

Dyadic®: The “One-Stop Shop” From Eukaryotic Gene Discovery to Commercial Manufacturing

The C1 Fungal High-Throughput Robotic Screening (HTRS) System and C1 Fungal Hyper-Producing Protein Expression System

The Challenge: Developing Products from DNA

Within the *eukaryotic* kingdom exists millions of organisms. These organisms represent a largely untapped source of potential genes that can be used to make new products of commercial value. But to date, only a small number of eukaryotic genomes have been sequenced and only a small fraction of these genes have been isolated and functionally characterized. Among those, even fewer have been translated into commercially viable products. The reasons for this are varied, but in general, most of today's *genomic* and *proteomic* R&D programs face **three major bottlenecks**:

Bottleneck 1

Ability to Rapidly Identify Viable Product Leads

Up to 90% of the *biodiversity* found on the earth, such as yeast, fungi, plants, insects, fish, and other animals including humans, are eukaryotic organisms¹, that is, they are multi-celled with a nucleus. The genes within these eukaryotic organisms generally contain introns. However, current methods for rapidly screening for new product leads – called High-Throughput Robotic Screening (HTRS) – often fail to recognize proteins from eukaryotic organisms. This is because currently used discovery organisms, primarily bacteria but also yeast on a limited basis, are unable to adequately process introns found in native eukaryotic genes. This failure leads to an inability to convert genomic sequences of eukaryotic genes into functional proteins, **which means that up to 90% of the world's potential product leads are still waiting to be discovered.**

Bottleneck 2

Producing Sufficient Protein for Laboratory and Application/Clinical Testing

Even when HTRS assays identify a protein with commercial potential, developers still face the challenge of making enough protein with which to work. If researchers are unable to make enough functional protein, it is impossible to continue research, development and applications testing work, including clinical trials for pharmaceuticals. **Many pharmaceutical and biomaterial research programs have been cancelled due to the inability to produce adequate quantities of these newly discovered biomolecules.**

Bottleneck 3

Difficulty in Bringing Biological Product Leads to Market

Due to the fact that different organisms express proteins differently, genes that produce active proteins in one living organism are often unable to make economically viable quantities of functional proteins when placed in another organism. Mass production technologies of today often require that genes discovered in a bacterial or yeast HTRS system be expressed in a completely different commercial production system, such as animal cell culture like Chinese Hamster Ovary (CHO), yeast or filamentous fungal systems. Consequently, there is no guarantee that a protein, once discovered, can ever be manufactured. **Bottlenecks in commercial scale production—a late stage in product development—are extremely costly and may lead to delays or cancellation of otherwise promising projects.**

¹ E.O. Wilson, F. Baird – The Current State of Biological Diversity “Biodiversity” National Academy of Sciences, National Academy Press, Washington D.C. 1988.

The Dyadic Solution – C1, the “One-Stop Shop”

Dyadic® International, Inc. has developed the foundation to overcome each of these monumental hurdles. Dyadic has developed ***Chrysosporium lucknowense* (C1)** to go from gene discovery to commercial manufacturing using the same host organism (see Figure 1). The C1 Fungal High-Throughput Robotic Screening (HTRS) System (Patent Application #WO 01/25468) and the C1 Fungal Hyper-Producing Protein Expression System (Patent Application #WO 00/20555) utilize the C1 organism to rapidly convert genomic libraries from the world's vast pool of eukaryotic DNA into functional biomolecules, leading to rapid gene discovery and commercial manufacture of valuable products.

Unique Features of the C1 Eukaryotic Technology Platform

The unique Dyadic C1 Hyper-Producing Fungal System was isolated from an alkaline-soil lake and then genetically modified to serve as an optimized eukaryotic host organism for the Dyadic HTRS and C1 Protein Expression Systems. It is being developed to:

- Take DNA from virtually any eukaryotic or prokaryotic organism and translate it into protein.
- Produce enough protein to enable gene discovery and assay screening, utilizing existing HTRS equipment.
- Manufacture the protein in commercial quantities.

■ Discovery ■ Optimization ■ Manufacturing

DYADIC®
II

© Sept. 2001

All rights reserved.

Dyadic® is a registered trademark of Dyadic International, Inc.