for SH2 domain-containing cDNAs that functionally interact with FceR ITAMs. The assay picked up several previously identified SH2-encoding cDNAs (Grb10, Grb-4, Nck, and the p85 subunit of PI-32 kinase), and also several novel SH2 domain-containing open reading frames (ORFs). One of these, the SH2-B ORF, has the unique property that it can bind (as part of a fusion protein) to both Igβ and Igγ ITAMs in a manner distinct from that of the SH2 domains of either Syk or Lyn. The full length SH2-B ORF encodes a protein of 757 amino acids containing a single SH2 domain as well as several proline-rich domains. While the function of this new member of the family of SH2 domain-encoding proteins in cellular signaling is unknown, its identification by the yeast tribrid system provides ample demonstration of the potential of this new method and opens the possibility of discovering even greater numbers of proteins whose assembly into functional multimeric complexes is dependent upon posttranslational modification. Thus the yeast tribrid system allows researchers not only to explore structural components and cellular architecture but also to study the regulatory mechanisms of protein assembly.

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COMMENTARY ON RESEARCH

Marilyn Wiebe

A new use for the mycoprotein organism

Fusarium graminearum is a welcome addition to the list of potential host organisms.

Filamentous fungi have emerged in recent years as alternatives to bacteria and yeasts for the production of heterologous proteins, primarily because they can secrete large amounts of correctly glycosylated enzymes.[1-3] In this issue (p.1479), Royer and colleagues[4] report the addition of *Fusarium graminearum* to the growing list of potential filamentous hosts for the production of heterologous proteins.

While efficient transformation procedures for *Aspergilli* have been available for more than a decade, and transformation systems for a diverse range of other filamentous fungi have been developed in the past five years, *Aspergillus niger*, *Aspergillus oryzae*, and *Trichoderma reesei* still dominate as hosts for the production for heterologous proteins. *F. graminearum* is therefore a welcome addition to the list of potential host organisms: The use of this species may represent a significant step toward the large scale production of heterologous proteins in continuous culture.

The strain (A3/5) of *F. graminearum* that Royer and his colleagues[4] used to produce fungal trypsin, cellulase, and lipase has been used for the past 10 years in the production of Quorn mycoprotein,[5] a textured protein preparation used as a meat substitute in various "vegetarian" products. As a food component, *F. graminearum* is generally recognized as safe, a potential application advantage of this organism. Quorn is produced in large scale continuous flow culture.[6]

The promoters controlling production of heterologous proteins often allow for growth-correlated production[7,8] (rather than production in stationary phase). Thus, the use of an organism that can be easily produced in a continuous flow culture (turbidostat) at optimum growth rates would maximize production. Withers and colleagues[9] recently demonstrated that at least some fungal transformants can be very stable in long-term continuous-flow cultures. If the environmental conditions are optimized, even less stable transformants can produce consistent enzyme concentrations. Thus, continuous-flow culture may be a realizable option for production of heterologous proteins.

Furthermore, it is becoming clear[1,7] that the widely used *Aspergillus* species are not suitable hosts for the production of all heterologous proteins, as they may fail to correctly process or secrete some enzymes. Morita and colleagues[7,10] have developed *Acremonium chrysogenum*, which is used industrially in the production of cephalosporin C, as a host organism to secrete heterologous enzymes to avoid possible complications of using plant-pathogenic *Fusaria*. The A3/5 strain of *F. graminearum* however, is demonstrably nonpathogenic to wheat and maize (the hosts of the wild-type fungus) and has been rigorously tested for toxicity in both animals and humans.[5] Both *A. chrysogenum* and *F. graminearum* A3/5 have been shown to correctly produce a *Fusarium* alkaline protease, that neither *A. niger* nor *A. oryzae* produced efficiently.

It is interesting to note that both Royer and colleagues[4], and Morita and colleagues[7] found that a *Fusarium* alkaline protease promoter was a strong promoter providing efficient signal sequences for secretion, even though in both cases the promoter and signal sequences were heterologous. *A. chrysogenum* secreted alkaline protease in gram quantities per liter,[7] and human lysozyme in milligrams per liter.[10] The development of these, and other filamentous fungi, as host organisms clearly represents an important advance for industrial-scale production of heterologous products.

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