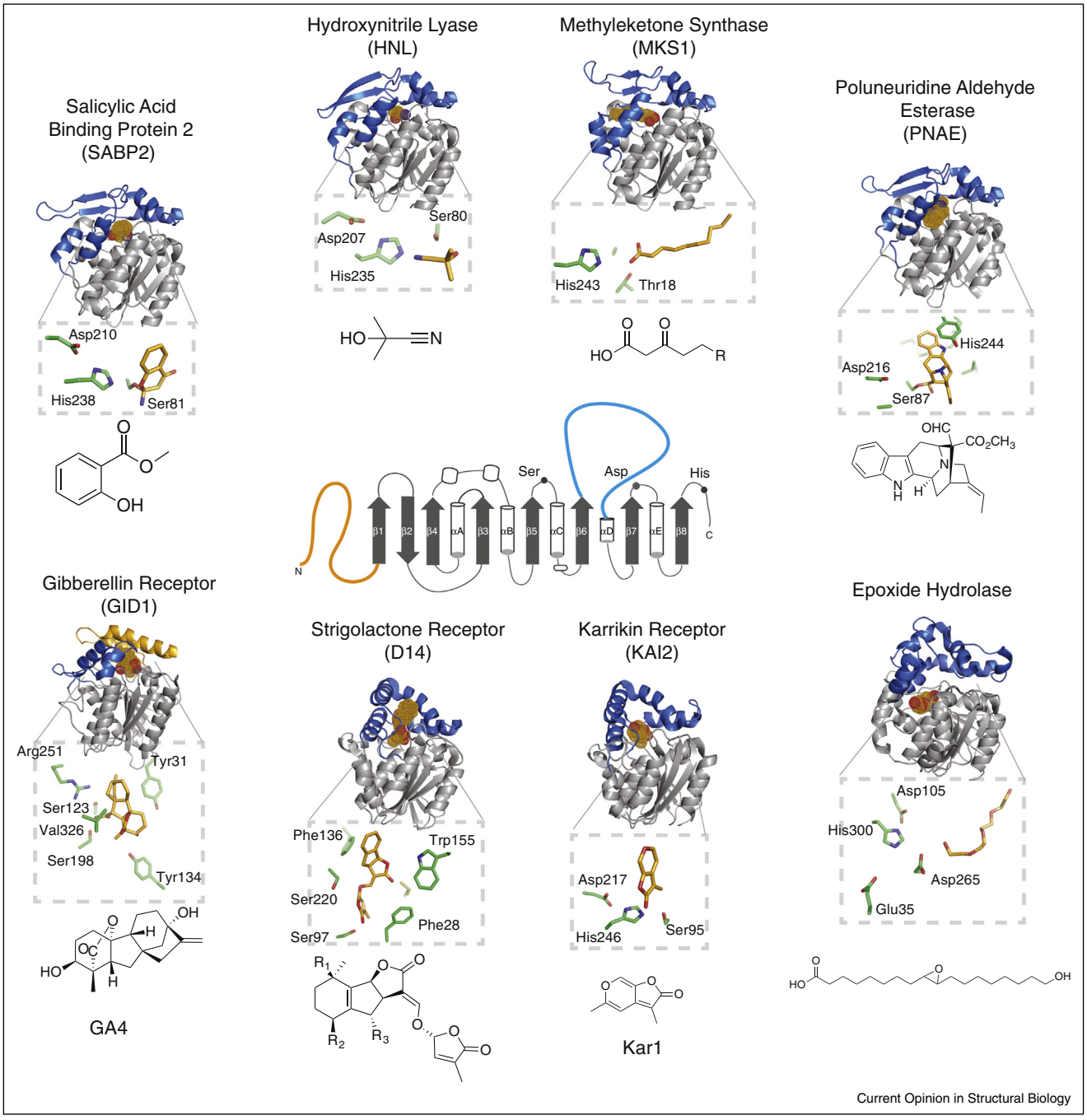
Introduction

Serine hydrolases are one of the most prevalent enzyme families constituting approximately 1% of the human genome [1•]. The core catalytic machinery of these enzymes is composed of a conserved Ser/His/Asp(Asn) catalytic triad and a transition state stabilizing oxyanion hole provided by the peptide backbone [2]. The majority of these enzymes fall into the large alpha/beta hydrolase (ABH) fold superfamily, first classified in 1992 [3]. This protein superfamily is found in all domains of life serving catalytic roles in primary and specialized (secondary) metabolism as esterases, thioesterases, lipases, proteases, dehalogenases, haloperoxidases, and epoxide hydrolases [4–6]. Our understanding of the catalytic and non-catalytic versatility of this family continues to expand. As enzymes, ABHs are classically responsible for the hydrolysis of ester and peptide bonds. However, ABHs also participate in the breaking of carbon–carbon bonds [7], decarboxylation reactions [8•,9–11], and the fascinating cofactor-independent dioxygenation of heteroaromatic rings [12•].

The core fold of ABHs is an 8-stranded β-sheet surrounded by α-helices. Structural and functional variation is typically dependent on additional structural elements, often referred to as lid domains (Figure 1) [4]. The number of β-strands and α-helical segments vary, but the intervening loops carrying the catalytic Ser, His, and Asp/Asn residues are the most conserved features defining the ABH family. Nevertheless, across all three domains of life, ABH family members often share surprisingly low sequence identity (e.g. 6.2% identity/9.3% similarity between *Pseudomonas* sp. dienelactone hydrolase and wheat serine carboxypeptidase II) while maintaining a highly conserved three-dimensional core architecture (Figure 1).

Due to their sessile nature, plants rely on a diverse repertoire of specialized, often taxon-specific metabolites and sophisticated signaling systems to communicate and survive in ecosystems challenged by a myriad of biotic and abiotic factors. The adaptability of the ABH fold has allowed it to serve as an exemplary scaffold for the evolutionary 'design' of additional enzyme chemistries and biological functions in the green plant lineage. Recent discoveries include hydroxynitrile lyases [7,13], polyneuridine aldehyde esterase [11], and methyl ketone synthase [8•,9,10]. Notably, the alpha/beta hydrolase fold also functions as bona fide ligand receptors in the strigolactone, karrikin-smoke receptor, and gibberellin response pathways [14•,15•,16•,17•,18,19]. Despite mounting evidence for the importance of these enzymes in plant physiology and specialized metabolism, the *Arabidopsis thaliana* (thale cress or mouse-ear cress) genome alone contains hundreds of uncharacterized ABH-like genes (Figure 2). Notably, only a small number of ABH structures from all green plants have been experimentally determined. This review seeks to provide a representative overview of the diverse functions of the ABH superfamily in the green plant lineage, with a focus on unique structural elements recently uncovered in plant ABHs related to unanticipated

Figure 1



Structural overview of ABH proteins in the plant kingdom. The 2D structure format of alpha/beta hydrolases is indicated in the center of the figure. N-terminal regions (orange) and inserted lid domains (blue) correspond to the 3D structures surrounding the 2D outline. The surrounding ABH structures are intended to demonstrate the diversity of currently solved structures from the green plant lineage. Some ABHs may not contain complete catalytic triads, therefore their active site region along with their catalytic residues are shown with their co-crystallized substrates. The ligand in each structure is represented as dots and colored by atom with carbon — bright orange, oxygen — red, and nitrogen — blue. A close-up of the active site is shown below each, oriented to best view the ligand and catalytic/relevant residues, rather than to remain in the same orientation as the cartoon full view. Chemical structures of the biologically relevant ligands/substrates are also shown. PDB codes are as follows: SABP2 (1XKL), HNL (1SCQ), MKS1 (3STU), PNAE (3GZJ), Epoxide Hydrolase (2CJP), KAI2 (3JKM), D14 (5DJ5), GID1 (3EBL).