Tapping into Plant-Associated Microbial Diversity
Janne Kerovuo, Ph.D.
Agriculture Matters

30% — Portion of greenhouse gas emission related to Agriculture

40% — Share of worldwide employment in Agriculture (70% of the “bottom billion”)

70% — Share of worldwide water withdrawals from Agriculture

10,000 — Years of historical food production that must be matched in the next 50 years

925,000,000 — Hungry people today

Source: World Economic Forum: Realizing a New Vision for Agriculture
Constrained Resources

**Water availability** — 30% crop production at risk by 2025

**Land** — Arable land is running out and poor soil health threatens the yields

**Climate change** — Yields potentially depressed 20%+ in many areas

**Poor education, nutrition, and health** — Low productivity, earning potential, capacity of rural development

*Source: World Economic Forum: Realizing a New Vision for Agriculture*
Agradis was founded in 2011 by Synthetic Genomics Inc. (SGI) and Plenus SA de CV to capitalize on the tremendous agricultural and genomic strengths of both companies. Agradis licensed technologies from Synthetic Genomics Inc. and Plenus SA de CV in 2011. SGI’s CEO, J. Craig Venter, Ph.D. and Plenus’ CEO Alfonso Romo, co-chairs of the Agradis Board of Directors, bring with them extensive experience in developing and commercializing cutting edge technologies. They also share a common vision that new agricultural products developed sustainably and efficiently are one of the most pressing needs for society today. This was one of the driving forces for the formation of Agradis.
## Agradis Management Team

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<tr>
<th>Position</th>
<th>Key Achievements</th>
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<tbody>
<tr>
<td><strong>CEO</strong></td>
<td>Proven track record of commercializing global crop production technologies</td>
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<tr>
<td>Alejandro Rodriguez</td>
<td>President and COO of Seminis Vegetable Seeds</td>
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<td><strong>President</strong></td>
<td>Business development, venturing, and marketing experience with Syngenta / Zeneca</td>
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<tr>
<td>Tom Christensen</td>
<td>BS Agronomy, MS Plant Physiology, MBA</td>
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<tr>
<td><strong>Senior Director of Plant Breeding</strong></td>
<td>Significant achievements in plant breeding and agronomic improvement in various crops</td>
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<tr>
<td>Julian Barrera</td>
<td>BS Plant Breeding, MS Genetics</td>
</tr>
<tr>
<td><strong>Senior Director of Microbial Solutions</strong></td>
<td>Industrial biotechnology R&amp;D management experience at Danisco, Diversa, and Synthetic Genomics</td>
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<tr>
<td>Janne Kerovuo</td>
<td>PhD Biochemistry</td>
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Agradis’ Crop Production Technologies

**Microbial Solutions; Crop Protection**
- Microbes, their products and genes that control plant pests
- First target is the *Fusarium* fungus
- Secondary targets include fungi that cause stalk rots, rusts, and blights

**Microbial Solutions; Yield Enhancement**
- Microbes that increase plant growth rates and yield
- First targets are broad acre field crops
- Achieve through nutrient efficiencies and plant growth stimulants

**Plant Breeding; Genetic Improvement**
- Traditional and molecular assisted breeding
- Castor bean as first target for molecular breeding approach
- Sweet sorghum improvement initially through breeding
Agradis Microbial Solutions Vision

We are tapping into plant-associated microbial diversity to develop superior and sustainable microbial products for Agriculture.

We use our innovative technologies to discover novel microbial plant growth enhancers and biocontrol agents.

First targets: corn and wheat yield enhancement and crop protection.
## Modes of Action of Biocontrol of Crop Pests

<table>
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<th>Mode of Action</th>
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<td>Competing for nutrients / space</td>
<td>Beneficial microbes outcompete pathogens, preventing infection and damage to the crop</td>
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<tr>
<td>Secreting antimicrobial compounds</td>
<td>Beneficial microbes secrete compounds inhibiting or eradicating crop pests</td>
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<tr>
<td>Parasitizing the pest</td>
<td>Beneficial microbes parasitize crop pests, preventing damage to the crop</td>
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<tr>
<td>Inducing host plant defenses</td>
<td>Beneficial microbes induce systemic resistance, enabling crops to protect against pests</td>
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Modes of Action of Crop Yield Enhancement

Nutrient fixation & utilization
- Beneficial microbes fix nitrogen for the crop and/or enhance mineral nutrient uptake (e.g. $S^0$ – oxidizers)

Nutrient solubility
- Beneficial microbes increase solubility of inorganic nutrients (e.g. P, K, Fe) and improve crop’s ability to utilize nutrients

Plant growth stimulant production
- Beneficial microbes secrete compounds that act as plant growth stimulants and improve tolerance of abiotic stress
Microbial Discovery and Development Cycle

- Sample collections
- Microbial isolations
- In vitro characterizations
- Plant-microbe selections
- In planta trials
- IP protection
- Multi-location field trials
- Product development and registration
- Partner
- Market demonstration
- Product launch
- Target identified

Sample collections
Microbial isolations
In vitro characterizations
Plant-microbe selections
In planta trials
IP protection
Multi-location field trials
Product development and registration
Partner
Market demonstration
Product launch
Target identified
Microbial Culture Collection

• Targeted sampling from diverse biotopes and environments around the world

• Proprietary isolation and cultivation of plant-associated microbes (rhizosphere, endosphere, phyllosphere)

• Agradis Microbial Culture Collection contains > 4,000 unique, characterized microbes (>200 different genera), continuously growing

• The most systematic culture collection of plant-associated microbes: “Poaceae Microbiome”
Genomics Tools

- Next-Gen sequencing technologies coupled to state-of-the-art Bioinformatics tools to study plant-microbe interactions

- **Genome sequencing** – Identify sequences that set our novel microbes apart from existing strains

- **Metagenomics** – Study the microbial communities present in natural and agricultural soils

- **Transcriptomics** – Identify novel genes and pathways involved in plant-microbe interactions

- Develop IP around novel genes/pathways

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Archetype™
Metagenomics, Soil Analysis and Field Performance

- Metagenomic and soil chemistry analysis of field trial sites linked to the performance of microbial treatment
- Understanding the efficacy (and non-efficacy)
- Tailored Microbial Solutions in the future?

Field Soil, St. Paul, Minnesota  
Field Soil, Lincoln, Nebraska
Microbial Characterization - Efficacy

• HTP *in vitro* biocontrol screens against major plant pathogens which cause diseases such as:
  – *Fusarium* Head Blight
  – Root Rot, Crown Rot and Stalk Rot
  – Take-All
  – Anthracnose
  – Gray Mold, *etc.*

• HTP *in vitro* screens for potential plant growth enhancement activities, including:
  – Plant growth hormone production
  – P-solubilization
  – N-fixation
  – 2,3-butanediol production
  – ACC deaminase activity, *etc.*

• *In planta* screens for major plant diseases; the collection screened for *Fusarium* head blight biocontrol

• *In planta* screens for corn and wheat yield enhancement
Microbial Seed Coating

• Targeted and cost-effective application method

• Microbes must be compatible with other seed coating agents

• Microbes are mixed with a biopolymer and coated on the seed in desired dosages

• As the seed germinates, the microbes colonize and form beneficial association with the developing plant

• Plant-associated beneficial microbes provide growth enhancement and protection from pests throughout the growing season
3rd Party FHB Efficacy Screening

- Microbial seed treatments and microbial foliar sprays tested in greenhouse trials for FHB reduction

- The wheat heads are challenged by *Fusarium graminearum* conidia
  - After challenge, FHB severity is monitored
  - Commercial biocontrol agents used as controls/benchmarks

- Agradis microbes significantly reduce FHB severity as foliar spray applications and as a seed treatment
  - Late season disease biocontrol as a seed treatment

"COMPOSITIONS AND METHODS FOR CONTROLLING HEAD BLIGHT DISEASE"
U.S. Provisional Patent Application
Agradis Microbial Solutions Summary

• The most systematic microbial collection for given plant family (*Poaceae*) generated and characterized using our proprietary technologies

• Novel plant associated microbial diversity captured

• Coupling genomics and Next-Gen-Sequencing technologies with a very powerful Bioinformatics platform to differentiate in the field

• *In planta* efficacy of microbes as biocontrol agents and crop yield enhancers demonstrated in greenhouse and field trials

• Agradis Microbial Solutions Technologies provide robust microbes, microbial products and genes for biocontrol agents, yield enhancers, insecticidal, herbicidal, and nematocidal agents