Dr Parimal Swamy

MD 1989 (Jabalpur Medical College)

Post Graduate training in Cardiology, Critical Care, Diabetology, Respiratory Medicine & Nephrology

Diploma in Preventive Health Care, Certified Cardiac Rehab Specialist, Graduate of Master Clinician Program in Diabetes, W.H.O. accredited P.G Diploma in Diabetes Management, Certificate of Excellence in Diabetes Care & Diploma in Peak Performance Training

Holds design rights for Manual Nebulizer, Biological Age Assessment Tool, CardioFitness Analyzer ™ & Variable IV Insulin Protocol © for ICU.

Designed Asthma Control & Treatment Card (ACT) ®.

Two podium and poster presentation in European Respiratory congress. Presented paper in ADA 2017. Received best paper award in World Congress on Diabetes in 2017.

Authored three books- Emergency Medicine, An Introduction to Neurofeedback Training & Synchronized Integrated Meditation

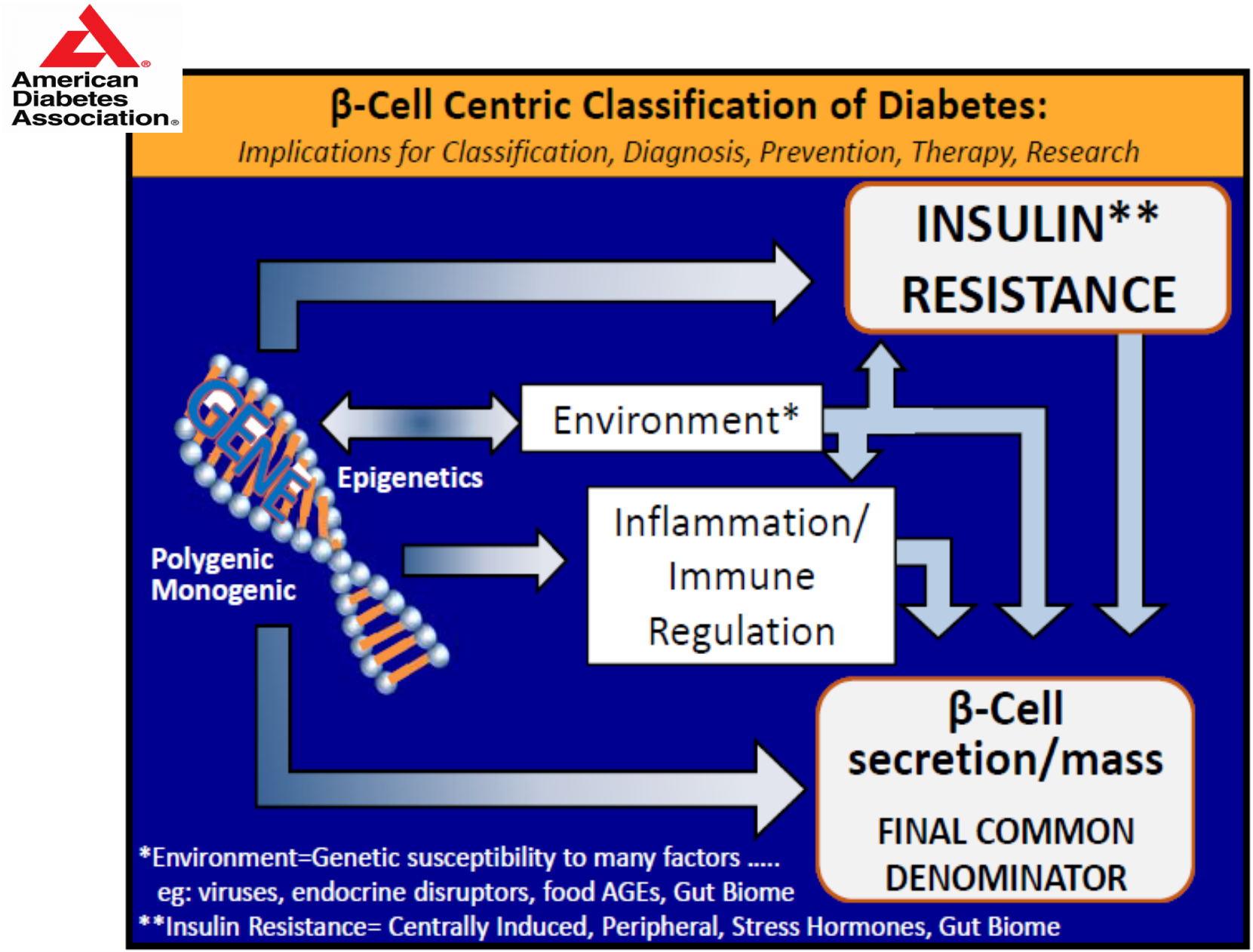
Presently Consultant Physician Jabalpur Hospital & Research Center, Associate Professor of Medicine HDCI-Jabalpur, heads Saksham Yoga™-Mind Body Training, Corporate Fitness Trainer for many organizations

Beta Cell Activation

(Is it possible to reverse diabetes)

Hope V/s Reality

Dr Parimal Swamy


β-Cell Centric Classification of Diabetes:
Implications for Classification, Diagnosis, Prevention, Therapy, Research
INSULIN** RESISTANCE
Environment*
Epigenetics
Polygenic
Monogenic
Inflammation/ Immune Regulation
β-Cell secretion/mass
FINAL COMMON DENOMINATOR
*Environment=Genetic susceptibility to many factors .....
eg: viruses, endocrine disruptors, food AGEs, Gut Biome
**Insulin Resistance= Centrally Induced, Peripheral, Stress Hormones, Gut Biome

Diabetes Reversal : Primary Mechanism (!)

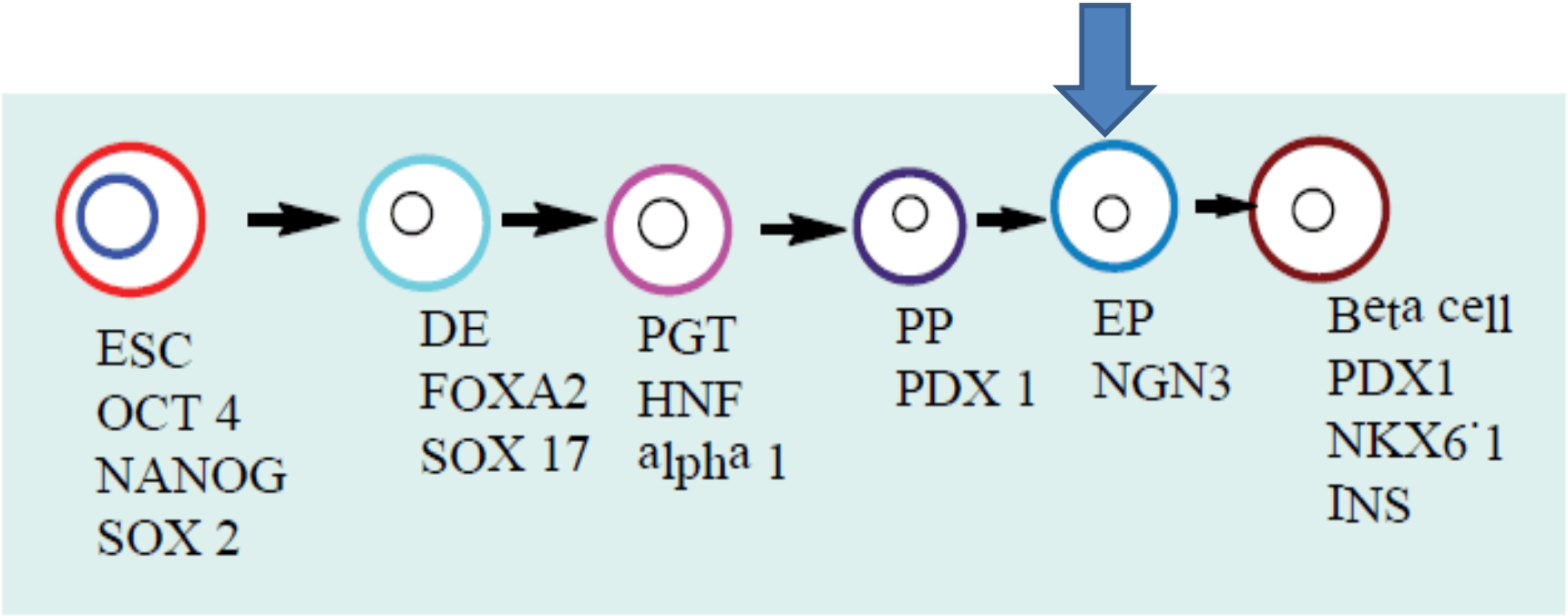
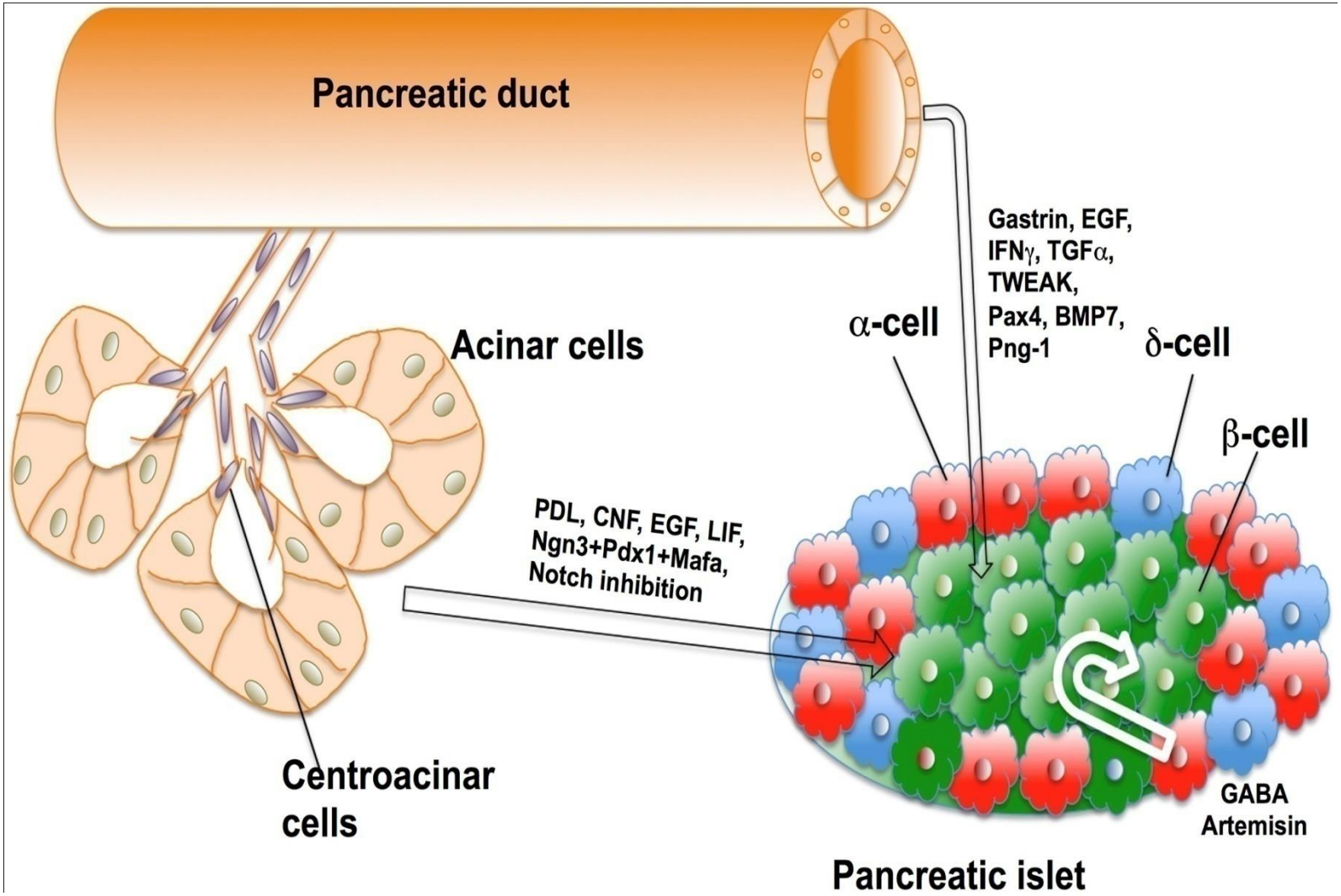


Figure 1: An overview of pancreas development pattern and principal transcription factors involved. ESC (embryonic stem cell), DE (definitive endoderm), PGT (primitive gut tube), PP (pancreatic progenitor), EP (endocrine progenitor).

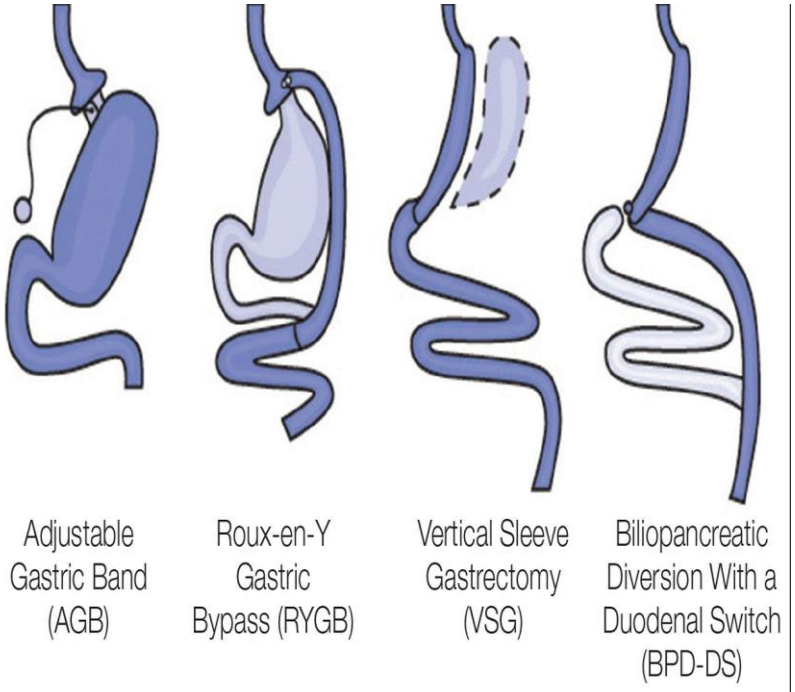


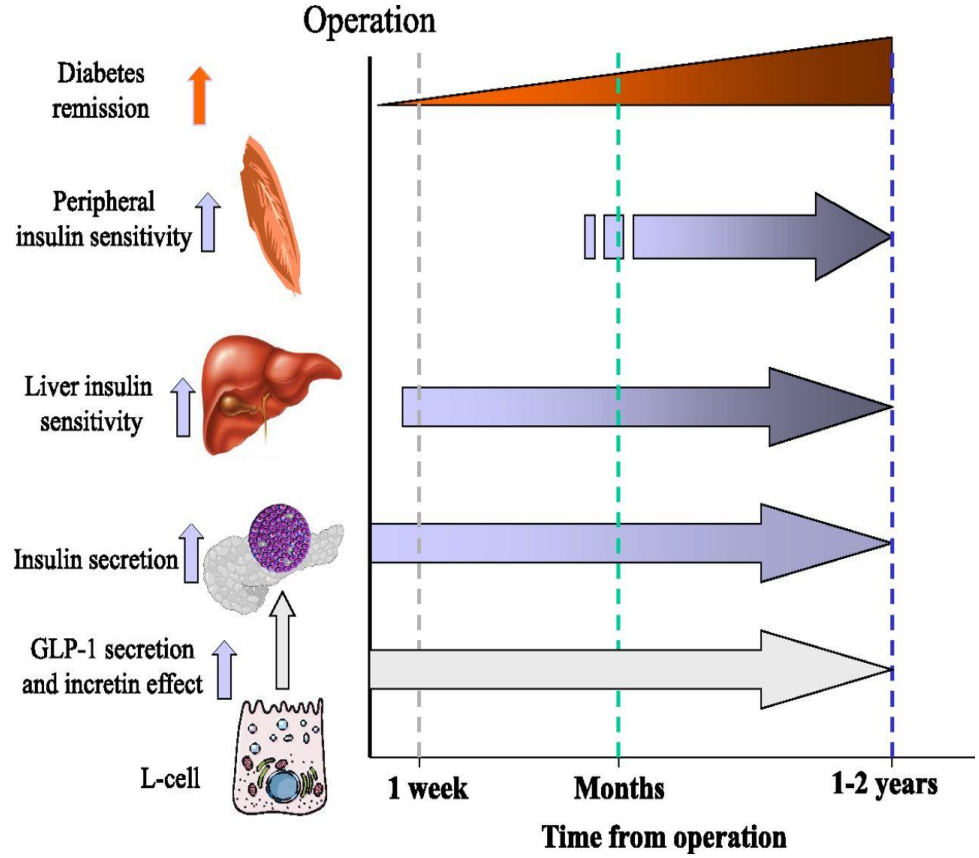
Cell Metabolism 2018 27, 57-67DOI: (10.1016/j.cmet.2017.08.007)

Clinically applicable, logically possible ,evidence based (some still experimental) but safe Beta Cell Activation interventions

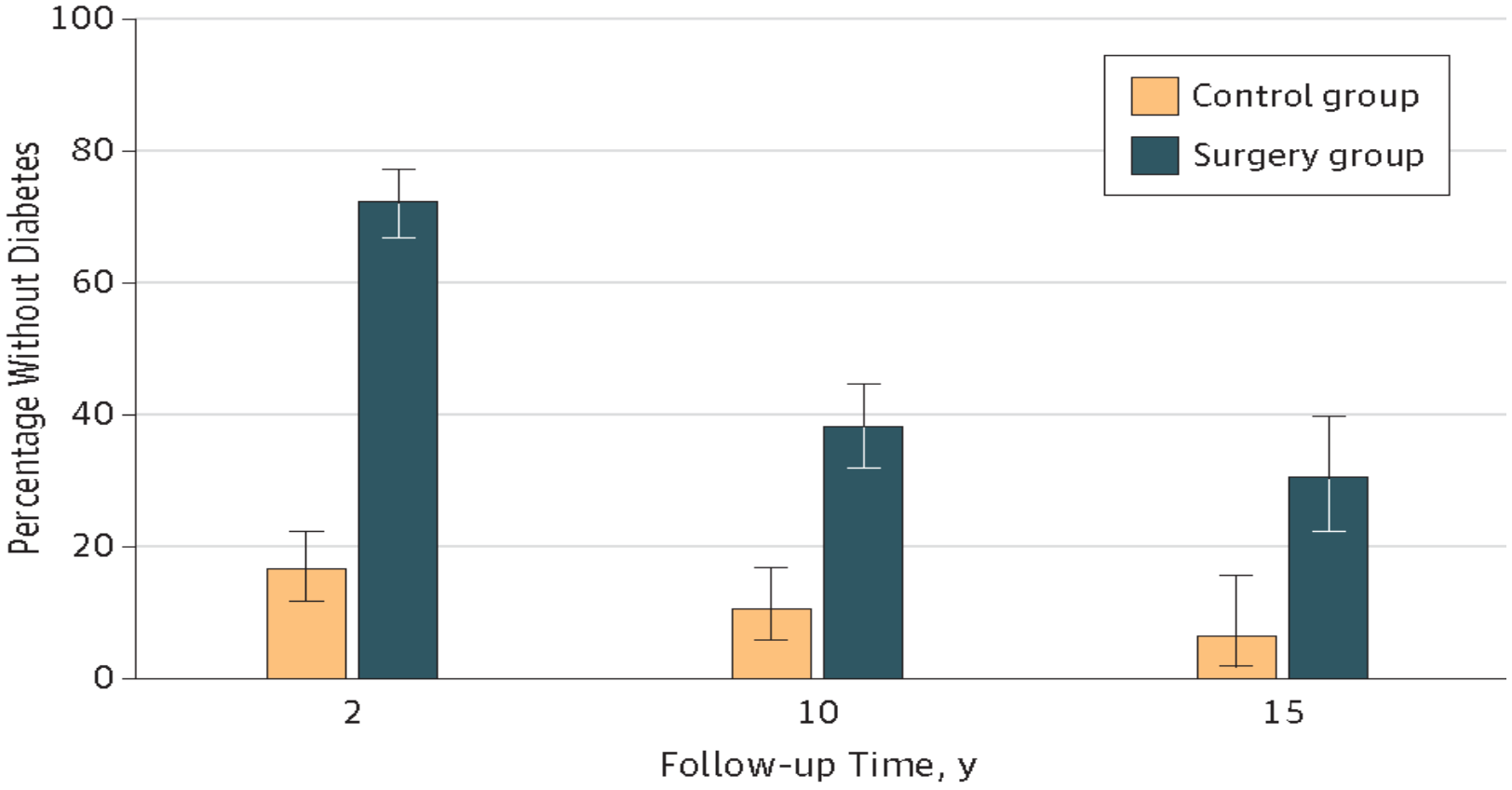
- **Bariatric procedures**
- **Established pharmacological compounds & other agents**
- **Exercise**
- **Diet- VLCD,KETO,LCD, Fasting mimicking diet**

Bariatric Intervention : ! Easiest Diabetes Reversal





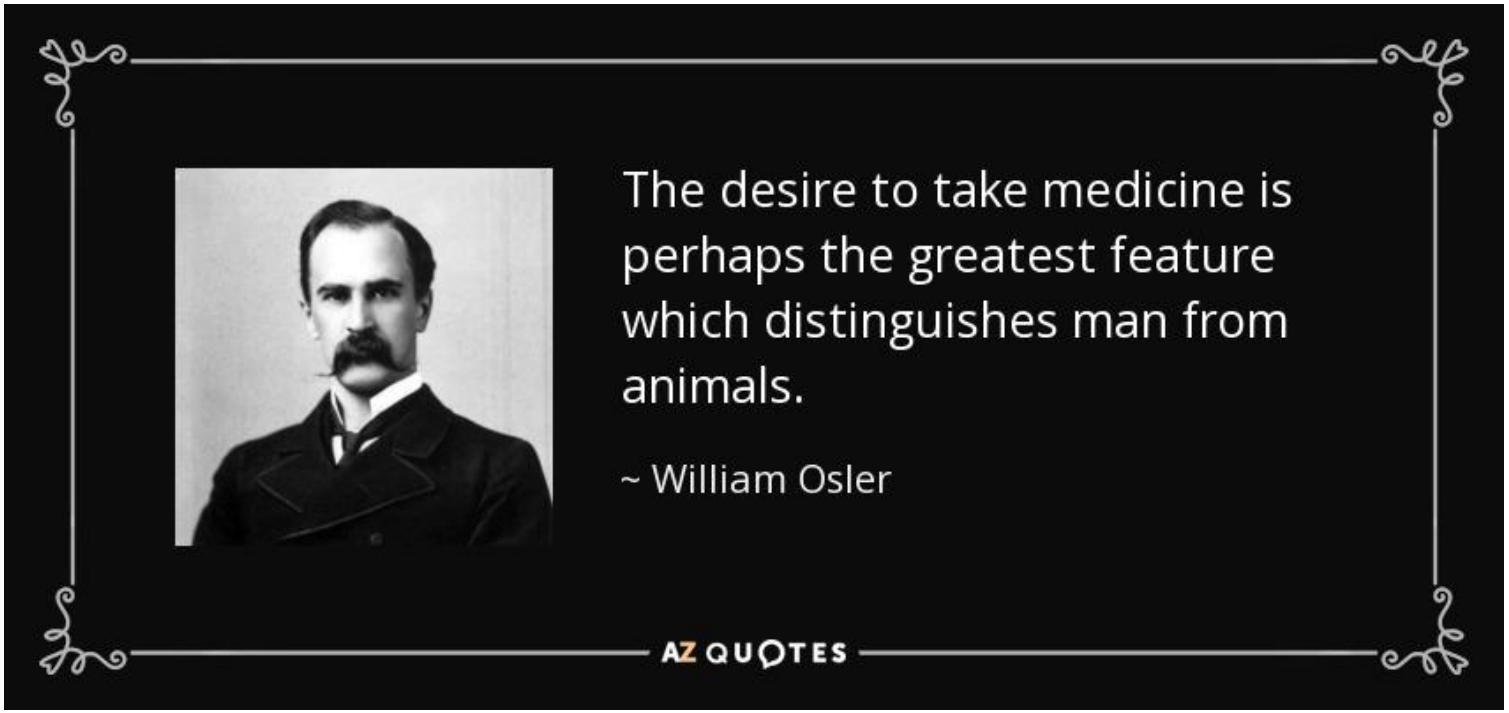
Bariatric Intervention : ! Easiest Diabetes Reversal



Total participants			
Control	207	135	62
Surgery	303	236	115
Odds ratio (95% CI)	13.3 (8.5-20.7)	5.3 (2.9-9.8)	6.3 (2.1-18.9)

Association of Bariatric Surgery With Long-term Remission of Type 2 Diabetes and With Microvascular and Macrovascular Complications (June 11, 2014; JAMA Network)

Diabetes Reversal : Drugs

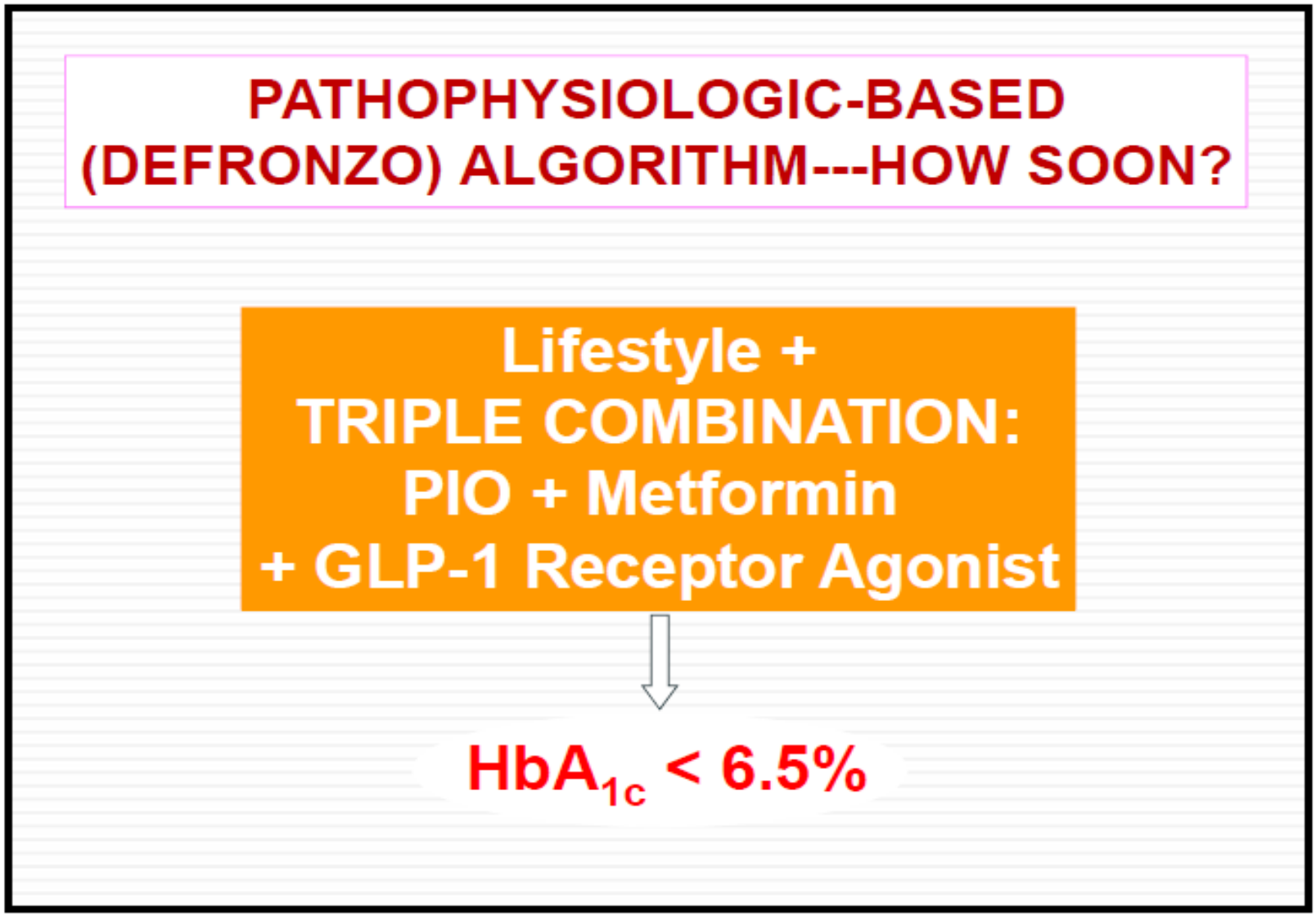


Logic for Combination therapy-
Use the least number of agents that treat most number of mechanisms of hyperglycemia(without stressing the Beta cells)

Pharmacologic Agents	Incretin Regulation			Insulin Resistance			Kidney	Brain	Colon/ Biome	Stomach/ Small Intestine	Immune Dysregulation/ Inflammation
	Beta Cell	Alpha Cell	Incretin Defect	Muscle	Liver	Adipose					
GLP-1RA	√	√	√	√	√	√		√		√	√
DPP4-I	√	√	√								√
Pioglitazone/ TZD	√			√	√	√					
SGLT2-I	√			√	√	√	√				
Metformin					√				√		
Bromocriptine-QR				√	√	√		√			
Pramlintide		√						√		√	
AGI										√	

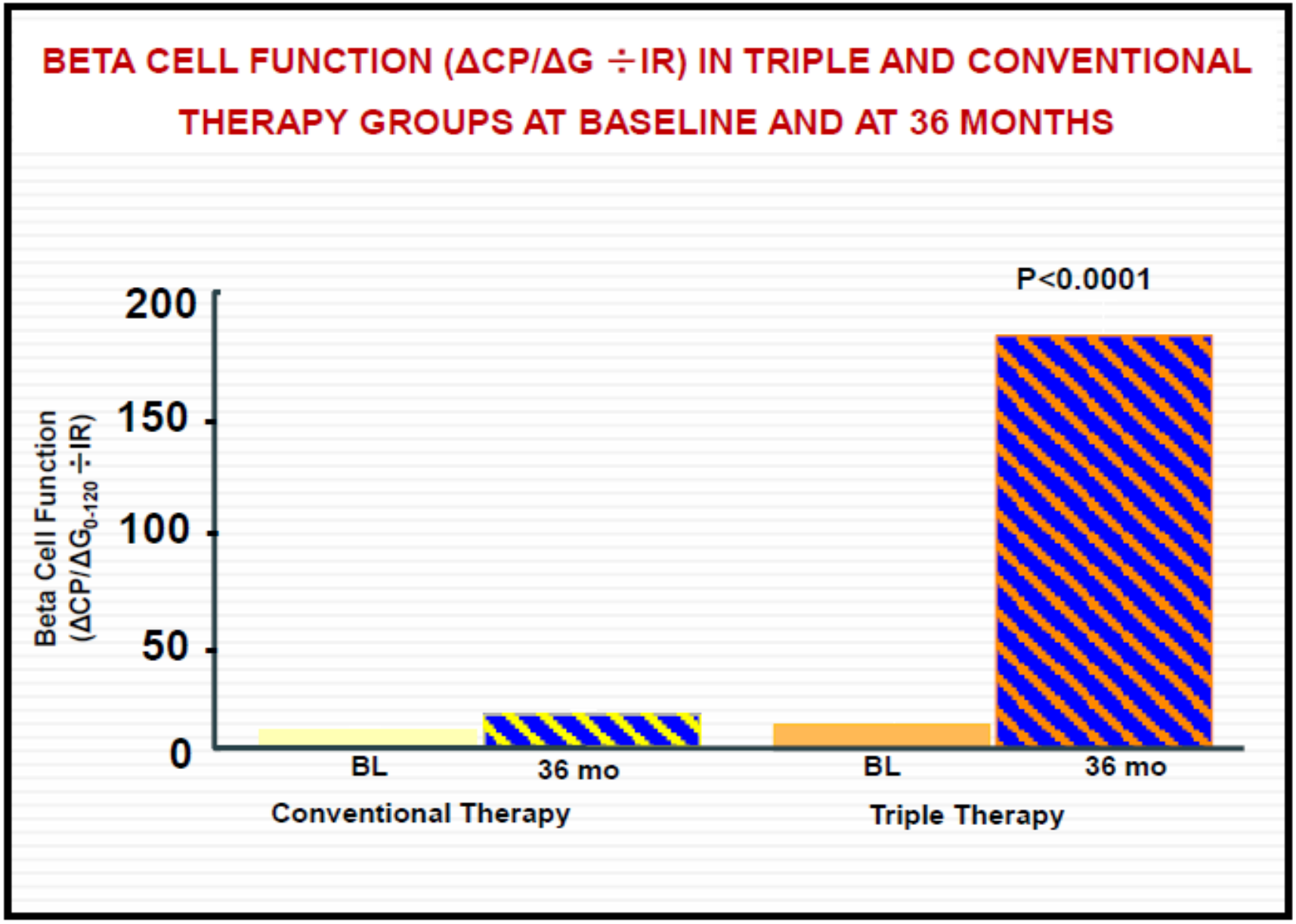
Diabetes Reversal : Drugs (Clinically Applicable)

- GLP 1 Analogues (injectable)
- Pioglitzone
- Gliptins
- SGLT 2 inhibitors
- GABA supplementation
- Phytochemicals
- Early intensive insulin therapy(only in selected cases)



Type 2 diabetes can be prevented with early pharmacological intervention.

Diabetes Care. 2011 May;34 Suppl 2:S202-9



Type 2 diabetes can be prevented with early pharmacological intervention.

Diabetes Care. 2011 May;34 Suppl 2:S202-9

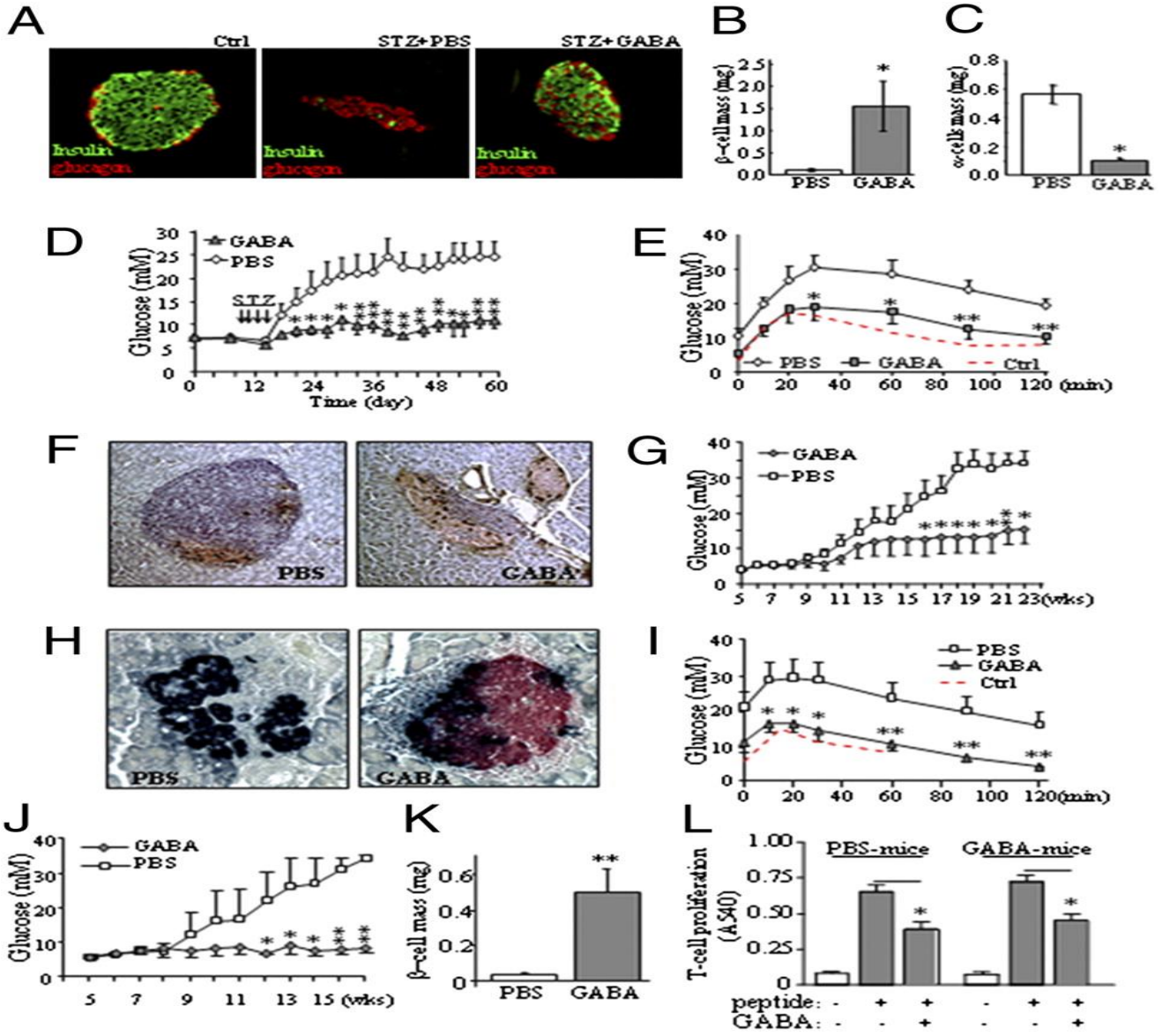
Table 3. List of the chemicals that enhance the proliferation rate and reduce beta cell apoptosis resulting in the conservation of beta cell mass

Nature of chemicals	Proliferation enhancer	Apoptosis inhibitors
Small molecules	GKA	N/A
	calcium signaling	
	adenosine signaling	
	WS6	
Hormones	insulin	insulin
	lactogen signaling	estrogen
	incretin	incretin
	betatrophin	triiodothyronine
Phytochemicals	N/A	resveratrol
		PPAG
		flavonoids
		glutathione peroxidase mimetics

GKA – glucokinase activator; N/A – not applicable; WS6 – compound name with molecular formula C29H31F3N6O3; PPAG – phenylpropenoic acid.

Increasing beta cell mass to treat diabetes mellitus. Adv Clin Exp Med. 2018 Sep;27(9):1309-1315.

GABA preserves β-cell mass and prevents diabetes in MDSD and NOD mice.



Nepton Soltani et al. PNAS 2011;108:28:11692-11697

©2011 by National Academy of Sciences

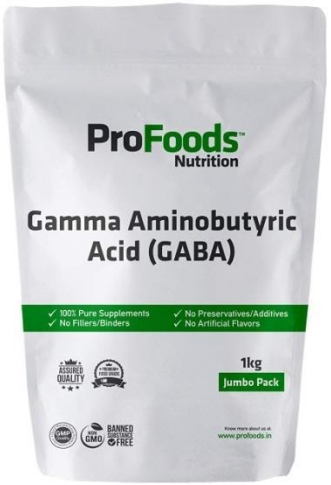
GABA: Ready for prime time!?

Long-Term GABA Administration Induces Alpha Cell-Mediated Beta-like Cell Neogenesis

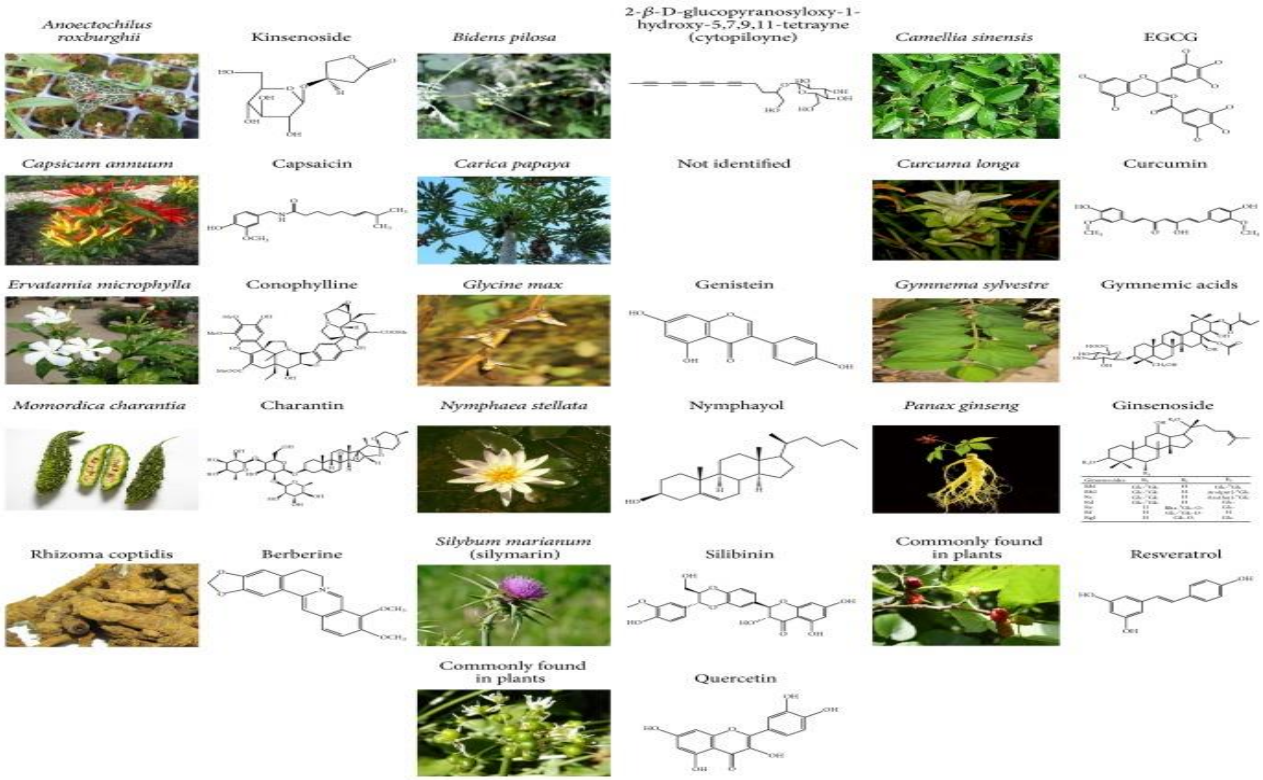
Volume 168, Issues 1–2, 12 January 2017, Pages 73-85.e11

GABA Promotes Human β-Cell Proliferation and Modulates Glucose Homeostasis

Diabetes 2014 Dec; 63(12): 4197-4205.



Plant-Derived Compounds Targeting Pancreatic Beta Cells for the Treatment of Diabetes



Evid Based Complement Alternat Med. 2015; 2015: 629863.

Phytotherapy in the Management of Diabetes:A Review; Molecules. 2018 Jan 4;23(1)

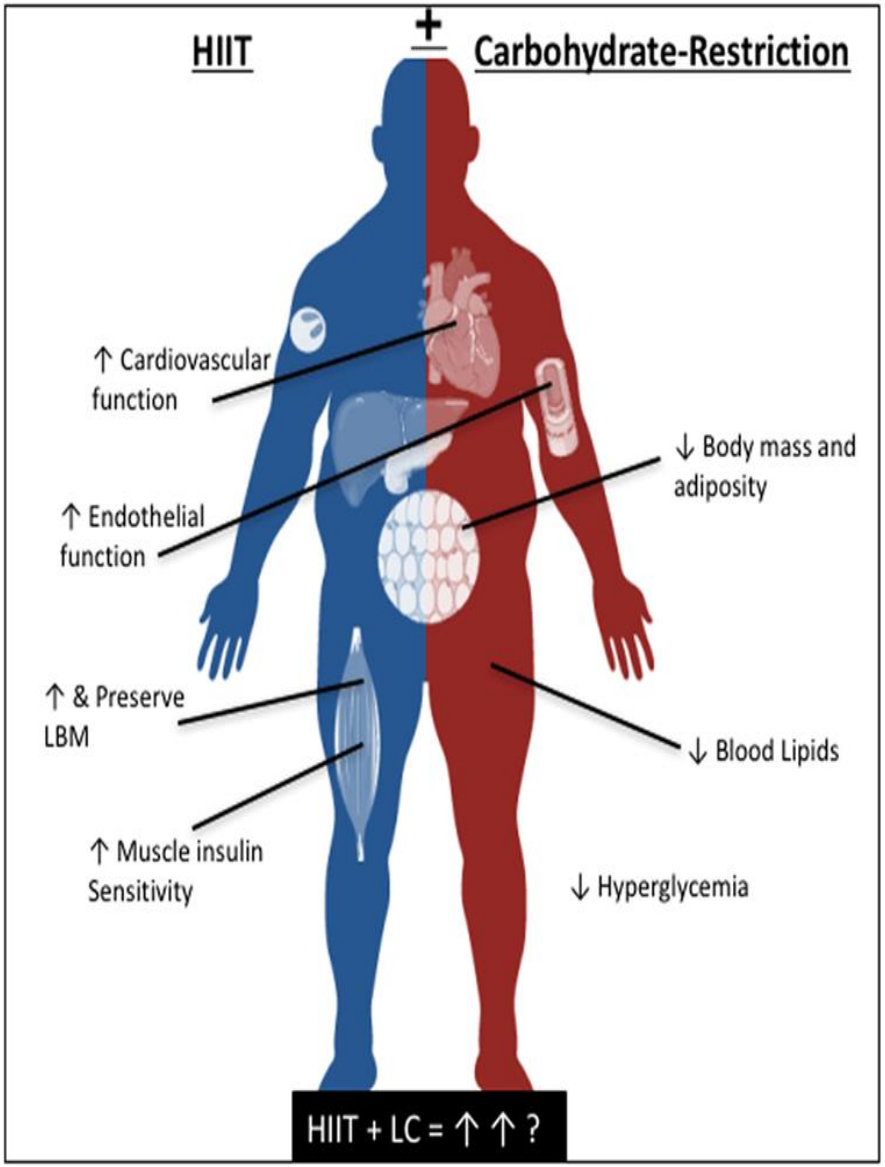
Exercise

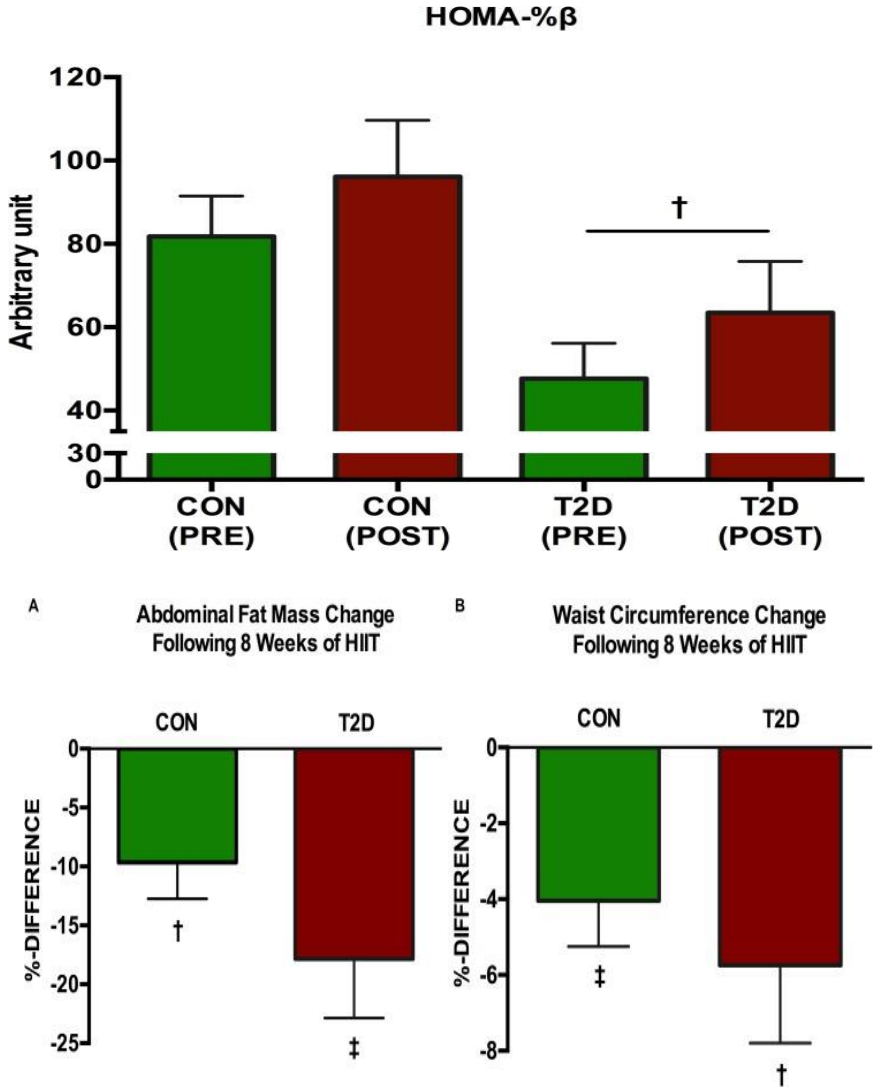
30 minutes 5 days a week ?

When ?How?

Carbohydrate-Restriction with High-Intensity Interval Training: An Optimal Combination for Treating Metabolic Diseases?

Front. Nutr., 12 October 2017



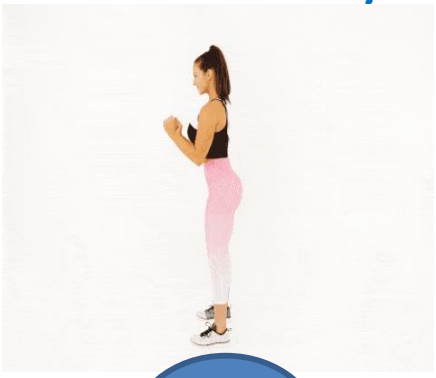


High Intensity Interval Training Improves Glycaemic Control and Pancreatic β Cell Function of Type 2 Diabetes Patients

PLoS One. 2015; 10(8): e0133286.

It takes only THREE minutes to remain Diabetes Free!

Short Resistance Activity



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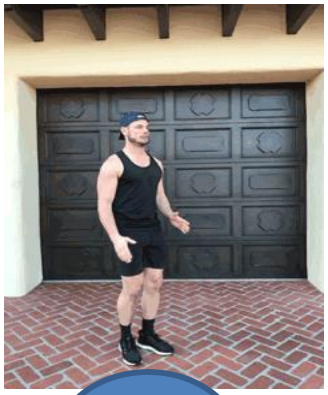

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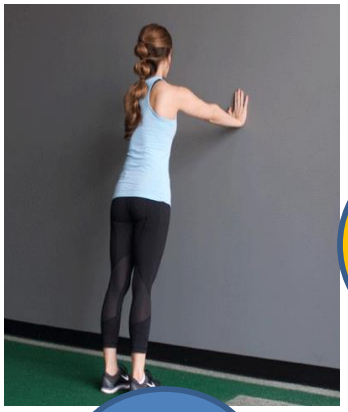


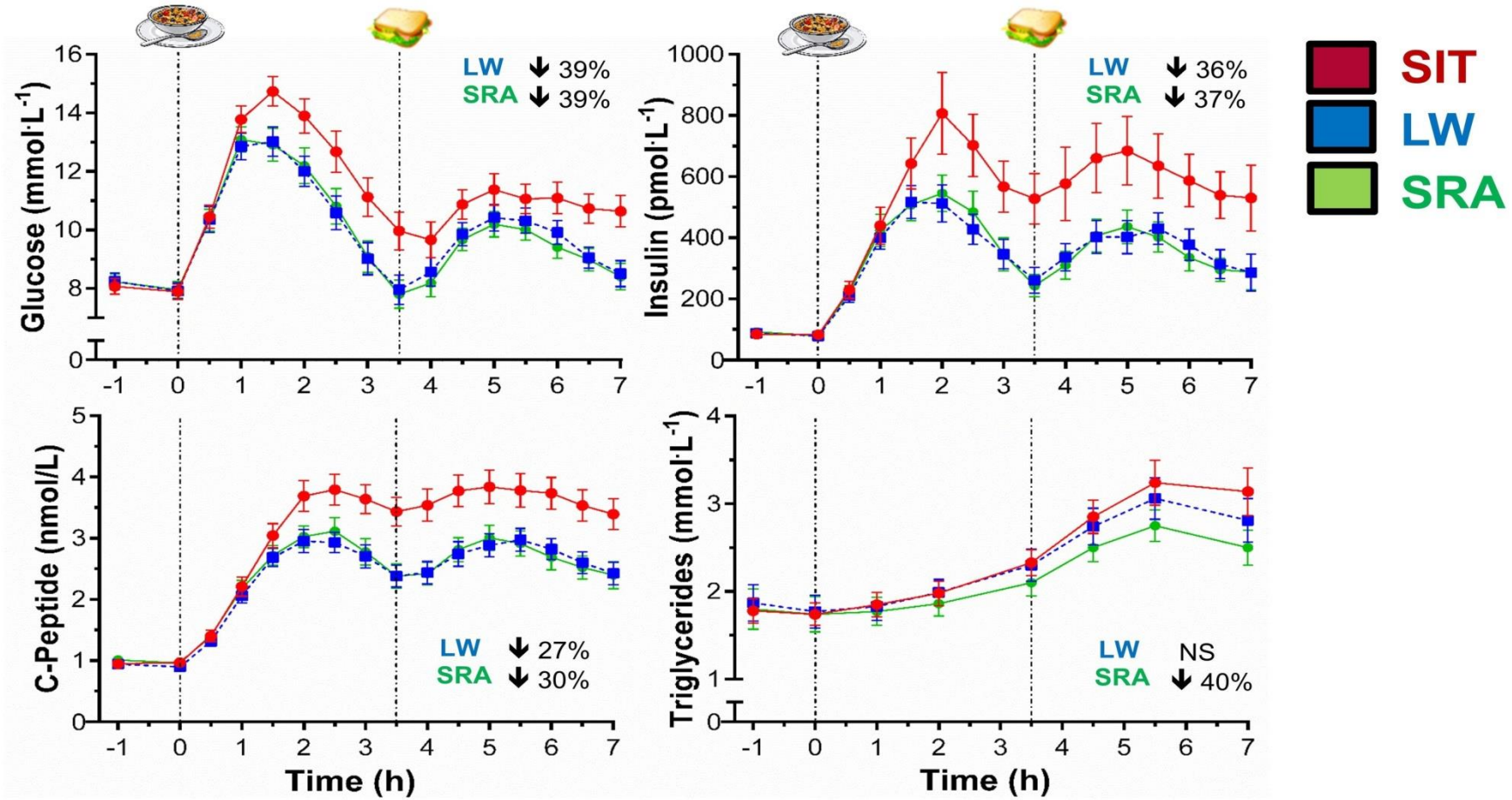
10

X 3

Breakfast----------Lunch----------Evening snack----------Dinner

Beta Cell Preservation
Hormonal Balance
Heart Age
Brain Health
Emotional Balance
Anti-aging gene expression

Short (Repeated)Resistance Activity : Activating Unique Enzymatic Pathways !



Benefits for Type 2 Diabetes of Interrupting Prolonged Sitting With Brief Bouts of Light Walking or Simple Resistance Activities(Diabetes Care 2016 Jun; 39(6): 964-972)

Food : The Final Frontier in Diabetes Reversal

When diet is wrong
medicine is of no use;
When diet is correct
medicine is of no need.

~Ayurvedic Proverb

HOW LOSING WEIGHT CAN REVERSE DIABETES

This was deduced from a study conducted between July 25, 2014, and August 5, 2017, among 298 people aged 20-65 and diagnosed with the disease in the past six years

149 were put on **weight management programme**. Anti-diabetic and blood pressure lowering drugs were all stopped at the start of it. The rest continued with best practice care, including medication

3-step programme

Step I
Low-calorie formula diet (825-853 calories daily) for **3-5 months**

Step II
Stepped food introduction **(2-8 weeks)**

Step III
Ongoing support for weight loss maintenance with strategies to increase physical activity

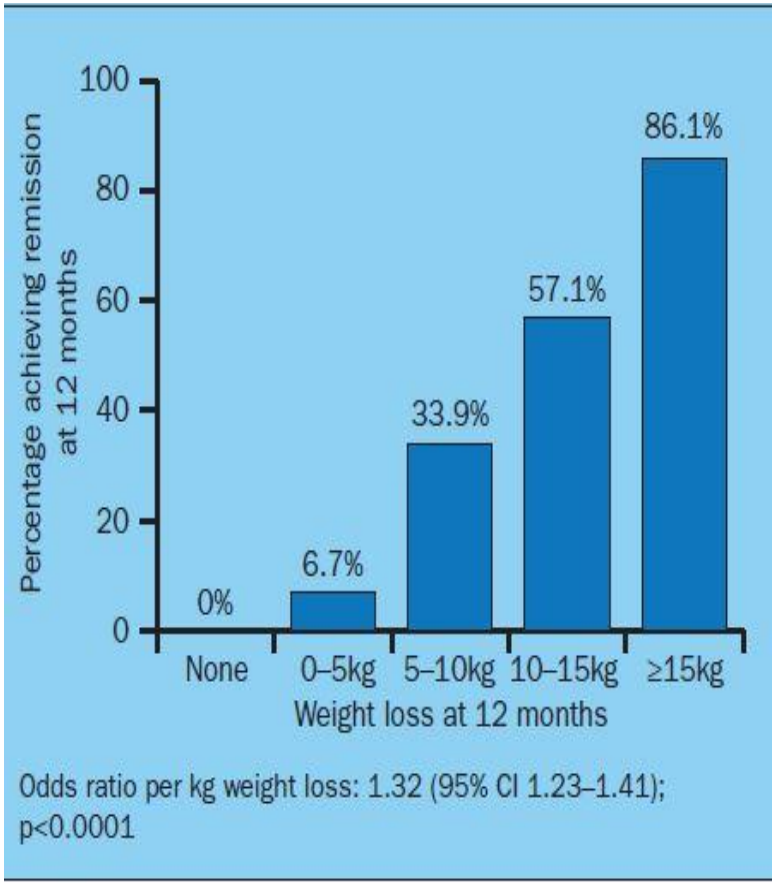
A year later

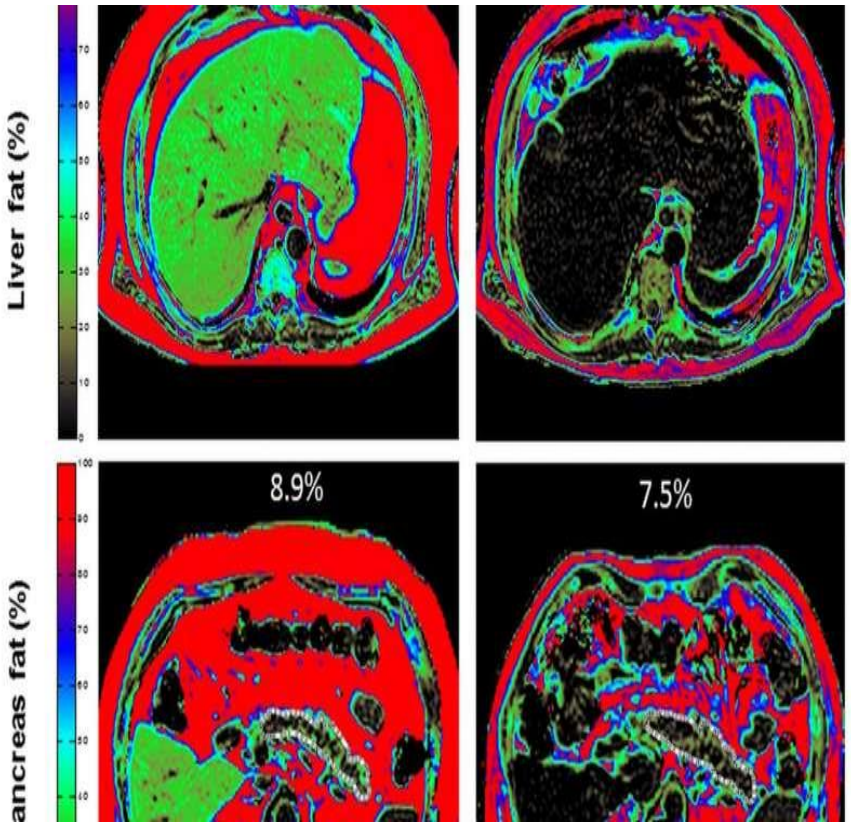
46% of participants who lost weight significantly didn't have diabetes—the highest in those who lost over 15 kilos

The Diabetes Remission Clinical Trial reported return and persistence of non-diabetic blood glucose control in **46%** of people with type 2 diabetes of up to 6 years duration.

LANCET;Volume 391,541-551, February 10, 2018

Weight Loss + Fat (Liver/Pancreas) Loss =Diabetes Remission





Primary care-led weight management for remission of type 2 diabetes (DiRECT): an open-label, cluster-randomised trial

LANCET; Volume 391,541-551, February 10, 2018

Eating Fat to Eliminate Fat (& diabetes)!

	Diet Type (per 2000 kcal)	Carbs (g)	Protein (g)	Serum BOHB (mM)*
Indian Standard Diet(!)	High carb, low fat	300 **(60% or more)**	75	0.05
ADA standard (!)	Mediterranean	200 **(50%)**	100	0.1
	Paleo	100	150	0.2 – 0.3
Fat approx .160 gm	**Well-formulated ketogenic diet**	**35 (!) 7%)**	100	1.0 – 3.0
	Total starvation (fasting > 7 days)	0	0	4.0 – 7.0

Hallberg SJ, McKenzie AL, Williams PT, et al. Effectiveness and safety of a novel care model for the management of type 2 diabetes at 1 year: an open-label, non-randomized, controlled study. Diabetes Ther. 2018;9:583-612

Eating Fat to Eliminate Fat (& diabetes)!

- 349 adults with T2D enrolled: Intervention = 262. 92% obese/ Control: n = 87, 82% obese, DM duration 8 years
- HbA1c declined from (7.6 ± 0.09% to 6.3 ± 0.07%, P < 1.0),
- Weight declined **13.8 ± 0.71 kg** (P < 1.0)
- **T2D medication prescription** other than metformin **declined** from 56.9 ± 3.1% to 29.7 ± 3.0% (P < 1.0).
- **Insulin** therapy(30%) was reduced or eliminated **in 94%**
- **Sulfonylureas were entirely eliminated**
- No adverse events were attributed to the CCI.
- **hsCRP – (-) 39% (P< 1.0)**
- **Triglycerides - (-) 24% (P < 1.0)**
- **HDL-cholesterol - (+) 18% (P < 1.0)**
- LDL-cholesterol (+) 10% (P = 5.1)
- **Serum creatinine and liver enzymes (ALT, AST, and ALP) declined (P ≤ 0.0001),** and apolipoprotein B was unchanged (P = 0.37).
- CONTROL participants had no significant changes in biomarkers or T2D medication prescription at 1 year.

Hallberg SJ, McKenzie AL, Williams PT, et al. Effectiveness and safety of a novel care model for the management of type 2 diabetes at 1 year: an open-label, non-randomized, controlled study. Diabetes Ther. 2018;9:583-612

J Nat Sci Biol Med. 2017 Jan-Jun; 8(1): 60–63.

High rates of diabetes reversal in newly diagnosed Asian Indian young adults with type 2 diabetes mellitus with intensive lifestyle therapy

Vijaya Sarathi, Anish Kolly, H. B. Chaithanya, and C. S. Dwarakanath

Department of Endocrinology, Vydehi Institute of Medical Sciences and Research Center, Bengaluru, Karnataka, India

	Baseline	3 months	1 year	2 years
Fasting plasma glucose (mg/dl)	223.78±52.56	99.31±14.26	100.53±14.64	94.71±9.59
Postprandial plasma glucose (mg/dl)	345.37±67.24	133.12±25.19	135.59±13.45	140.31±18.87
Glycated hemoglobin %	10.6±1.5	6.1±0.3	5.9±0.4	5.9±0.5
Drugs (no drugs/metformin/insulin/ metformin + dipeptidyl peptidase 4 inhibitors)	4/25/3/0	24/6/0/2	24/6/0/2	22/8/0/2
Weight (kg)	73.84±9.25	68.87±8.8	67.28±6.32	66.18±5.91

	Reversal (*n*=24)	No reversal (*n*=8)	*P*
Age (years)	24.83±3.34	25.37±2.82	0.66
Fasting plasma glucose (mg/dl) at diagnosis	222.84±57.42	225.9±36.9	0.839
Postprandial plasma glucose (mg/dl) at diagnosis	338.22±73.08	366.48±41.94	0.193
Glycated hemoglobin % at diagnosis	10.7±1.3	10.6±0.9	0.897
Calorie intake (kcal) at diagnosis	2452.08±310.86	2358.75±299.87	0.464
Calorie intake (kcal) at 3 months	1339.58±178.65	1785.75±228.89	0.003
Change in calorie intake (kcal) at 3 months	1112.50±257.67	450.00±68.11	<0.001
Weight (kg) at diagnosis	76.75±10.15	72.87±14.71	0.5
Weight (kg) at 3 months	69.33±10.4	67.62±13.62	0.7
Change in weight (kg) at 3 months	7.41±2.1	4.25±1.16	<0.001

FMD (fasting Mimicking Diet)

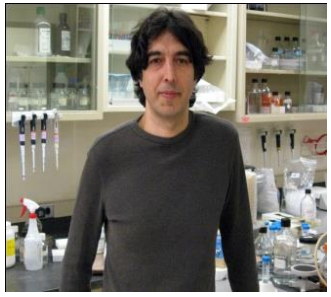
USC Diet : Stem Cell Activation

Day 1 : 1000 calories ; Day 2-5 : 725 calories

Day 1: 10 to 16 calories per kg bodyweight, 10% protein, 56% fat, 34% carbs
Days 2 – 5: 7 to 11 calories per kg bodyweight, 9% protein, 44% fat, 47% carbs

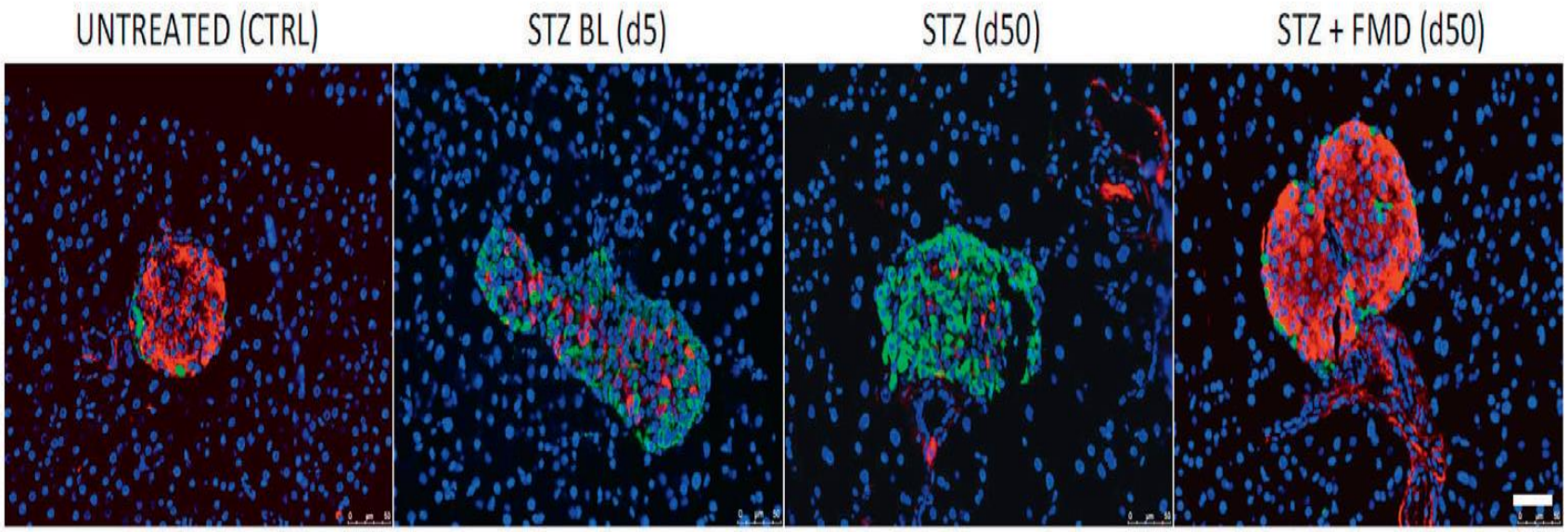
for 5 days

At least four times a year



Valter Longo
Director of the
USC Longevity Institute

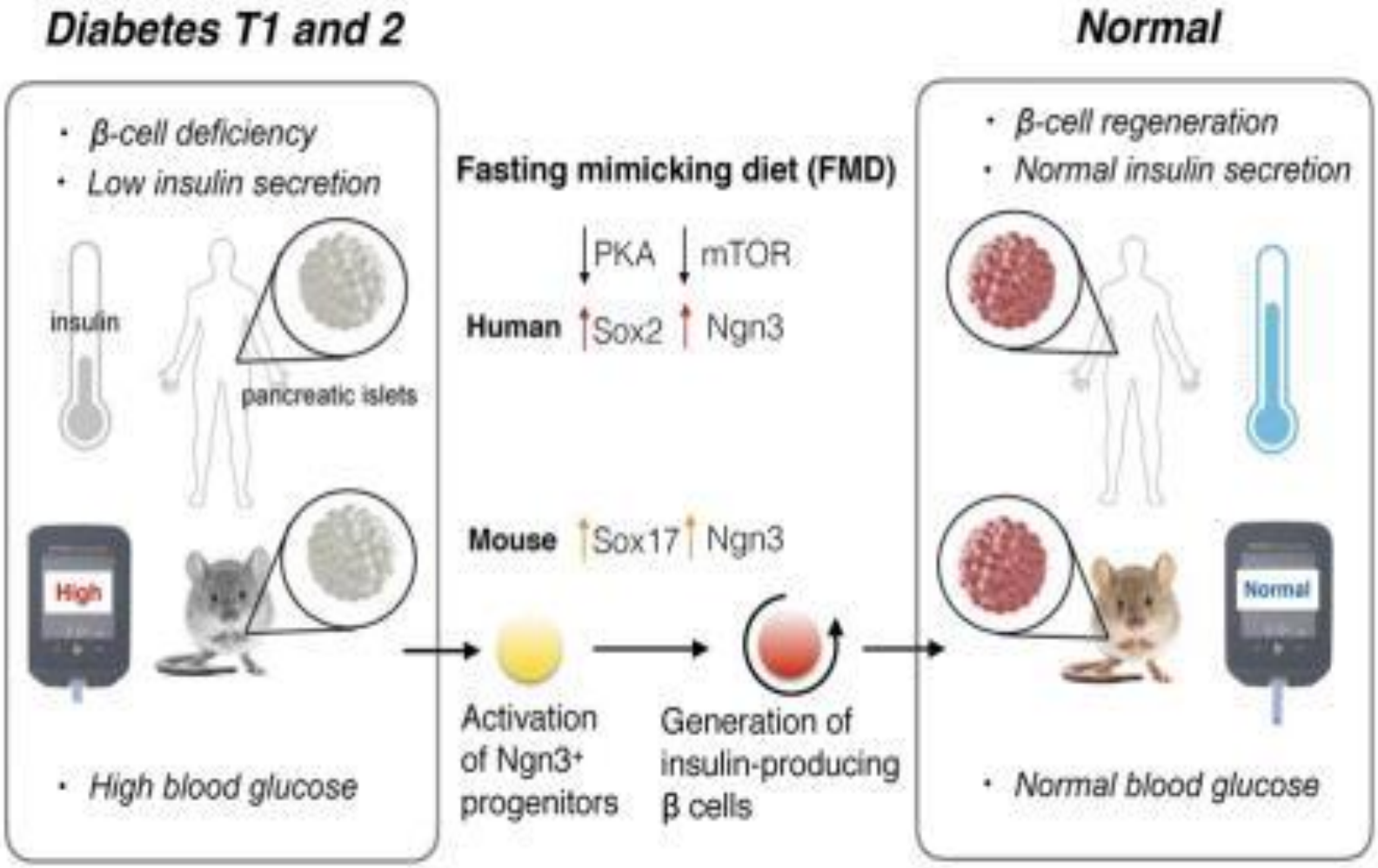
Mild Ketosis : Diabetes Reversal



(FMD= Fasting Mimicking Diet)

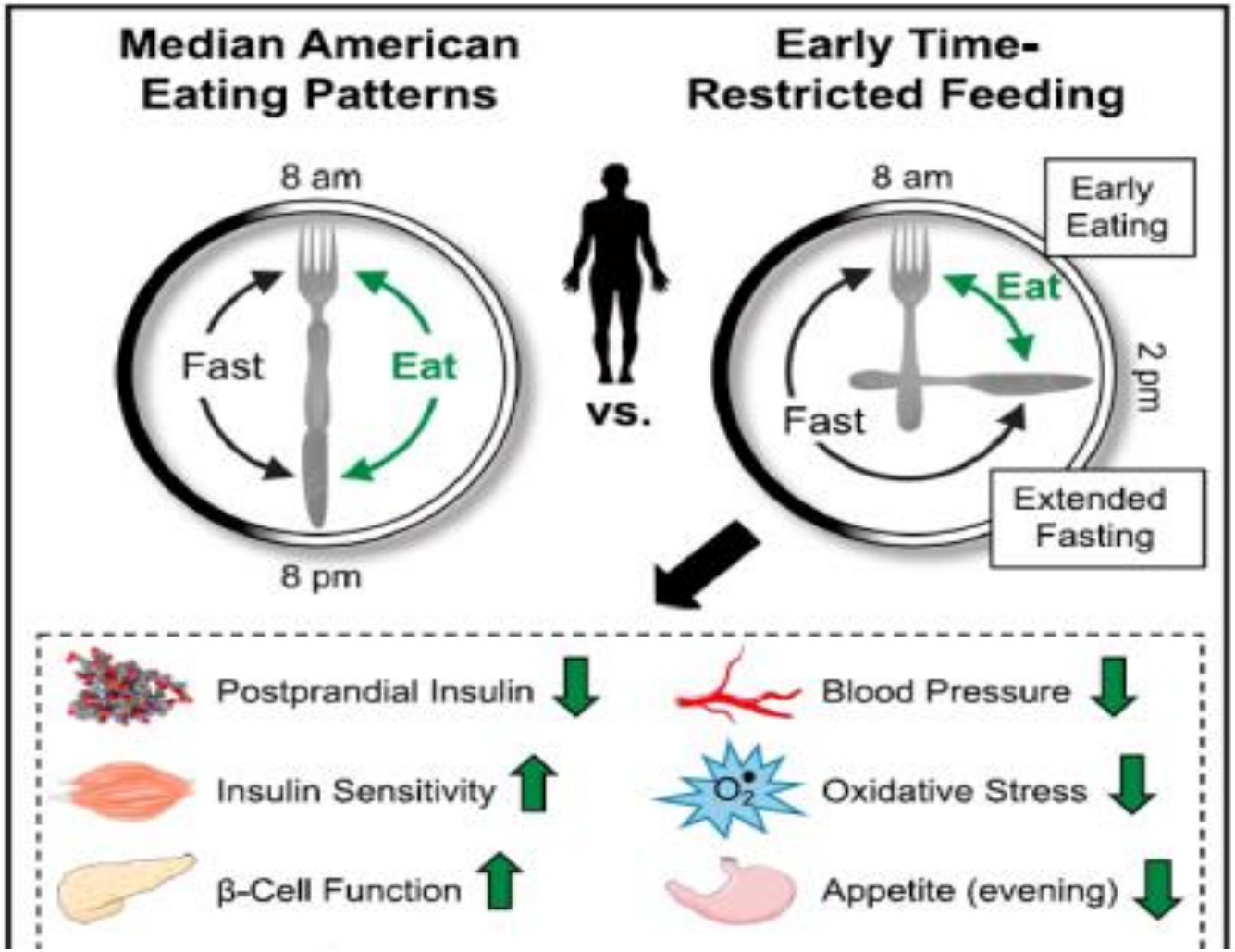
Fasting-Mimicking Diet Promotes Ngn3-Driven β-Cell Regeneration to Reverse Diabetes
CELL ; Volume 168, ISSUE 5, P775-788.e12, February 23, 2017

Mild Ketosis : Stem Cell Activation



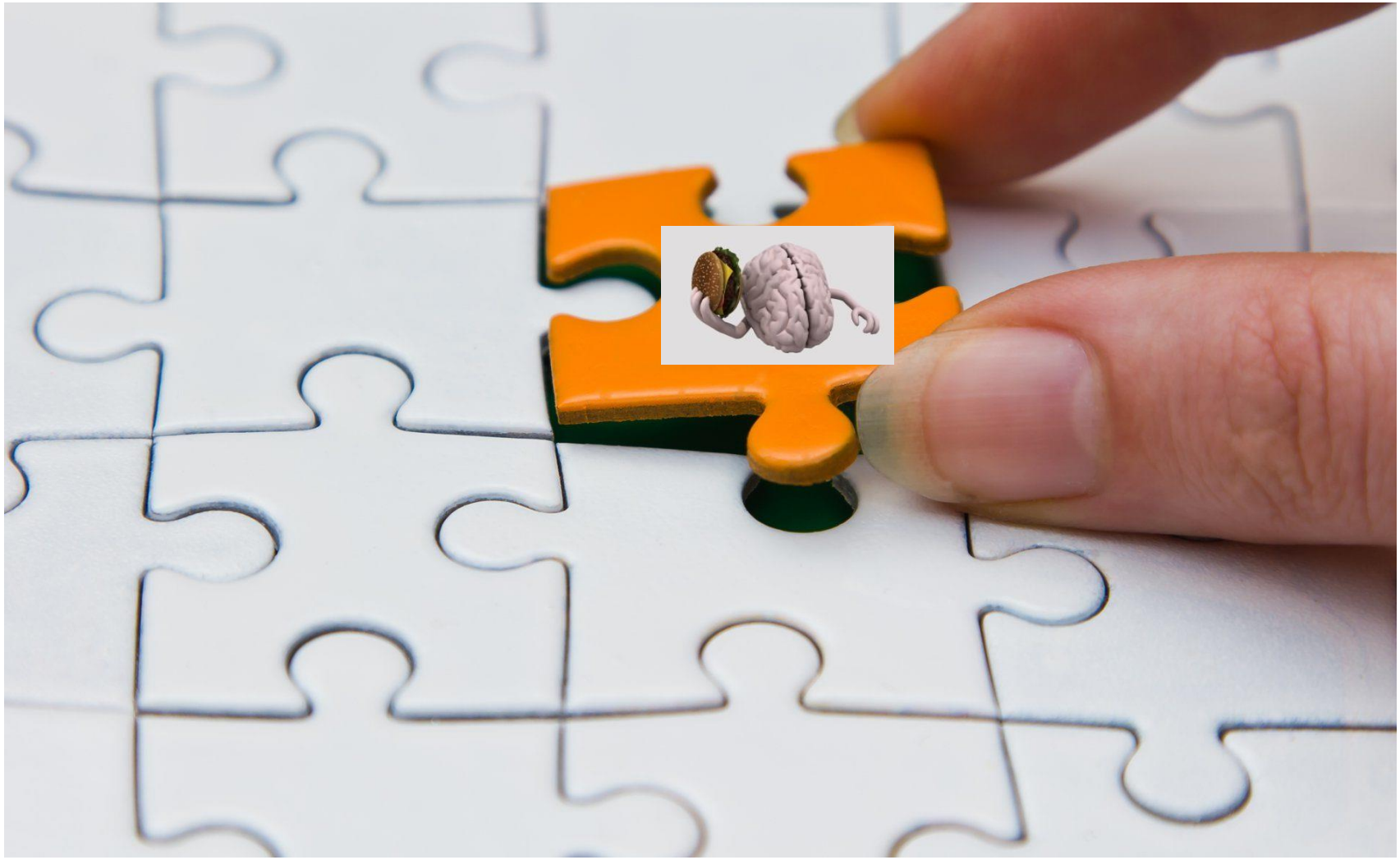
Fasting-Mimicking Diet Promotes Ngn3-Driven β-Cell Regeneration to Reverse Diabetes
CELL ; Volume 168, ISSUE 5, P775-788.e12, February 23, 2017

Time Restricted Eating : Beta Cell activation



Early Time-Restricted Feeding Improves Insulin Sensitivity, Blood Pressure, and Oxidative Stress Even without Weight Loss in Men with Prediabetes(May 10, 2018; Cell Metabolism)

You can offer Beta Cell Activation to your patients BUT…….

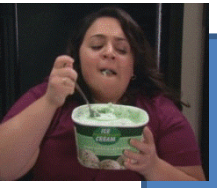


Beta Cell Activation=Diabetes Reversal=Significant Lifestyle Changes=Ensuring Adherence= Making Your Patients Like the Lifestyle Changes

- **Brain** is the most selfish organ in the body(& it is the most powerful one also!)
- Even slightest uncertainty in environmental stimuli can propel brain to induce a state which is conducive to diabetes (& inflammation & endothelial dysfunction & atherosclerosis) so that it quenches the thirst of brain for energy (glucose)
- Problem of nonadherence is a NEUROLOGICAL state & not psychological
- Willpower(& traditional patient education) can not solve nonadherence
- **Bio-behavioral interventions** can modulate brain state to implement strategies of Beta Cell Activation

1.Uncertainty and stress: Why it causes diseases and how it is mastered by the brain ;Progress in Neurobiology 156 (2017) 164–188
2.International Journal of Obesity (2015) 39, 1188–1196
3.How Should We Think About the Role of the Brain in Glucose Homeostasis and Diabetes? ;Diabetes 2017 Jul; 66(7): 1758-1765

Blueprint of Beta Cells Activation



1.VLCD (2-12 weeks)
2.Well formulated KETO diet
3.LCD
4. Carb Cycling (low to moderate)

---

4. FMD (5 days/3 months)

Time Restricted Eating
-*-*-*-*-*-*-*-*-*-

→10% weight loss
→Fat loss from liver & pancreas
→Prolonged or intermittent mild ketosis

1. Combination of Beta Cell preserving drugs
2. GABA

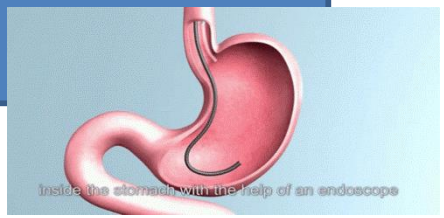
Phytochemicals

Bio-Behavioral Manipulation

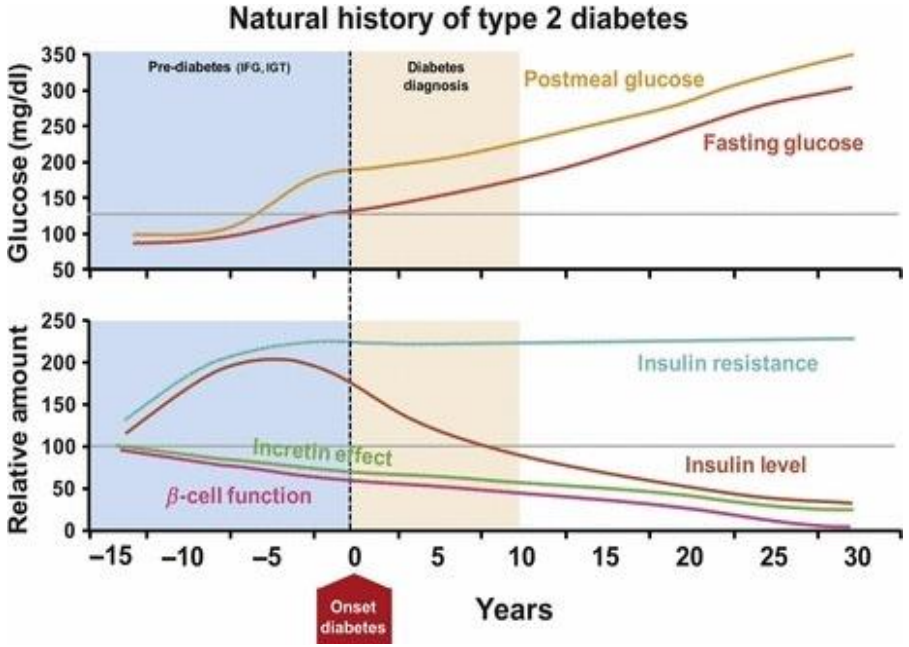
1. Interval training
2. Endurance exercise with periodic weight training
3. Short Resistance Activity

Coupled with low carb diet
(Protein & fat before exercise /daily carb <150 gm

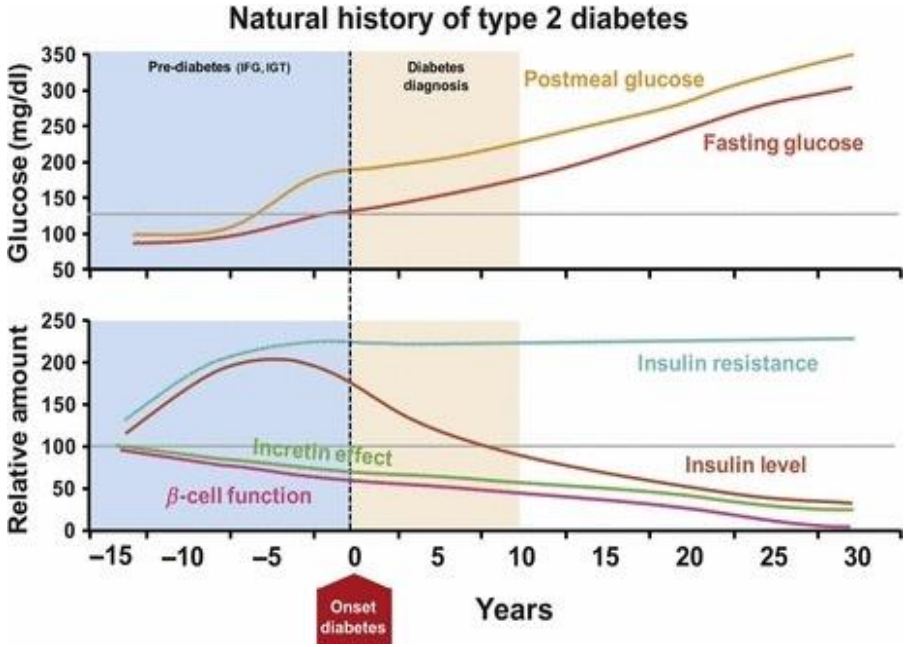
Bariatric Procedures



Do You Still Think Diabetes is Characterized by Relentless Progression of Beta Cell Dysfunction in All Patients?



Your Message to Patients?!



Thank You….