Producing Protein and Plastics from Methane, a Sustainable Platform for Biotechnology

Bio World Congress
July, 2017
Thermodynamics and Economics of Carbon

Banholzer, W. et al. Chem Eng Progress, March 2008, S7-S14

- All products are downhill from methane
  - *Key challenge is controlling the reaction, as full combustion is favored*
- Methane is an advantaged feedstock relative to carbohydrates or CO\textsubscript{2} for making diesel or other reduced products
- Methane is one of the cheapest sources of high-energy carbon
Low-Cost, Non Food-Based Carbon Offers an Advantaged Feedstock...

- Available from **multiple sources**: natural gas, biogas from MSW, ag waste, wastewater treatment
- **Homogeneous** – doesn’t vary due to weather or growing conditions
- **Transportable** – pipeline transport is cheap, reliable, and efficient
- **Infrastructure** – pipeline transport infrastructure is available globally
- **Affordable** – natural gas in the North America is the world’s cheapest source of carbon
  - Current U.S. natural gas forward curve shows gas <$3.75 per MMBtu through 2029
- As a green house gas, methane is **84x more potent** than CO\textsubscript{2} in the short term

**Historical price comparison on an equivalent MMBtu basis**

Methanotrophs in Nature

Aerobic methane-oxidizing bacteria (methanotrophs) are widely distributed in the environment and play a key role in the cycling of the potent greenhouse gas methane. They oxidize much of the methane produced by the anaerobic metabolism of methanogenic archaea before it escapes to the atmosphere, thereby mitigating the effects of global warming. Methanotrophs have been isolated from many different environments, including freshwater and marine environments, soils, sediments, acidic peatlands, rice paddies, landfill, alkaline soda lakes, hot springs, cold environments, and even from highly acidic, thermophilic environments.

Methylococcus capsulatus Bath current “work horse”

- Gammaproteobacteria, type I methanotroph
- Relatively fast growth rate (methane:oxygen mix)
- Genome sequence available
- Amenable to genetic manipulation
- Only methanotroph proven at commercial scale
- Variety of formats for strain testing: 24-well plates, pressure bottles, 2L fermenters
- Amended media and optimized feeding strategies produce high cell densities in small scale.
Calysta’s Platform: Strain Engineering

Calysta has developed a set of novel engineering tools for methanotrophs:

- Reporter genes

<table>
<thead>
<tr>
<th>Empty Vector</th>
<th>P16hps Comet</th>
<th>PT5 Comet</th>
<th>Pm ph Comet</th>
<th>Pm ph Dasher</th>
<th>Pm ph Magenta</th>
<th>Pm ph Purple</th>
</tr>
</thead>
</table>

- Plasmids that replicate both in methanotrophs and in *E. coli*
- Constitutive and inducible (low/med/high) promoters
- Techniques for chromosomal knockin and knockouts

Different promoter gene-fusions with synthetic fluorescent and chromogenic proteins (non-*Aequorea*) expressed in *M. capsulatus*
Calysta’s Integrated Bioplatform

- Low-Cost, Abundant Feedstock
- Biology
- Reactor Design
- Products/Marks

Methane (Nat Gas or Renewable)
Proprietary Tools/Algorithms
High Mass Transfer Gas Reactors
Industrial Partnerships
Making Everything from Plastics to Protein

Research
- Future Food
- N-butanol
- Biodiesel
- Butadiene
- Crotonate
- ω-3 fatty acids
- Fatty alcohols
- 3-hydroxypropionate
- 1,3 BDO
- 3-hydroxybutyrate
- polyhydroxybutyrate
- polyhydroxyalkanoates

Development
- Nutritional Supplements
- Palatants
- Probiotics
- L-amino acids
- Lactate
- Succinate
- Pentamethylene diamine
- Isoprene
- Malate
- 2,3 BDO
- Acetate
- Acetoin
- Autolysate

Commercial
- FeedKind®
- FeedKind® terra
- FeedKind® pet

Legend:
- Chemical products
- Nutritional products
The Calysta Opportunity

• Calysta’s FeedKind protein can help address one of the greatest threats to global growth: food security
• Proprietary fermentation platform for producing protein and other nutritional products
• High quality FeedKind protein has been extensively validated in aquaculture, the most demanding and fastest growing food production system in the world

• Experienced team with proven track record of successful execution across multiple disciplines
• World-class partners and investors including Cargill, Mitsui and Temasek
• Construction of the world’s largest gas fermentation facility underway in Memphis, Tennessee, U.S
Food Security Is the Issue of the Future

By 2050, 9.6B people will demand 75% more protein than currently available

2006 Protein Demand

63.9 million tonnes

2050 Protein Demand

110.8 million tonnes

“Our research shows people will spend one-third of any increase in incomes on a more varied high-protein diet”

Greg Page – Former Chairman of Cargill

Demand for Protein is on the Rise Globally

The global protein ingredients market for animal feed and human food and beverage is $40B growing at 5-6% per year

Two Problems...One Solution

Food Security

Global Warming

• No agricultural land use
• 77-98% less water than agricultural products
• 40% improved CO₂ emissions compared to combustion of methane

FeedKind protein does not compete with the human food chain
• No animal derived ingredients
• Helps mitigate global warming losses at 5% of global GDP (IPCC 2014)

“Future Fit Feed”
Independent Analysis Confirms Environmental Benefits

Assessment of environmental impact of FeedKind™ protein

Table B: Impacts of feed ingredients in relation to protein content

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Protein content (%DM)</th>
<th>CO₂e emissions (kgCO₂e/kg)</th>
<th>Water consumption (m³/kg)</th>
<th>Land occupation (m²/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FeedKind™ Powder</td>
<td>71</td>
<td>2.2</td>
<td>0.01</td>
<td>0.00</td>
</tr>
<tr>
<td>Fish meal (medium)</td>
<td>64</td>
<td>2.6</td>
<td>0.02</td>
<td>0.01</td>
</tr>
<tr>
<td>Soy protein concentrate</td>
<td>66</td>
<td>0.8</td>
<td>0.14</td>
<td>6.66</td>
</tr>
</tbody>
</table>

- Comparable impacts to fishmeal
- Dramatically improved water and land footprints compared to agricultural products

http://www.carbontrust.com/media/672719/calysta-feedkind.pdf
Source: Carbon Trust, 2016
FeedKind® is a Natural, Non-GMO Protein Source Offering Significant Differentiating Benefits

Naturally occurring microorganisms metabolize methane as their sole source of carbon and energy, producing a nutritious, high-protein biomass

Multiple Monetization Opportunities:

<table>
<thead>
<tr>
<th>Supply Chain</th>
<th>Consumer</th>
<th>Sustainability</th>
<th>Under development</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Traceable</td>
<td>• Non-GMO</td>
<td>• No agricultural land use</td>
<td>• Amino acid modifications</td>
</tr>
<tr>
<td>• Consistent product</td>
<td>• Natural fermentation process</td>
<td>• Little water use</td>
<td>• Omega-3</td>
</tr>
<tr>
<td>• Year round production</td>
<td>• Reduced fish-in / fish-out ratio</td>
<td>• Additive to the human food chain</td>
<td>• Prebiotic and probiotic effects</td>
</tr>
<tr>
<td>• Long shelf life</td>
<td>• Saturated fatty acids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Reduced enteritis from plant proteins</td>
<td>• No animal based ingredients</td>
<td></td>
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EU Approval Already Received for Use in Fish and Livestock:

**EU Feed Registration:**

<table>
<thead>
<tr>
<th>12.1.2</th>
<th>Protein from Methyloccocus capsulatus (Bath), Alcaligenes acidovorans, Bacillus brevis and Bacillus firmus</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Protein product of fermentation with Methyloccocus capsulatus (Bath) (NCIMB strain 11132), Alcaligenes acidovorans (NCIMB strain 12387), Bacillus brevis (NCIMB strain 13288) and Bacillus firmus (NCIMB strain 13280) (†) on natural gas (approx. 91 % methane, 5 % ethane, 2 % propane, 0.5 % isobutane, 0.5 % n-butane), ammonia, and mineral salts, the crude protein is at least 65 %.</td>
</tr>
<tr>
<td></td>
<td>Crude protein</td>
</tr>
<tr>
<td></td>
<td>Crude ash</td>
</tr>
<tr>
<td></td>
<td>Crude fat</td>
</tr>
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</table>
FeedKind Has a Superior Nutritional Profile When Compared to Other Fishmeal Alternatives

Major aquaculture feed ingredients and indicative pricing

Source: FAO Feed ingredients and fertilizers for farmed aquatic animals, 2009.
Ultra-efficient carbon conversion, with every ton of FeedKind sold providing a ~10x upgrade to the price of the carbon-equivalent input.
FeedKind Protein Commercial Samples Shipping Worldwide from Teesside UK Plant

- Over 5 tonnes of FeedKind protein already produced in 2017
- Shipping commercial samples to customer and partners worldwide
- Facility is a “scale-down” of the original Tjeldbergodden, Norway reactor, demonstrated to produce at a rate of 10,000 mtpa
- Successful maintenance of 8+ weeks of continuous fermentation, meeting design parameters for key commercial metrics such as yield and productivity
- Partnered with Center for Process Innovation (“CPI”) to provide on site services and well trained staff

Ground Has Broken on 1st Commercial Plant in Memphis, Tennessee

• Collaborating with Cargill on what will be the world’s largest gas fermentation facility, occupying 37 acres of Cargill’s 69-acre property on President’s Island in Memphis

• Modular design lends itself to phased construction process: 20 fermenters, each similar in size to a football field end zone, plus several dryers, each approximately the height of a six-story building

• 20,000 mtpa Phase I coming online Q1 2019, with total production capacity of 200,000 mtpa by 2021
Calysta Commands a Leading IP Position, Creating Significant Barriers-to-entry

• **46 granted** patents with **over 100 pending** applications covering more than **22 patent families**

• Strong claims covering proprietary reactor design that have already invalidated one potential competitor’s patent

• Broad claims granted in 2016 covering biological production of any chemical from natural gas

• Aggressively filing on new gas fermentation reactor designs and improvements

• Continuing to develop new applications for products across species and markets