Open Science and/or Compliance – What Future do We Want for Computational Biology?

Impuls Talk “Digital Sequence information, Open Access, and Sustainable Benefit Sharing: Scientific Input to International Policy Decisions”

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Brussels, March 10, 2020

NUTRITION · HEALTH · SUSTAINABLE LIVING

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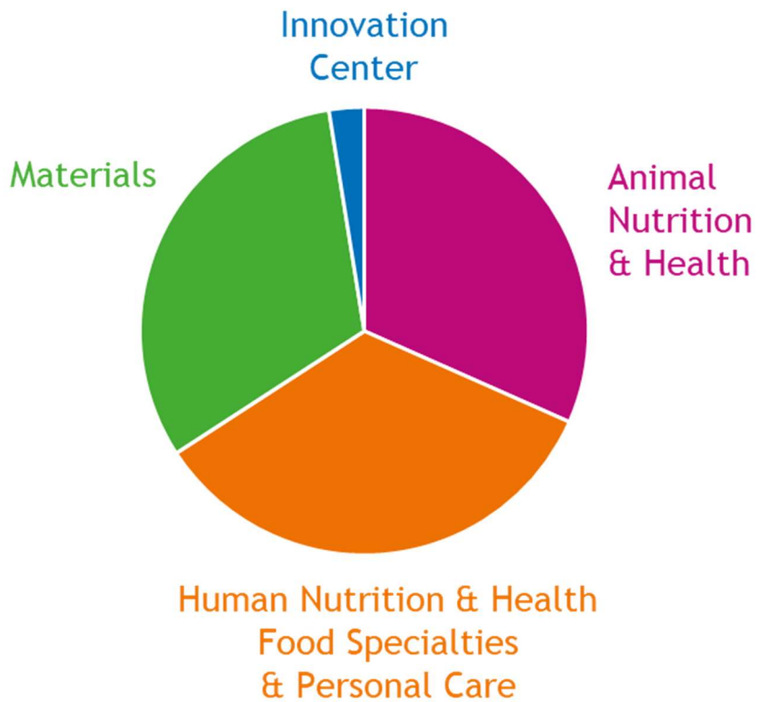
DSM is a Purpose-Led Science-Based Company in Nutrition, Health and Sustainable Living



- #1 Supplier of vitamins, nutritional lipids, carotenoids, nutraceutical ingredients and custom nutrient premixes
- Production methods: chemical synthesis, fermentation/biotechnology, extraction from biological materials

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The Nature of Products in the Food and Feed Industry

Product Information

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***life'sDHA*™ 100mg Vegetarian Capsules**

Composition

	1g contains
Fill Material	
DHA Algal Oil	411.7 mg
High Oleic Sunflower Oil	83.2 mg
Tocopherols	1.5 mg
Natural Flavor	1.0 mg
Sunflower Lecithin	0.9 mg
Ascorbyl Palmitate	0.2 mg
Shell Material	
Water	209.6 mg
Modified Corn Starch	114.9 mg
Glycerin	72.6 mg
Carrageenan	54.5 mg
Sorbitol	46.9 mg
Caramel	2.5 mg
Beta Carotene	0.5 mg

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Omega-3 fatty acids provide key lifelong health benefits:

- DHA is important for the brain and eyes; while
- DHA and EPA together promote cardiovascular health.

Typically, products contain **multiple components**, with each component potentially being derived from **multiple GRs**, and/or involving **multiple pieces of "DSI"** ⇨ How to determine the value of each individual component?

Human milk oligosaccharides (HMOs) support digestive, immune and cognitive development by modifying the gut microbiota.

GRAS Notice No. 749 for 2'-*O*-fucosyllactose: "Coding fragments from 4 donor species were synthesized *in vitro* and inserted into the host strain."

Table 4: Coding DNA Fragment Inserts

Gene	Origin	Length (as bp)	Function	Insertion site
fucT2	*Helicobacter pylori*	900	Fucosyl transferase	Disrupted *ldhA* gene
sucP	*Bifidobacterium adolescentis*	1517	Sucrose phosphorylase	Disrupted *pfkA* gene
frk	*Zymomonas mobilis*	906	Fructokinase	Disrupted *adhE* gene
cscB	*Escherichia coli*	1248	Sucrose transporter	Disrupted *agp* gene

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Use of "Genetic Resource Sequence Data" (GRSD) by DSM

nature biotechnology

ARTICLES

Nature Biotechnol. 25, 221-231, 2007

Genome sequencing and analysis of the versatile cell factory *Aspergillus niger* CBS 513.88

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The filamentous fungus *Aspergillus niger* is widely exploited by the fermentation industry for the production of enzymes and organic acids, particularly citric acid. We sequenced the 33.9-megabase genome of *A. niger* CBS 513.88, the ancestor of currently used enzyme production strains. A high level of synteny was observed with other aspergilli sequenced. Strong function predictions were made for 6,506 of the 14,165 open reading frames identified. A detailed description of the components of the protein secretion pathway was made and striking differences in the hydrolytic enzyme spectra of aspergilli were observed. A reconstructed metabolic network comprising 1,069 unique reactions illustrates the versatile metabolism of *A. niger*. Noteworthy is the large number of major facilitator superfamily transporters and fungal zinc binuclear cluster transcription factors, and the presence of putative gene clusters for fumonisin and ochratoxin A synthesis.

(12) **United States Patent**
Bailey et al.

(10) **Patent No.: US 7,851,199 B2**
(45) **Date of Patent: Dec. 14, 2010**

(54) **PRODUCTION OF CAROTENOIDS IN OLEAGINOUS YEAST AND FUNGI**

(75) Inventors: **Richard Bailey**, South Natick, MA (US); **Kevin T. Madden**, Arlington, MA (US); **Joshua Trueheart**, Concord, MA (US)

(73) Assignee: **Microbia, Inc.**, Lexington, MA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 465 days.

(21) Appl. No.: **11/385,580**

(22) Filed: **Mar. 20, 2006**

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Protein Engineering vol.13 no.1 pp.49–57, 2000

From DNA sequence to improved functionality: using protein sequence comparisons to rapidly design a thermostable consensus phytase

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Naturally-occurring phytases having the required level of thermostability for application in animal feeding have not been found in nature thus far. We decided to *de novo* construct consensus phytases using primary protein sequence comparisons. A consensus enzyme based on 13 fungal phytase sequences had normal catalytic properties, but showed an unexpected 15–22°C increase in unfolding temperature compared with each of its parents. As a first step towards understanding the molecular basis of

and 63°C (see below), we were interested in developing a rapid procedure to increase the unfolding temperature and thus the thermostability of phytases.

Increasing the thermostability of an enzyme usually requires combining multiple amino acid exchanges, each of which slightly increases the unfolding temperature of the protein. The main problem, however, is the identification of the relevant amino acid residues. In general terms mutations that increase thermostability may, for example, result in formation of hydrogen bonds, salt or disulphide bridges, increase the hydrophobic packing or the α-helix or β-sheet stability or stabilize β-turns or flexible termini or loops (for review see Jaenicke *et al.*, 1996). Despite extensive knowledge of the general mechanisms governing protein stability (Dill *et al.*, 1989; Dill, 1990; Fersht and Serrano, 1993; Matthews, 1993; Cordes *et al.*, 1996) no rapid and reliable procedures are available for increasing the thermostability of a given protein. For successful thermostabil-

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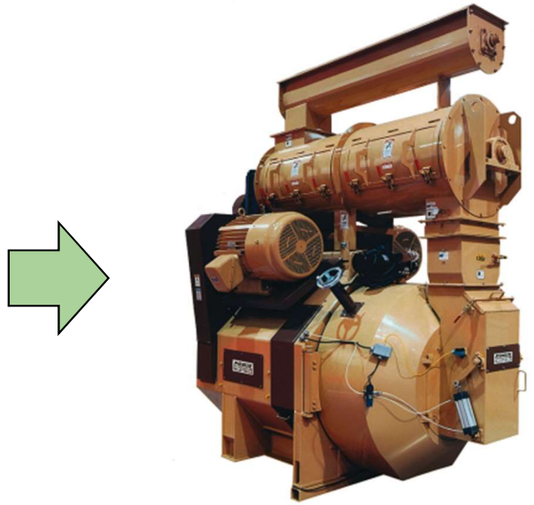
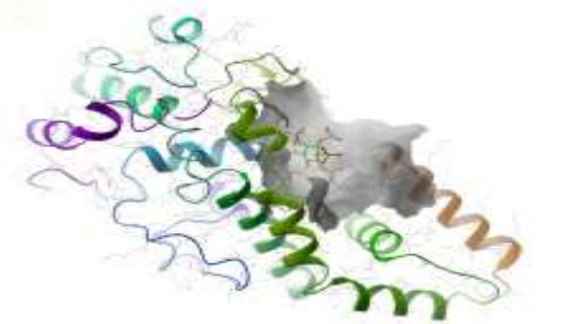
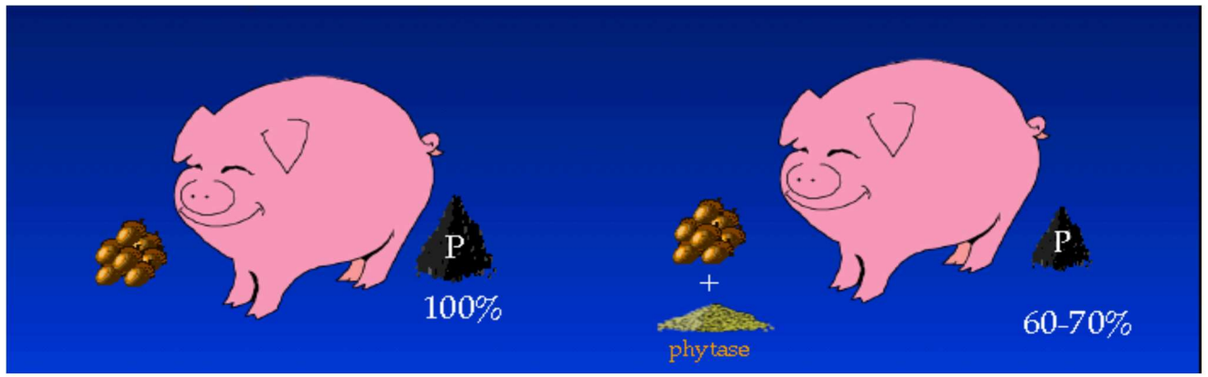
The Need for Heat-Stable Phytases



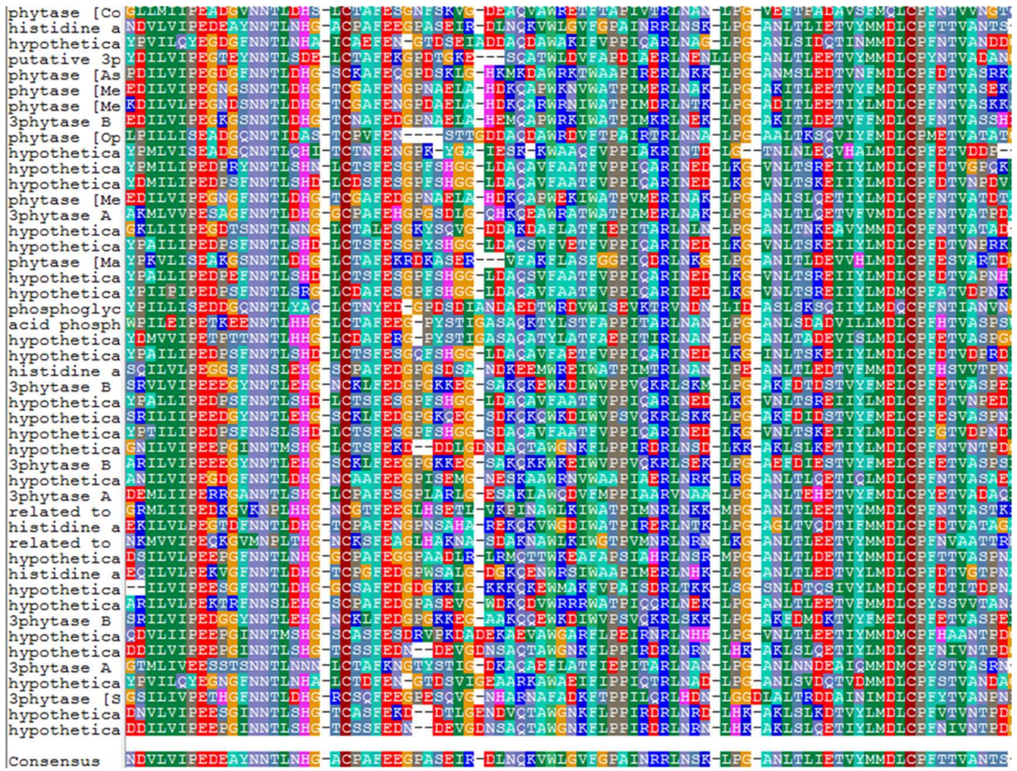


3D structure of *Aspergillus niger* phytase (accession code 3k4q) with phytate in the catalytic site (the grey area)



The Process for Generating a Heat-Stable Phytase

1. Determine the consensus sequence based on a sequence alignment of 153 pre-selected homologous phytase amino acid sequences
2. Develop the consensus phytase into a commercial product



The Main Challenges Requiring Careful Consideration

CBD/NP Challenge	Implications for typical Food/Feed Products, or for a Consensus Phytase
Built on national sovereignty	Access restrictions by, and/or negotiations required with multiple provider countries
Stacking obligations	How to determine the value of each individual component/sequence? How to assign the "fair" share of benefits to each of the provider countries?
Eternal obligations	The above issues turn even worse over time, as products are typically further improved
No homology threshold	… and even if used only transiently, benefit sharing obligations may perpetuate …

Overall, these challenges represent a serious threat for timely addressing the global health, environmental and socio-economic challenges that this planet is facing!

High legal certainty, lean governance and processes, and clear cut-off criteria are considered essential to generate the most desirable outcome for all!

Before rushing into any sort of compromise, it is crucial to very carefully analyze all options and to consider all impacts

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