JDRF Perspective on Closed Loop

Aaron J. Kowalski, Ph.D.
Assistant Vice President
Treatment Therapies
Juvenile Diabetes Research Foundation International
Presenter Disclosure

Aaron Kowalski

Disclosed no conflict of interest.
The First Generation of an Artificial Pancreas
JDRF Artificial Pancreas Consortium
APP Consortium

Peter Chase – UCHS Colorado

Stuart Weinzimer – Yale

Bruce Buckingham – Stanford

Boris Kovatchev & Marc Breton – UVA
Claudio Cobelli – U. Padova
Eric Renard – U. Montpellier

Howard Zisser – Sansum
Moshe Phillip – Schneider Children’s Med Car

Frank Doyle – UCSB

Ed Damiano – Boston University

Ken Ward – Oregon Health and Sciences Unit.

Roman Hovorka – Cambridge

Rick Mauseth – Benaroya Institute

Tim Jones – Unit of Western Australia
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*Jaeb Coordinating Center - Tampa
Current Areas of Research Focus

Control-to-Range
- A system that would minimize hypo and hyperglycemic excursions

Nocturnal Pump Shut-off
- A system that would predict impending nocturnal hypoglycemia and suspend insulin delivery for up to 2 hours

Overnight Closed-Loop Control
- A system that would control blood glucose while sleeping

Dual Hormone
- A bihormonal system with insulin and glucagon, amylin, or other hormones
APP Strategy – Iterative Increases in Automation

1. Very Low Glucose Insulin Off Pump
   - Pump shuts off when user not responding to low-glucose alarm

2. Hypoglycemia Minimizer
   - Predictive hypoglycemia causes alarms followed by reduction or cessation of insulin delivery below low threshold

3. Hypoglycemia/ Hyperglycemia Minimizer
   - Same as Product #2 but added feature allowing insulin dosing above high threshold (e.g., 200mg/dl)

4. Automated Basal / Hybrid Closed Loop
   - Closed loop at all times with meal-time manual assist bolusing

5. Fully Automated Insulin Closed Loop
   - Manual meal-time bolus eliminated

6. Fully Automated Multi-Hormone Closed Loop

START

END
APP Strategy: Low Glucose Shut-off System

1. **Very Low Glucose Insulin Off Pump**
   - Pump shuts off when user not responding to low-glucose alarm

2. **Hypoglycemia Minimizer**
   - Predictive hypoglycemia causes alarms followed by reduction or cessation of insulin delivery below low threshold

3. **Hypoglycemia/ Hyperglycemia Minimizer**
   - Same as Product #2 but added feature allowing insulin dosing above high threshold (e.g., 200mg/dl)

Graph:
- **BG – mg/dL**
  - Alarm #1
  - Alarm #2 - No response at threshold – Insulin off for up to 2 hours
- **Time**
APP Strategy: Predictive Hypoglycemia System

1. Very Low Glucose
   - Insulin Off Pump
   - Pump shuts off when user not responding to low-glucose alarm

2. Hypoglycemia Minimizer
   - Predictive hypoglycemia causes alarms followed by reduction or cessation of insulin delivery below low threshold

3. Hypoglycemia/Hyperglycemia Minimizer
   - Same as Product #2 but added feature allowing insulin dosing above high threshold (e.g., 200mg/dL)

**Predictive** alarm on impending hypoglycemia – No response – alarm plus insulin reduced or off for up to 2 hours
APP Strategy: Hyper/hypo Minimizer System

1. **Very Low Glucose**
   - Insulin Off Pump
   - Pump shuts off when user not responding to low-glucose alarm

2. **Hypoglycemia Minimizer**
   - Predictive hypoglycemia causes alarms followed by reduction or cessation of insulin delivery below low threshold

3. **Hypoglycemia/ Hyperglycemia Minimizer**
   - Same as Product #2 but added feature allowing insulin dosing above high threshold (e.g., 200mg/dL)

**BG – mg/dL**
- Predictive alarm on impending hypo or hyperglycemia
- No response – Alarm plus insulin increase or reduction to bring glucose level back into range

Minimize time in “Red” zones
Technology: Capabilities and Gaps
System evolution will be technology dependent

1st Generation AP Systems

1. Very Low Glucose a
   Insulin Off Pump

2. Hypoglycemia
   Minimize

3. Hypo/Hyper
   Minimize

4. Fully Automated
   Insulin
   Closed Loop

5. Basal / Hybrid
   Closed Loop

2nd Generation AP Systems

3rd Generation AP System

6. Fully Automated
   Anti-insulin
   Closed Loop

START

END
Needs Assessment: 1st Generation AP Systems

- Finalized algorithmic approach
- Defined clinical and regulatory path
- Pathway to commercial availability
Sensors
- Improved accuracy and reliability
- Differentiated redundancy (beyond Glucose Oxidase)
- Calibration free

Algorithms
- Continuously optimizing
- With and without meal bolus

Pumps
- Performance feedback information

Needs Assessment: 2nd Generation AP Systems

![System evolution will be technology dependent](image)
Needs Assessment: 3rd Generation AP Systems

- Multi-hormone therapies
  - Approved soluble and pumpable complementary hormones/drugs (i.e. glucagon)
- Dual chamber pump
- Sensors
  - Single port sensing and infusion
  - Implantable long life sensors

System evolution will be technology dependent
Regulatory Approval – Key Area of Focus

- Gaining regulatory approval will be challenging
  - Conservative FDA
    - Novel product to treat serious disease
    - Subject to highest regulatory oversight
  - Progress has been slow on approval of academic research

- What JDRF is doing:
  - Meet frequently with key staff at FDA
  - Review and approve all submissions from academic sites before they are sent to FDA
  - Convene a clinical recommendations panel of experts to address key clinical questions
Insulin & Other Hormones
Glucose-modulating Drug Initiative: Strategy & Priorities

- Improved insulins
  - New insulins that work faster
  - New and improved delivery tools (i.e. intradermal, inhaled, intraperitoneal)

- Other hormones
  - Glucagon, Amylin, Leptin, others

- New pathways
  - Glucose-responsive insulins
  - Repositioned drugs: Holistic approach needed to achieve overall metabolic health (i.e. Incretins, Metformin, SGLT2 inhibitors)
Sensor Development Initiative

Juvenile Diabetes Research Foundation
and
The Helmsley Charitable Trust

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JDRF-Helmsley Sensor Initiative: Request for Expressions of Interest

- **Sensor Performance**
  - Approaches should focus on overall improved sensor accuracy and reliability with significant attention to performance in the hypoglycemic range

- **Form Factor**
  - Minimize the burden of wearing a sensor, with consideration to use in all people with diabetes from infants to the geriatric population

- **Examples of pertinent topics include:**
  - Advanced glucose measuring technologies
  - Advanced methods of calibration or universal calibration
  - Alternate modes of sensing
  - Improved form factor – miniaturization
  - Advanced algorithms for improvement to sensor data
  - Improved hypoglycemic accuracy and reliability
  - Measurement redundancy
  - Reduced warm up time
  - Failure detection
  - Comprehensive communication capabilities
Summary

- Artificial Pancreas system testing is occurring in humans across the globe
- Near-term solutions exist to reduce hypoglycemia exposure
- Today’s technologies will allow for first automated dosing of insulin
- Technological improvements will allow for more automated approaches
- Hormones beyond insulin will be important as we move beyond automated insulin delivery towards more “artificial pancreas”-like systems/approaches
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- JDRF Artificial Pancreas Consortium Members

- Industry
  - Abbott Diabetes, Animas, BD, DexCom, Insulet, Medtronic, Roche,
For more information

See the JDRF Artificial Pancreas Project Website:

www.artificialpancreasproject.com

Or email

akowalski@jdrf.org