The Voice of the Donor for a Cure

Juvenile Diabetes Cure Alliance

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The Diabetes Research Institute's BioHub Initiative

Conclusions:

→ The DRI recently introduced its BioHub research initiative with a goal of developing a biological cure for type 1

→ This cure approach integrates several technologies that are currently in development

→ Many individual projects within the BioHub represent Practical Cure research

→ The BioHub is a clear step in the right direction for Practical Cure development, but there are meaningful opportunities to refine this effort

Organizations of Focus:

American Diabetes Association (ADA)

Diabetes Research Institute Foundation (DRIF)

JDRF

Joslin Diabetes Center (Joslin)

TAKE ACTION NOW

Ensure it's for a Cure

✓ **Specify** for Practical Cure research. Use our letter at www.thejdca.org/

✓ **Call** us for an advisory meeting at 212-308-7433

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This is a special report on the BioHub initiative spearheaded by the Diabetes Research Institute (DRI), with the DRIF being an important source of funding for the program. The JDCA is sharing its views on this new development in response to numerous inquiries that we have received from Alliance members who regularly read our reports.

What is the BioHub?

The BioHub is a cell-based approach to curing type 1. It is designed to allow a person to achieve insulin independence through the transplantation of insulin-producing islets. The goal is to create "an integrated "mini organ" that mimics the native pancreas, containing thousands of insulin-producing cells that sense blood sugar levels and release the precise amount of insulin needed in real time."[1] The BioHub is designed to eliminate the need for harsh systemic immune suppressing drugs to prevent rejection of the implanted islets.

Concurrent with the introduction of the BioHub program, **the DRI, and by extension the DRIF, adopted a definition of a cure** which outlines the goals that the initiative seeks to deliver. **The DRIF is the only one of the four major type 1 diabetes charities that has established a cure definition**. As defined by the DRI, a cure would mean:

> "The ability to restore natural insulin production and normalize blood sugar levels without imposing other risks."[2]

Although a time goal is not associated with the BioHub' s delivery of a cure, the DRI expects to achieve conclusive results for key projects by 2025 if they are fully funded.

Multiple components

The BioHub is an integrated platform that contains four distinct areas of funding. The DRIF has a funding goal of $65 million for BioHub research. The four funding areas with the targeted funding amounts are:

1) Site selection—$14 million
   Site selection research seeks to identify an optimal location in the body for implanting the islets, or to develop a device that could house them.

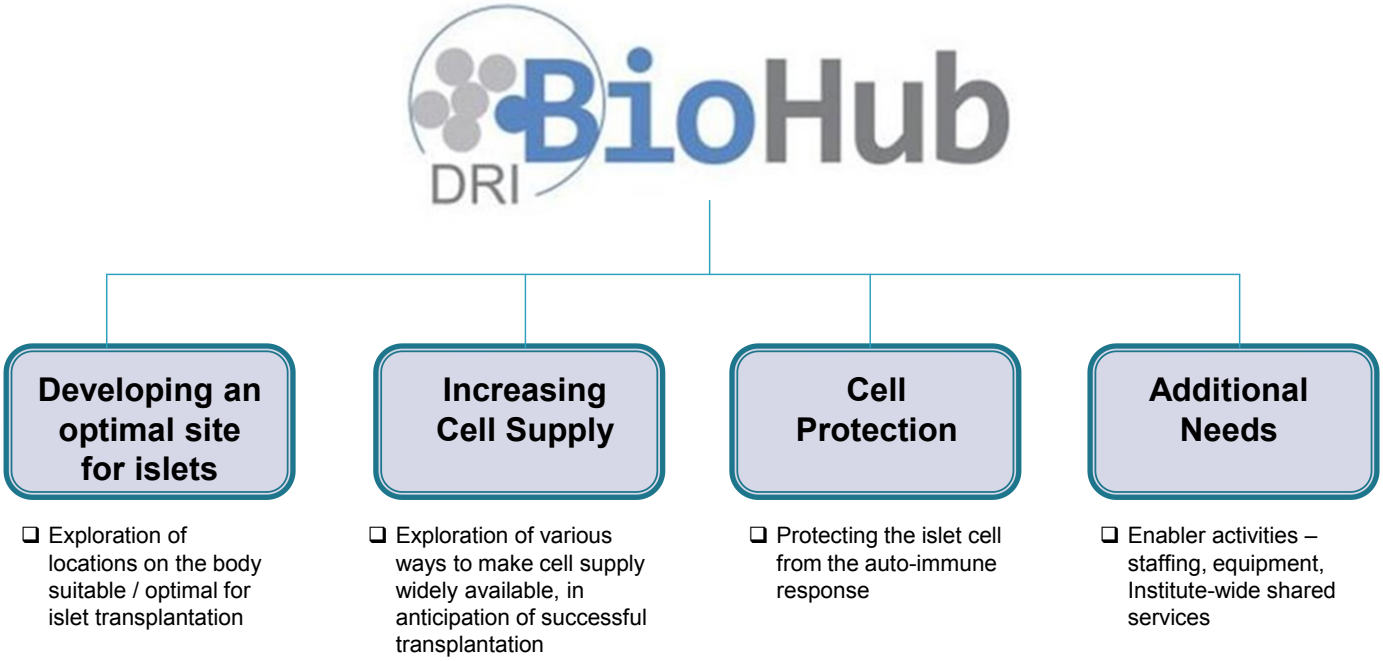
2) Cell protection—$ 26 million
   Cell protection focuses on shielding the islets from an autoimmune attack, which might involve:
   - → encapsulating the cells
   - → a low-dose localized immune suppressing drug
   - → agents that allow the immune system to tolerate the implanted islets

3) Cell supply—$6.5 million
   This area of research focuses on developing an abundant source of insulin-producing cells for transplant. Potential sources might include stem cells, donor islets, and porcine islets.

4) Additional needs—$18.5 million
   Unspecified additional needs include expenses associated with conducting research, like lab equipment and staffing.

There are many individual projects within the BioHub initiative, some of which are interconnected (the appendix on page 5 lists key projects within each of the four funding areas).[3] One strength of the BioHub is that if one project were to fail, there are others that could take its place. Therefore, **the viability of the entire initiative is not dependent upon one individual project**.

The following diagram depicts the major components of the BioHub:



All of the technologies that are represented in the BioHub diagram are in development today, but to varying degrees. The DRI expects that select projects could advance to human clinical trials by 2014. Although conclusive results for key components may be achieved by 2025, no time goal has been adopted and the BioHub's ultimate success cannot be assured.

JDCA's view of whether the BioHub is Practical Cure research

Practical Cure research is defined by outcomes, and specifically the potential to deliver the following outcomes by 2025:

- → no blood glucose monitoring beyond once per week
- → A1c levels between 5-7%
- → an unrestricted diet with no carb counting
- → worry free sleep
- → low risk and little to no side effects
- → reasonable meds if the solution is pharmacological or a fast recovery if it is surgical

Positive characteristics

- → The DRI/DRIF have adopted a definition of a cure
- → It is endeavoring to deliver what cure donors want
- → It is outcome based
- → Utilizes existing technology platforms
- → Integrates many individual projects into one conjoined objective
- → Not dependent on one technology

The JDCA believes that **the majority of the projects in two of the major funding areas, site selection and cell protection, are Practical Cure research**. Most projects in these areas are designed to shield transplanted islets from an autoimmune attack and ensure their survival and functionality, key elements in the development of a Practical Cure that is based on islet transplantation.

Areas of concern

- → It is not time bound
- → Details of the utilization of the $65 million remain vague
- → Ensuring the best global talent is participating as appropriate, even outside the DRI
- → Opportunity to further rationalize the number of projects in the cell protection area
- → Additional needs funding of $18.5 million is unclear

Many projects in two of the four major funding areas are not Practical Cure research. Projects that target an increasing cell supply are not Practical Cure research because having a large supply of islets is not a cure, in our view. A larger source of functional islets would make an eventual cure that is based on islet transplantation technology more widely available, but simply having more islets would not deliver a Practical Cure to one person. The funding category called "additional needs," includes projects that are oriented more toward general researcher funding and Institute-wide equipment needs and may not be specifically focused on delivering a Practical Cure.

Summary and Conclusion

The DRI's BioHub effort is an integrated approach toward type 1 cure development. This initiative offers promising opportunities and endeavors to do what cure donors want. Many projects within this broad initiative are examples of Practical Cure research, which the JDCA ardently advocates. Although the approach exhibits positive characteristics, there are also concerns whether donor money is being utilized for its maximum benefit.

The JDCA is not aware of any other major diabetes charity taking an approach to cure development that is similar to the BioHub. We would like to see more charities fund integrated cure approaches like this. In particular, we would like to see all the organizations adopt a Practical Cure initiative that identifies and prioritizes projects that endeavor to deliver Practical Cure outcomes within a reasonable timeframe. **Importantly, as is always the case, donors who seek a Practical Cure can support this type of work by stipulating that their contributions to the charity of their choice be used only for Practical Cure research**.

Appendix: Individual BioHub Projects

Site Selection

◊ Omentum as Alternative Site for Islet Transplantation
◊ Silicone Scaffolds for Islet Transplantation
◊ Venous Sac as Alternate Site
◊ Autologous Plasma plus Recombinant Human Thrombin

Cell Protection

◊ Facilitating Cells for Tolerance
◊ Encapsulation with Conformal Coatings
◊ Double Shrink-Wrapped Cells
◊ Using Oxygen Generating Biomaterials
◊ Functionalized Nanoscale Coating for Encapsulation
◊ Immunomodulatory and Regenerative Effects of Mesenchymal Stem Cells on Allografts
◊ Using Myeloid Derived Suppressor Cells for Tolerance
◊ Regulatory T Cells
◊ CCL21 Suppressing the Immune Attack
◊ Autologous Stem Cells with Mesenchymal Stem Cells Mesoblast Infusion
◊ Localized Immunomodulatory Drugs
◊ Active Tolerance Induction without Immunosuppression Using Donor Bone Marrow
◊ Suppression of SMAD7
◊ Stem Cell Educator

Cell Supply

◊ Xenotransplantation/Porcine Islets
◊ Adipose Cells
◊ Transdifferentiation/Acinar Tissue/Precursor Cells
◊ Biliary Tree Ducts
◊ Super Islets
◊ Oxygen Sandwich for Islets
◊ Replication of Human Islet Cells

Additional Needs

◊ Rapid Response Team
◊ Fellowship Fund
◊ Equipment Fund
◊ Institute-wide shared core services

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Endnotes

1. Diabetes Research Institute Foundation BioHub Case Statement "Reaching the Biological Cure". Page 3.

2. Diabetes Research Institute Foundation BioHub Case Statement "Reaching the Biological Cure". Page 3.

3. Diabetes Research Institute Foundation BioHub Case Statement "Reaching the Biological Cure". Pages 14-15.

Analyst Certification

The JDCA analyst responsible for the content of this report certifies that with respect to each organization covered in this report: 1) the views expressed accurately reflect his own personal views about the organizations; and 2) no part of his compensation was, is, or will be, directly or indirectly, related to the specific views expressed in this research report.

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