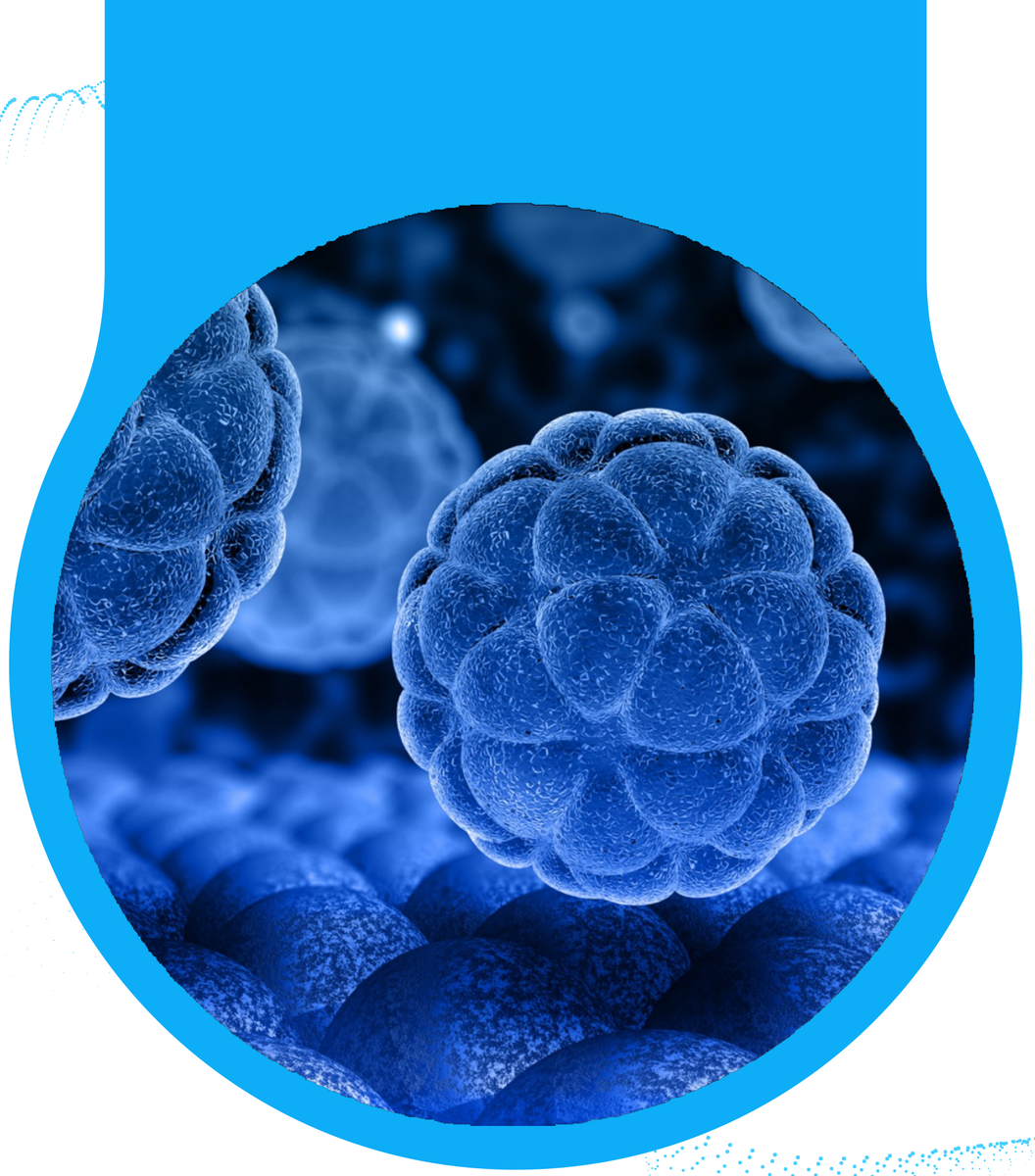
Med Masters Discussion on Body Composition

PROJECT Y
BIOTECH

Disclaimer

This presentation and the information contained within are not meant to provide any sort of instruction, medical indication or application, or constitute legal advice. We are not attorneys so please always consult your attorney for advice on all things related to running your business.

The topics contained herein are presented in overview format and are designed for discussion. This will assume a base-level knowledge of cellular biology and energy systems.



Agenda

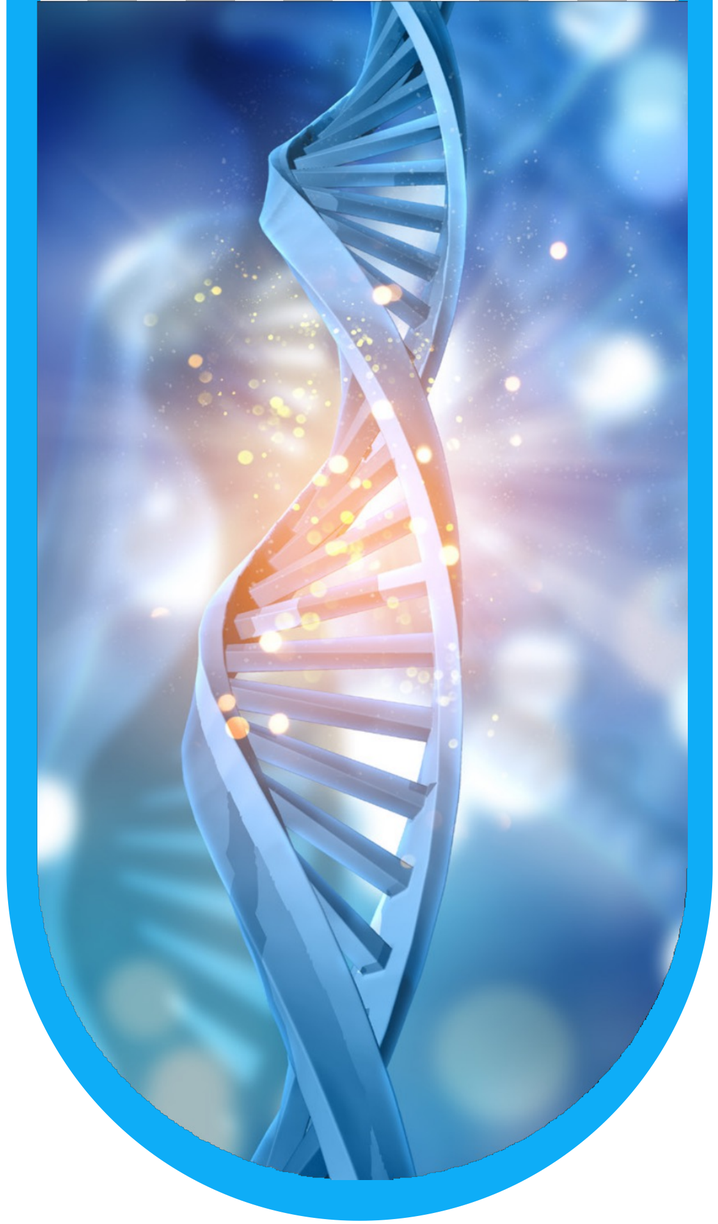
01 Shift from Weight Loss to Body Composition
- GLP-1 RA review
- Importance of lean mass
- Metabolic Syndrome

02 Energy Systems
- Phosphagen
- Glycolysis
- Aerobic

03 Peptides Related to Body Comp
- Anti-catabolic
- MDP’s
- Notable mentions

Goals of Body Composition Programs

If your "life-span" is relative to anti-aging and super longevity, then your "health-span" could be viewed as relative to your quality of life over time. Body composition is integral for both of these goals.



Quality AND Quantity

Life-span doesn't sound as appealing when you consider the potential of some duration of that time being spent enduring pain, disease, and other complications. With a proper understanding of your available toolkit and execution of a personalized strategy, you and your patients can plan for immediate performance enhancement, long-term vitality, and everything in between.

Shifting from Weight Loss to Body Comp

GLP-1 RA (GLP-1/GIP; GLP-1/GIP/Glucagon…etc)

- GLP-1 qualification (per insurance) is BMI of +30 or +27 with a co-morbidity (like type 2 diabetes)
- BMI is useless and often counter-productive when considering a body composition program
  - BMI = weight in kg divided by height in meters sq (kg/m2)
  - More effective methods for assessing fat versus lean mass would be
    - Calipers
    - Bio-electrical impedance
    - Hydrostatic Weigh
    - DEXA

Weight Loss to Body Comp cont'd

GLP-1 RA's simply eliminate hunger

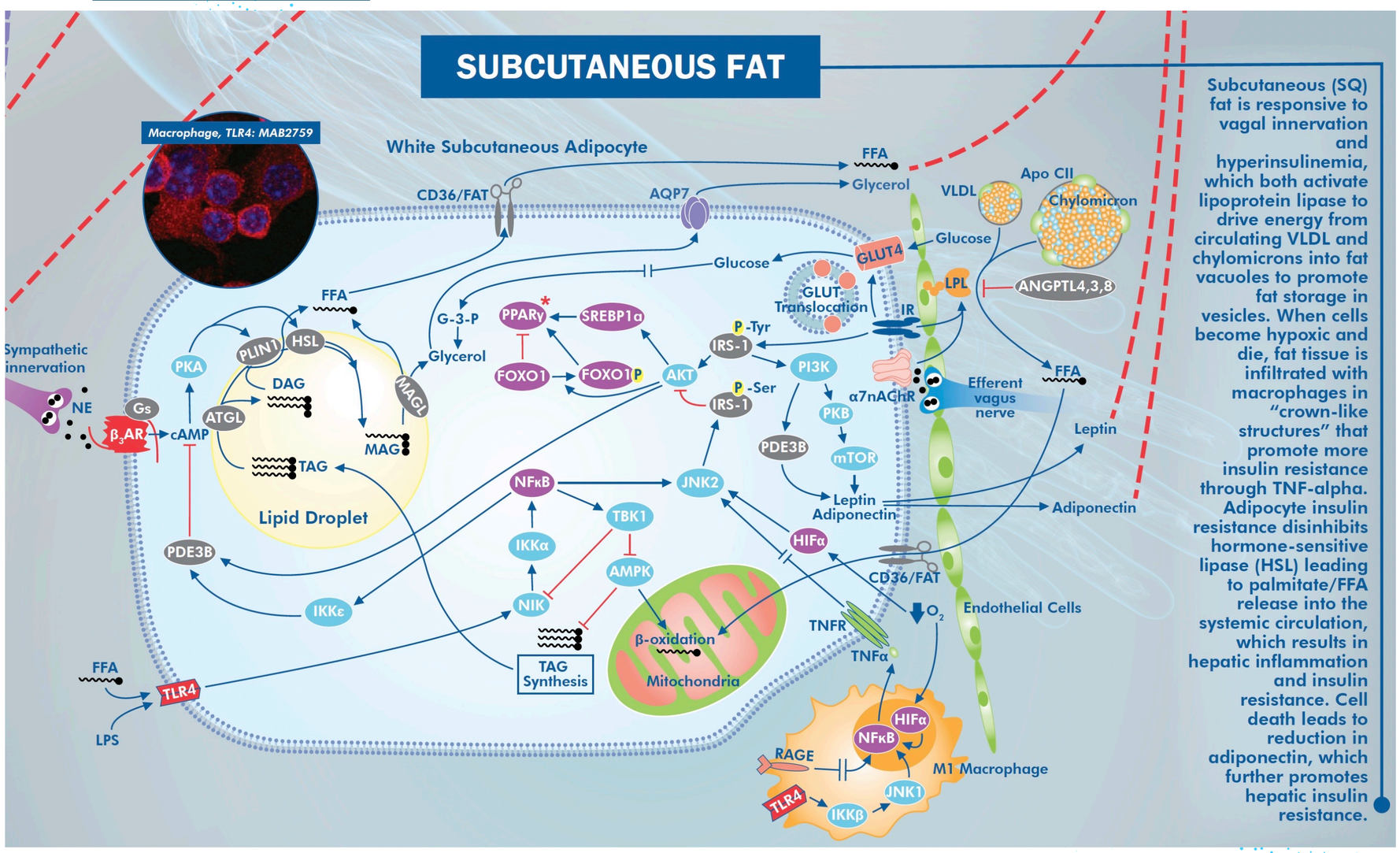
- GLP-1 activates POMC/CART neurons and indirectly inhibits NPY/AgRP neurons, ***which can reduce food intake. GLP-1 receptor agonists (GLP-1RAs) can also influence brain regions that regulate feeding, such as reward centers***.
  - Stimulate the pancreas to release insulin from b cells, which **regulates blood sugar**. It suppresses glucagon secretion from a-cells
    - Useful for type 2, not so much for type 1
    - Type 2 often can go hand in hand with "lack of commitment to a program." Afterall, you can handle type 2 diabetes on your own with the right will power
  - Slows digestion by reducing gastric emptying, decreasing blood sugar spikes and increases "feelings of fullness"
    - Insulin spiking is also a storage mechanism for the body, so preventing this is ideal for reducing the transition of caloric intake to stored fat

Weight Loss to Body Comp cont'd

When you stop eating…

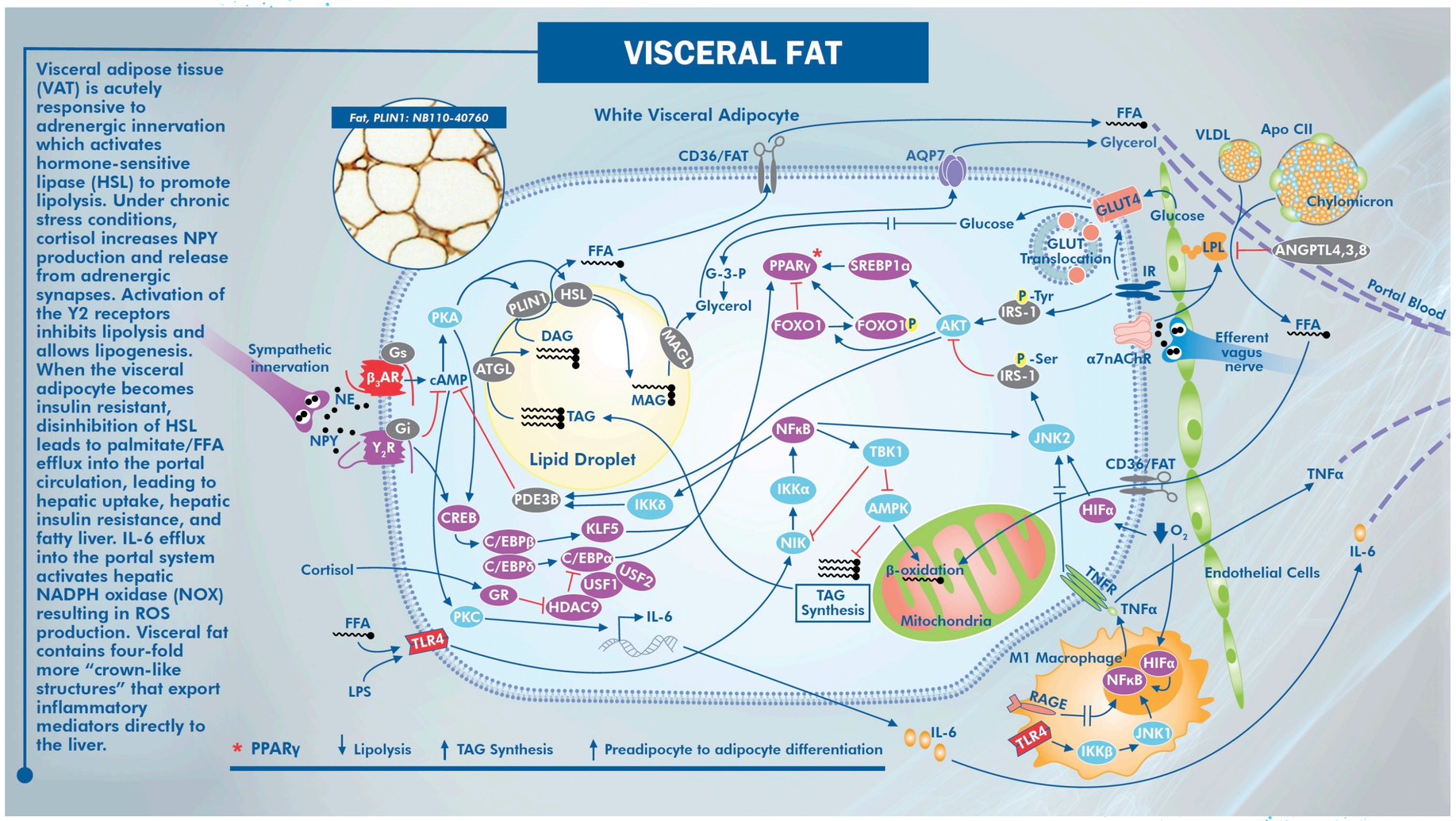
- Reduced caloric intake below your daily expenditure (BMR + Output) results in weight loss, however, **it is non-specific**
- Muscle is easier to metabolize than fat. Fat is a protective storage mechanism and there are genetic/ancestral reasons for holding on to fat storage
  - Dieting below caloric requirements will result in a catabolic state without supplementation and/or resistance training
- Without focusing on lipolytic and anti-catabolic augmentation, you risk losing significant muscle mass
  - Ozempic butt
  - Ozempic face
  - Osteoporosis
  - Reduced metabolic output
  - Instability
  - Fatigue
  - Etc…

Subcutaneous Fat



- Most commonly discussed and visible
- Hips, thighs, belly, butt
- Genetic pre-disposition to preferred storage locations (love handles versus inner thighs)

VISCERAL FAT



- Surrounding organs, very dangerous
- Capable of secreting pro-inflammatory cytokines and chemoattractant molecules that attract and reprogram immune cells to an inflammatory phenotype, further exacerbating inflammation
- Contributes to the development of atherosclerosis and metabolic syndrome.
- Typically visceral fat builds up once sub-cutaneous storage is exceeded. This is another genetic variable that can also be influenced

Metabolic Syndrome

- **Metabolic Syndrome**: Cumulative effects of linking ectopic fat storage, inflammation, insulin resistance, and liver dysfunction with defective lipid and glucose trafficking.
  - Common resultant disease states are Type 2 diabetes, non-alcoholic fatty liver disease, and cardiovascular disease.
  - Metabolic syndrome, in turn, increases the risk of cancer, neurodegeneration, and other diseases
- Three drivers of metabolic syndrome are subcutaneous fat (obesity), visceral fat (stress), and hepatic fat (dietary)

Lean Mass

- Muscle mass naturally fades with age, resulting in higher fall risk and all cause mortality
- Muscle naturally shunts glucose from the bloodstream, improving overall metabolic health
- Muscle requires more calories to maintain, which is another metabolic rate factor
- Resistance training provides an *elevated metabolic rate* for longer than cardio (post-exercise)
- Resistance exercise triggers AMPK
- Resistance training helps improve bone density (reducing frailty)
- Ideally, you do both because cardio training has its own benefits as well
  - VO2 max is difficult to improve without combining training styles
  - VO2 max is a great indicator of health and longevity

Unpopular Opinion: Resistance training is *more impactful* than cardio for weight loss and longevity

Energy systems – Phosphagen

- Phosphagen System
  - ATP-CP (Adenosine triphosphate – Creatine Phosphate)
  - CP is stored in skeletal muscles. It donates a phosphate to ADP to make ATP.
  - ATP: ADP + CP = ATP + C
  - No carbs/fats used
  - Anaerobic
  - 10 seconds of all out expenditure, rapid fatigue

Energy systems – Glycolysis

- Blood sugar or muscle glycogen (stored glucose) forms pyruvate
- Blood sugar is used before glycogen, since it doesn't require glycogenolysis
  - No need to access storage when it's readily available in the blood
- One molecule of broken down glucose makes two molecules ATP
- Pyruvate either becomes lactate (muscle cramp), or acetyl CoA (mitochondrial production of more ATP)
  - Lactate wins out when the need for oxygen is greater than the supply, such as during anaerobic exercise)
  - Lactate reduces pH, which then acts through negative feedback to inhibit ATP production
  - Think about "aiming for 120 BPM during extended fat-specific exercise"

Energy systems – Aerobic Pathway

- Slowest, but most efficient access to ATP
- Requires oxygen
- Krebs cycle – Electron Transport Chain – Mitochondrial Respiration
- Carbohydrates – glucose and glycogen via glycolysis – pyruvate – acetyl CoA – Krebs cycle – electron transport chain – ATP and water are produced
  - Oxidative Phosphorylation produces **36 ATP per every molecule of glucose**
- Fat metabolism compared to glucose and glycogen:
  - Triglycerides – free fatty acids and glycerol (lipolysis) – long chain carbon atoms (triglycerides) are transported to mitochondria to produce acetyl-CoA (beta oxidation). Then Krebs cycle and same process as above
  - **Accessing stored fat for energy is NOT the most immediate source of energy and must be accessed strategically, especially in people who are not accustomed to engaging these energy production pathways!**
  - Analogy:
    - Old carbureted engine at altitude with 87 octane and dirty fuel injectors. A/F ratio will be off, spark may not ignite properly, misfires, inefficient use of fuel, low output and inefficient conversion of fuel to energy
    - New fuel injected engine, proper tune for exact delivery of fuel and air, 93 octane, higher output and more efficient conversion of fuel to energy

PEPTIDES RELATED TO BODY COMP

AOD 9604

- Last 15 amino acids in human growth hormone
- Lipolytic activity for more specificity than pure “weight loss”
- No concerns of chromosomal aberration or genotoxic activity
- No adverse effects on insulin sensitivity (compared to HGH and the chain reaction related to IGF)
- Non dose-respondent

PEPTIDES RELATED TO BODY COMP

Tesamorelin/Ipamorelin

- GHRH (pituitary) and GHRP (grehlin) combo
  - No secretion of ACTH (adrenocorticotropic hormone) or Cortisol (stress hormone, fat storage, catabolic)
- Hypothalamus sends GHRH to the anterior pituitary to release HGH, as well as somatostatin which is an HGH inhibitor (this is how the body stays in balance, and why exogenous HGH supplementation is dose-respondent)
- HGH in turn signals the release of IGF-1, which has it's own negative feedback loop to prevent additional HGH release
  - Natural pulsatile release of HGH throughout the day and night
- Ipamorelin has a low propensity to increase hunger compared to other GHRP's
  - Even less when added to a GLP-1RA regimen
- Ipamorelin was originally developed by Novo Nordisk
- Tesamorelin is FDA Approved for visceral adipose reduction in AIDS and HIV patients
  - Largely misrepresented need for high dosing based on this approval

Mitochondrial Derived Peptides (MDP's)

Humanin

- Discovered when screening for proteins that have a protective effect against amyloid-b (arguably the leading marker for Alzheimer's and potentially impactful for other type-3 diabetes/neurodegenerative disease states)
- Anti-apoptotic effects
- Increases glucose-stimulated insulin release
  - improving metabolism and subsequently improving body composition
  - Shuttles glucose out of the cell to be used for energy more efficiently
- Can protect against Ischaemia-reperfusion injury through decreasing the generation of reactive oxygen species
- Humanin activates the receptor site that is responsible for activating Janus kinase (JAK). Therefore it would follow that anyone on a JAK inhibitor for rheumatic conditions should use caution with Humanin and perhaps avoid altogether, as this JAK STAT excitation could exacerbate the condition being treated

Mitochondrial Derived Peptides (MDP's)

Mots-C

SHLP (small Humanin-like Peptide)

- Promotes AMPK activation (biggest difference from Humanin)
  - Balances nutrient supply with energy demand
  - Important therapeutic agent for controlling metabolic syndrome, type 2 diabetes, obesity, cancer, etc.
  - AMPK maintains the balance between anabolic and catabolic programs for homeostasis under stress
  - AMPK mediates tumor suppressor effects of LKB! (upstream kinase); supports findings of other AMPK activating drugs like metformin
- GLUT4 expression in skeletal muscles
  - Glucose Transporter 4
  - Transmembrane protein moving glucose across the cell membrane
- Increased respiratory exchange ratio = increased glucose utilization (increased metabolic rate)
- Reduced hepatic lipid accumulation (fatty liver disease)
- Mainly acts on the Folate-AICAR-AMPK pathway, regulating energy metabolism, insulin resistance, inflammatory response, brown adipose tissue activation, muscular exercise, neuronal protection, and age-related pathologies
- Mots-C is newer and still being studied to understand various functions and mechanisms of action

Notable Considerations

MK-677 (Ibutamoren)

- GHRP-1 derived just like Ipamorelin, but has a **pronounced** effect on hunger activation
- Excellent for muscle building, not ideal for weight loss/body comp program due to increased appetite
- Orally available for easy dosing adjustments and cadence preferences
- Reasonably low side effect profile considering it is an oral
- Good amount of supporting data, well known in the bodybuilding community

Notable Considerations

IGF-1 LR3

- Extended half life compared to IGF-1
- Exogenous IGF supplementation will override negative feedback loop
  - Same concept as TRT versus HCG; HGH vs GHRH/GHRP etc
- Significant improvement in anabolic environment for muscle hypertrophy
- High likelihood of storing excess calories (it's insulin after all)
- Ideally this is only used by advanced-level consumers and practitioners
  - Risks of incorrect administration are high
  - Short cycles with strategic diet, exercise, and

Notable Considerations

BPC-157

- Not directly related to anabolic or anti-catabolic states
- Allows for improved blood flow, reduced inflammation, and transient tissue healing properties (which are best realized when combined with TB4)
  - Remodeling, reducing scar tissue. This is why the gut doesn't have scar tissue!
- Analogy of creatine supplementation used to reduce the number of steps required for cells to regenerate ATP; BPC doesn't "build muscle" any more than creatine "generates ATP." But they both allow these end goals to be achieved faster by reducing the down time between regeneration.
- **Cell proliferation of cultured tendon fibroblasts not directly related to BPC157 as evaluated by MTT assay. However the SURVIVAL of BPC157 treated cells was significantly increased under H_2O_2 stress**

Q&A

CITATIONS

https://physoc.onlinelibrary.wiley.com/doi/epdf/10.1113/JP274472

https://www.ncbi.nlm.nih.gov/books/NBK534267/

https://www.ideafit.com/personal-training/the-three-metabolic-energy-systems/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4487780/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7672939/

https://translational-medicine.biomedcentral.com/articles/10.1186/s12967-023-03885-2#:~:text=Activated%20MOTS%2Dc%20mainly%20acts,aging%20and%20aging%2Drelated%20pathologies.

https://www.transformyou.com/blog/what-is-the-connection-between-igf-1-and-hgh

https://my.clevelandclinic.org/health/articles/23309-human-growth-hormone-hgh

https://www.peptides.org/mk-677-vs-ipamorelin/

https://jofem.org/index.php/jofem/article/view/213/278

https://pubmed.ncbi.nlm.nih.gov/11146367/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4855276/

PROJECT Y
BIOTECH

THANK YOU!

This presentation has not been reviewed or approved by the FDA or any state or federal governing body. It is for informational purposes only and does not constitute the legal opinion of any company mentioned. This is not intended to be used as medical or legal advice.