



CIRM GRANTS FUND VITAL STEM CELL RESEARCH, DIRECT SIGNIFICANT FUNDS INTO STATE ECONOMY

The California Institute for Regenerative Medicine was established in 2004 through the passage of Proposition 71 - a statewide ballot measure, providing \$3 billion in funding for stem cell research at California universities and research institutions. CIRM uses bond proceeds to make grants and provide loans for stem cell research, research facilities and other vital research opportunities.

In its efforts to find a stem cell treatment or cure for juvenile diabetes, CIRM earmarked \$20 million for the creation of a Diabetes Disease Team comprised of research groups from a number of institutions, with the specific aim of getting a therapy for diabetes into clinical trials within four years.

The San Diego-based biotechnology company, Novocell, now called ViaCyte, was the principal recipient of the award, which takes the form of a loan. The Diabetes Disease Team, convened in 2009, also includes a group of scientists at the University of California, San Francisco (UCSF), led by Dr. Jeff Bluestone.

Ideally, the goal of type 1 diabetes

researchers is to replace lost beta cells, and attempts to do so have included the use of pancreatic transplants, beta cell (islet) transplants, and transplants of animal cells or tissues. Unfortunately, these approaches have been hindered by:

- The limited amount of donor tissue available;
- Recipient immune system rejection of donor cells;
- Autoimmune destruction of transplanted islet cells (T1DM is an autoimmune disease);
- Safety concerns over tumor formation and other side effects;
- Difficulties in generating normal islet cells from stem cells.

To help solve the first problem, the CIRM-funded Diabetes Disease Team has developed methods to make replacement beta cells from human embryonic stem cells, which can be reliably grown in large-scale batches. The embryonic stem cell-derived beta cells have been shown to cure experimental diabetes in mice and rats.

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Stem Cell Progress at UCI

Researchers Revert Adult Skin Cells to Stem Cell Stage Before Growing into Cardiac Muscle Cells

Scientists at the University of California, Irvine at the Sue and Bill Gross Stem Cell Center are working on a method to revert a human skin cell to a stem cell state while retaining the patient's own genetic composition. Preliminary studies have shown that this approach could be used to generate cardiac muscle cells at very high rate of efficiency.

However, a bottleneck in the production of these cells has been the inability to produce these induced cells efficiently in volume quantities. This project will develop new methods to produce iPSC at predictably higher rates, which can then be used for generation of other types of cells including insulin-producing islet cells for auto-transplantation (islet cells produced from patient's own stem cells via skin cells).

The UCI researchers are using proteomic (protein-mapping) tools to understand under which conditions proteins can develop cells into stem cells. With this knowledge, scientists hope to develop small-molecule agents to generate iPSC from the patient's own skin cells without genetic manipulation. The ultimate goal is to develop non-invasive tools into convenient and safe drugs for the production of iPSC from the patients' own skin cells.

DIRECTOR'S MESSAGE

Spring is a season of growth and renewal, and in this issue, I'm very pleased to share some of the exciting strides our researchers are making in the area of stem cell regeneration.



We have had success growing cardiac muscle cells from iPSC, a type of stem cell derived from adult skin cells. The progress that our scientists have made in less than one year, working with researchers at the Gross Stem Cell Research Center, is remarkable.

We are living in exciting times when it comes to biological and health sciences advances, especially here in California. Thanks to grants from the Center for Integrative Medicine (CIRM), researchers all across the UC are making enormous strides that will benefit a host of human diseases and conditions.

I want to take this opportunity to once again thank you for your continued support of all that we do at the UC Irvine Center for Diabetes Treatment and Research.

Ping Wang, MD
Center Director

In order to address the issue of donor-recipient compatibility, the Diabetes Disease Team has had some very encouraging initial success with several strategies, including administering the cells inside a simple device to shield the cells from immune attack, implantable under the skin, as well as next-generation pharmaceuticals that enable transplantation between unmatched individuals without major side effects. However, the long-term feasibility of such approaches will have to be studied.

With the critical proof-of-concept milestones behind them, the researchers are focusing on the crucial manufacturing and laboratory testing required to assure reliable production of a safe and effective product. If the data is promising, the next step is to seek FDA approval to test the product in humans.

CIRM-funded research projects – with \$1.1 billion so far – are moving toward these goals while creating more than 25,000 job years of new employment and more than \$200 million in new tax revenue. So, CIRM is growing the state's general fund, not depleting it.

The development of treatments and cures, for diabetes is a key target area of the Institute, according to Professor Alan Trounson, president of CIRM.

"This project engages over 30 scientists and physicians, as well as numerous associates and technicians, whose expertise covers all of the critical areas from process development and manufacturing to clinical testing of novel biomedical products – all aimed at treating and eradicating type 1 diabetes," said Trounson.

The Team funded by CIRM has well defined time lines and milestones aimed specifically at advancing any candidate product to an FDA submission. If successful, testing in diabetic patients could begin as early as three years from the project's initiation.

CIRM is also funding two other research groups investigating the differentiation of stem cells into islet cells. While researchers from UC San Diego are looking at the creation of new islet cells from embryonic stem cells, one at UCSF is coaxing re-programmed adult cells, so-called induced pluripotent stem cells or iPSCs, into generating human models of juvenile diabetes.

Despite the fact that substantial obstacles still must be overcome before stem cell therapy becomes a reality for diabetic patients, the initiatives taken by the CIRM represents a major effort to move the field forward.

Mission

To be a Center of integrity and responsibility dedicated to preventing diabetes, improving care and advancing science to find a cure.

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Save the Date

5th Annual Celebrate the Center Fundraiser
Thursday, September 22, 2011
5:30 p.m.
Balboa Bay Club & Resort
Newport Beach

Sugar Substitutes and Alternative Sweeteners

When it comes to sweetening foods there are two choices: “no-calorie” sweeteners (non-nutritive) or calorie-containing sweeteners (nutritive). The Food and Drug Administration (FDA), the U.S. government agency responsible for assuring the safety of food and food additives, determines if a sweetener is generally recognized as safe (GRAS). Since persons with diabetes are looking for low-glycemic sweetening alternatives, let’s take a look at what’s available and how they stack up.

No-Calorie Sweeteners (non-nutritive)

1. Aspartame: Equal, NutraSweet, SweetMate
2. Saccharin: Sweet’N Low, SugarTwin, Sweet Magic, Sucaryl
3. Sucralose: Splenda
4. Acesulfame-K: SweetOne, Sunette
5. Neotame
6. Rebaidioside (RebA): Stevia, Only Sweet, PureVia, Stevia in the Raw, SunCrystals, Truvia

All six of these no-calorie sweeteners are FDA approved and GRAS when consumed at ADI levels. The FDA establishes the Acceptable Daily Intake (ADI) for food additives. The ADI is the amount of food additive that can be eaten over a person’s lifetime without causing harm. These sweeteners do not cause brain tumors, cancer, multiple sclerosis or any other health problem.

Calorie-Containing Sweeteners (nutritive)

1. Sucrose: pure cane sugar, brown sugar, table sugar
2. Fructose: high fructose corn syrup, fruits, juices
3. Honey
4. Agave
5. Sugar alcohols: sorbitol, mannitol, xylitol, erythritol

These sweeteners can contain 2-4 calories per gram. If used in a large enough quantity they may contribute enough carbohydrate to the meal or snack to cause a rise in blood glucose levels. The sugar alcohols can have a laxative effect so should be used carefully, especially by persons with gastroparesis, dehydration or digestive problems.

Read Labels

Beware of products labeled “sugar free.” They may not contain a nutritive sweetener and can contain carbohydrate. For example, cranberry juice cocktail has 33 grams of total carbohydrate per 8 oz. serving. The “light” cranberry juice cocktail sweetened with aspartame contains 10 grams of total carbohydrate per 8 oz. serving. There is a significant reduction in carbohydrate but it is not reduced to zero.

A variety of nutritive and non-nutritive sweeteners are available today. The FDA monitors safety and approves food additives in the U.S. food supply. There is no evidence to date of any adverse side effects for any of these products when used in accordance to FDA established ADI.

As with any food there is the possibility of food intolerance and sweeteners are no exception. Aspartame contains the amino acid phenylalanine and individuals who are allergic to that amino acid may not tolerate products containing aspartame. The sugar alcohols can cause gas and diarrhea in some individuals. The best advice is to read labels carefully to select the best food or sweetener for you.



Nutty Agave Caramel Sauce

Low-glycemic sweetener agave nectar gives this recipe a caramely richness while the nut butter adds a flavorful, protein-packed punch

Ingredients

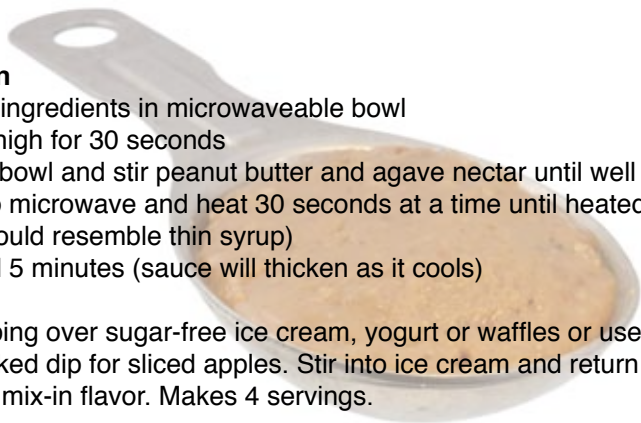
4 Tbsp Natural (no sugar added) peanut butter (almond, cashew, sunflower seed or any other nut butter)

4 Tbsp Blue Agave Nectar (available at most grocery and health food stores)

Preparation

1. Place all ingredients in microwaveable bowl
2. Heat on high for 30 seconds
3. Remove bowl and stir peanut butter and agave nectar until well blended
4. Return to microwave and heat 30 seconds at a time until heated through (mixture should resemble thin syrup)
5. Let stand 5 minutes (sauce will thicken as it cools)

Drizzle topping over sugar-free ice cream, yogurt or waffles or use as a protein-packed dip for sliced apples. Stir into ice cream and return to freezer for an easy mix-in flavor. Makes 4 servings.



Nutrition Information (per 1 Tbsp serving) / daily value (Exchange = 1 carb, 2 fats)

Calories: 149 Calories from Fat: 76 Total Fat: 8.4g / 12% Saturated Fat: 1.5g / 8%

Sodium: 12mg Total Carbohydrate: 15g / 7% (Dietary Fiber: 1g / 4% Sugars: 13g Protein: 3g)

Until There's a Cure...

Members of the community have been very supportive of our efforts to provide the best diabetes treatment available. And it is with your generosity that we will continue to further our mission to find a cure for diabetes. We hope you will join us in this quest. We welcome your support. To volunteer or to make a gift in support of patient care, education or research programs at the Center, please contact:

Rebecca Ford

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Sweeteners Overview

Brand Name	Generic	Glycemic Index	Safe Daily Consumption (per kg, body weight)	Cooking	Additional Info
Equal, NutraSweet, SweetMate	Aspartame	--	50mg/kg body weight/day	Loses sweetness when heated for long periods	Those with sensitivity to phenylalanine should avoid
Sweet'N Low, SugarTwin, Sweet Magic, Sucaryl	Saccharin	--	5mg/kg body weight/day	Yes	May leave bitter aftertaste
Splenda	Sucralose	--	5mg/kg body weight/day	Yes, results may vary	Also comes in sugar blends containing sucrose
SweetOne, Sunette	Acesulfame-K (AceK)	--	15mg/kg body weight/day	Yes, great versatility	
Neotame	Neotame	--	18mg/kg body weight/day	May lose some sweetness when heated	
Stevia, Only Sweet, PureVia, Stevia in the Raw, SunCrystals, Truvia	Rebaidioside (RebA)	< 1	2mg/kg body weight/day	Results may vary	
Agave nectar, blue agave nectar (derived from agave plant used to make tequila)	Agave nectar	15	N/A	Great for baking or cooking at high heat (caramelizes)	Contains calories and carbohydrates; slower absorption into bloodstream
ZSweet (sorbitol, mannitol, xylitol, erythritol)	Sugar alcohols (polyols)	0-13	N/A	Yes, but for best baking results, use half sugar, half polyol	May have laxative effect so those with gastroparesis, and digestive issues should use carefully. Contains calories and carbohydrate.