Thermograft™

Autologous Brown Adipose Tissue Therapy for the Treatment of Obesity and Type II Diabetes

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Ardent Cell Technologies is developing Thermograft – a therapy for obesity and type II diabetes. Thermograft transforms "energy-storing" white adipose tissue (WAT) into "energy-burning" brown adipose tissue (BAT). BAT naturally boosts metabolism through heat generation (thermogenesis) in response to cold or excess caloric intake. Clinical studies have shown that increasing BAT amount and activity can lead to body fat loss and improvement of diabetes symptoms, and is therefore a promising approach to counter the epidemics of obesity and type II diabetes [1-5].

The Opportunity and Unmet Need

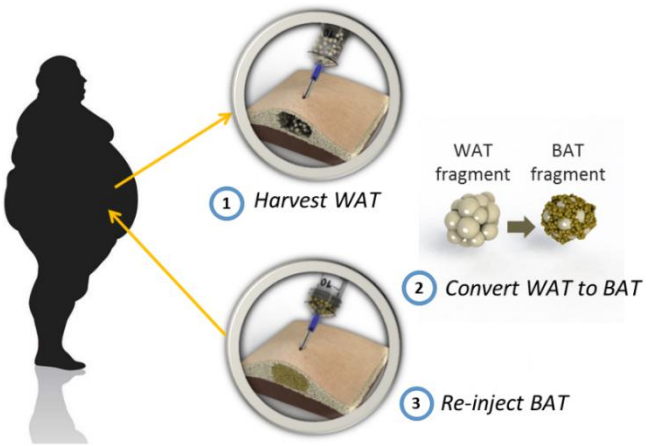
The obesity epidemic presents one of the most significant health and economic risks to the public. More than 2.1 billion people (~30% of the global population) are overweight or obese, and the annual costs associated with obesity are greater than $2T worldwide (2.8% of global GDP) and over $200B in the US alone [6, 7]. While obesity commonly leads to serious comorbidities such as type II diabetes and heart disease, weight loss can reverse or reduce risk of such conditions [8]. Current medical weight loss treatments such as drugs and bariatric surgeries are largely ineffective for maintaining long-term weight loss, while also exhibiting numerous potentially serious complications and side effects that limit their widespread use [9-11]. There remains a significant unmet clinical need for safer and more effective weight loss therapies.

The markets for obesity and type II diabetes treatments are some of the largest in healthcare. Global annual spending on weight loss products and services is estimated to reach $672B in 2015. Thermograft will compete mainly with medical weight loss and type II diabetes therapies, including prescription drugs and bariatric surgeries. The market for obesity therapeutics is predicted to grow at a CAGR of more than 35 percent from $0.4B in 2012 to $8.4B in 2022. The global obesity surgery device market is estimated at $1.4B in 2014, growing at a CAGR of 9.6% to reach $2.5B in 2020. Global sales of drugs for type II diabetes are expected to grow to over $80B within 10 years.

The Envisioned Product

Thermograft (for *thermogenic graft*) converts a patient's WAT to BAT outside the body using an automated device. The procedure adopts autologous fat-transfer procedures (widely practiced by plastic surgeons) to increase BAT in 3 steps:

1. A patient visits a surgeon who removes a small amount of excess WAT from under the skin using a syringe – a 30-minute in-office procedure under local anesthesia.
2. The WAT is transferred into the Thermograft single-use cartridge, which is then sent to Ardent where the WAT is converted to highly metabolic BAT by applying a set of "browning factors" in an automated process.
3. The issue is sent back to the surgeon after two weeks to reinject the BAT into the patient's subcutaneous WAT in a 2nd 30-minute in-office procedure under local anesthesia.



Following the Thermograft procedure, the resulting increase in BAT increases the patient's basal metabolism, burning large quantities of fats and glucose to induce weight loss, prevent weight regain, and improve diabetes symptoms. Thermograft can be performed in plastic surgeons' offices in a minimally-invasive and cost-effective manner, provides a controlled increase in BAT mass using autologous tissue with no immune rejection issues, introduces no systemic drugs into patients which could induce risky side effects, and can be easily manufactured and distributed.

Development and Milestones

Preclinical work at Columbia University supported by The National Institutes of Health and the Coulter Foundation Translational Research Partnership (a collaboration between Biomedical Engineering, the Weight Control Center, and Department of Plastic Surgery) achieved significant milestones in translation towards human clinical studies:

- A study of Thermograft in mice showing long-term function and persistence of the converted BAT after implant
- A study on human fat tissue showing that human WAT can be directly converted to BAT
- Development of an automated bioreactor device for WAT to BAT conversion in a single use, sterile closed system

Ardent Cell Technologies has received additional grant funding to develop the technology for human clinical studies. Ardent is currently seeking $1M to complete preclinical work towards an FDA Investigational New Drug (IND) application to initiate clinical studies that will demonstrate safety and of metabolic impact of Thermograft in humans. Following successful demonstration of Thermograft's impact on human metabolism, Ardent will seek partnerships with large biopharmaceutical firms to advance the technology to market.

Intellectual Property

Ardent is in discussions to license the following patent applications from Columbia University:

Patent Title	Filing Status
Injectable Brown Adipose Microtissues for Treatment and Prevention of Obesity and Diabetes (PCT/US2013/054587)	Provisional 8/2012, PCT 8/2013
Ex Vivo Browning of Adipose Tissue Therapy for Reversal of Obesity and Type II Diabetes (PCT/US2015/039917)	Provisional 7/2014, PCT 7/2015

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