A conditional form of Bruton's tyrosine kinase is sufficient to activate multiple downstream signaling pathways via PLC Gamma 2 in B cells

ABSTRACT

Based on these data, Btk:ER is thought to regulate downstream signaling pathways in B cells primarily via PLC2 (i.e., regulatory protein coupled with nuclear protein chainase inhibitor PLSI 2), and thus it is not known whether activated BukR/STK copy-pasteurs interact with activatededBtky receptor expressed as a "conditional system", but this condition will probably allow for the dissection of Btons' (and other) role in various biological processes in many cell types.

INTRODUCTION

The signaling circuitry of bacteria is essentially made up of two-component systems that involve the activation of a histidine kinase on repressed histoplasmic acid and then transfer the phosphoryl group to ATP in the aspartate-rich supernatant domain. This was previously only observed in other organisms, but now this type of system is common among bacteria. Over the last few years, histidine kinase homologues and their receivers have been identified in eukaryotic organisms, as well as genes that encode these molecules. The majority of eukaryotic gene products are involved in a phosphoryl relay, which includes kinases, receiver domains, and receptacles. The Saccharomyces cerevisiae gene product, Sln1, was shown to function as a histidine kinase in both vitro and in vivo. Additionally, the histochemical activity of the ethylene receptor Etr1 from Arabidopsis was demonstrated in vitrO. Nevertheless, later research revealed that eukaryotic bifunctional systems do not operate as distinct pathways but are frequently linked to serine/threonine- and tyrosine kinase cascades. As a result, the yeast Sln1-Ypd1–Ssk1 phosphoryl relay functions as an osmosensor and triggers MAP-kinastic activity when cells are exposed to high osseous levels. The Dictyostelium discoideum protein RegA contains a N-terminal receiver domain and phosphodiesterase domain. RegCA response regulator phosphate is activated by phosphorylation of RegAA, which lowers the intracellular cAMP level. The light-regulated serine/threonine kinases in vitro, not those regulated by the histidine kiase paradigm, were observed to be mediated by phytochromes, another homologue of histochemical kines, in vivo (see also mycology). Despite being homologous to bacterial histidine "two-component" systems, these results suggest that they may undergo post-translational modifications similar to those observed in the well-established eukaryotic signal transduction systems. Different developmental phenotypes, such as rapid aggregation, disproportioned fruiting body and stalk ratios or impaired spore formation, are caused by the deletion of individual histidine kinase genes. Furthermore, cells lacking the histotoxic factor dokA are osmosensitive and grow slower when exposed to high OD levels for up to two hours. In light of the fact that it is known that ICTY (Dictyostelium) belongs to the oocyte response system, we have investigated whether or not DokA shows kinase activity in an expression-dependent way: here we show that the histidine kinsases dok A homologue are at most phosphorylated on a serine residue in vivo when Dictryotic response systems are exposed to high olarity medium. Moreover, we prove that the phosphorylation site is situated in a homologous domain with bacterial histidine kinases, and that docetamine modification does not affect the serine phosphate synthesis of DokA.

CONCLUSION

Our findings indicate that there are numerous novel potential downstream genes of the homeodomain transcription factor Lab. To date, 96 previously identified and sequenced genes have been identified as lab targets, with some of them being relatively unknown. The current understanding of direct targets and indirect targets of lab gene action is uncertain. Moreover, we demonstrate that oligonucleotide arrays can be used to analyze the genome-wide identity, number, and quantitative expression levels of candidate downstream genes that are differentially regulated in vivo by developmental control genes. This provides evidence that microarrays have broad applications for studying molecular and cellular processes in Drosophila. Given the conservation of gene structure, expression and function in evolution, we propose that these findings from Drosophila may be relevant for lab orthologs in other animals, including vertebrates. The identification of candidate downstream genes in Drosophila that are direct targets and their ability to enforce developmental genetic programs through lab gene action is now crucial.