Osmotic stress-dependent serine phosphorylation of the histidine kinase homologue DokA

ABSTRACT

The first in vivo demonstration of a stimulus-dependent serine phosphorylation of an eukaryotic histidine kinase homologue was observed. This implies that DokA, while exhibiting typical structural traits of such bacterial systems, may be involved in the erythromycin-mediated signal transduction pathway.

INTRODUCTION

Many proteins have a modular structure that consists of multiple structural units, with immunoglobulin domains, EGF-like repeats and Fn3 modules being the most frequently found in extracellular regions. Fn3 modules and EGF-like repeats have been identified in members of the insulin receptor (IR) family. It is believed that the L domains of both IR and EGFR families are predominantly leucine-rich repeating, with legucine making up the majority at 10–16% of these residues. Moreover the 3D structure of the L1/cys-rich/L2 fragment of IGF-1R showed that the "L" domains were single–stranded right-handed -helices, with structural similarities to the pectate lyase (a right handed beta hislix) and ribonucleases inhibitor (AKA right hand beta-alpha superhelix). Ribonuclease inhibitor (RI) is recognized as a member of the superfamily of leucine-rich repeat proteins, while pectate lyases is not, despite similarities in their respective sequence patterns and 3D structures. The IGF-1R is listed as one of these proteins in the SCOP database, but it is absent from annotated sequence databases like SwissProt or SMART. In the same way, neither the IR or EGFR families' other L-domain containing proteins are listed as leucine-rich repeats in these data bases or in any recent summary of the complete protein tyrosine kinase family present in the human genome. The superfamily of leucine-rich repeat proteins is categorized into six subfamilies, including typical, RI-like, and CC. These subgroups have different lengths and consensus sequences of the repeats, as demonstrated in Fig. 1. Relatively, most of the LRR's have 22–25 amino acid residues of repeats, whereas RI, with its alternating 28 to 29 residue (but not significantly exceeding its usual range), is considered somewhat atypical; the family has also been extended to include the small proteoglycans which are composed of different combinations of two types of LRBs: 21 (S-type) and 26 (T-Type) amino acids. Fig. 1 shows the consensus sequence for an LRR, which is LxxLxLxxNx-Light-Laser-Labelle-Exeteragneagne-Chinese (refer to fig. 1) with high residue conservation at the first 11-12 residues and variable residencies (various examples include repeats where C was placed instead of N at (4th position in) and some by which I, V, M F, Y, A or C at positions indicated by L in the abovement of a consensus expressed as " Due to the diversity in sequence motifs among LRR proteins, the sequences of the L1 and L2 domains belonging to various IR and EGFR families were re-examined. The LOR motif is not easily identifiable when examining a single sequence, but becomes more evident when multiple sequence alignments are analyzed. The identification of conserved sequence motifs was significantly aided by the availability of the 3D structures of IGF-1R L1 and L2 domains, pectate lyase, and known LRR proteins RI and internalin 1B. The data indicates that pecktate protein lysis enzyme (APK) and EGFR protein syntheses from the IR and EFR families should be part of an expanding family of LRP-containing proteins.

CONCLUSION

Findings These studies suggest that PP5 plays a role in regulating GR nucleocytoplasmic shuttling and that the nuclear accumulation of GG is caused by suppressing DP5 expression without any hormone-mediated response. Hence, the previously reported increase in GR-induced transcriptional activity following ISIS 15534 induced suppression of PP5 expression may be due to the nuclear accumulation of highly bound gre (a type of genetic material) that is capable of binding DNA, but still requires agonist interaction to induce maximum transcriptionally active synthesis. The specific manner in which PP5 hinders the nuclear accumulation of GRs is still unknown, as it remains unclear whether it acts to prevent the nucleus from being expelled.