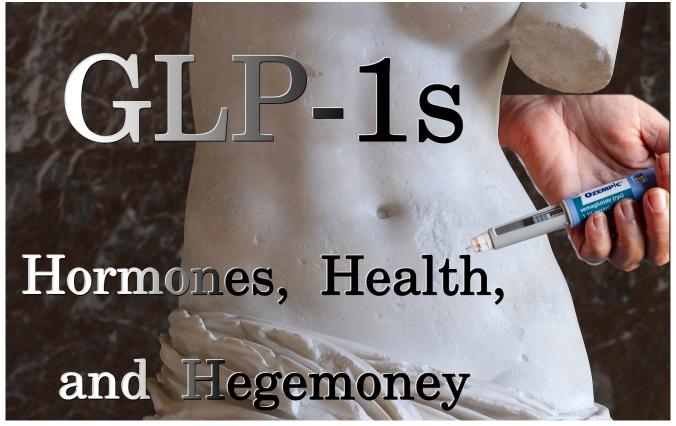


# What are GLP-1s?



On Hormones, Health, and Hegemony

What are GLP-1s? Maybe they stand for "God Loves Pharmaceuticals"? Seriously it's "Glucagon Like Peptide", but what does that even mean? For many Americans getting swept up in the new weight loss phenomenon borne of the Western pharmaceutical industry, this can be a lot to take in. And not all of it is self-explanatory: We hear that this miraculous drug, injected monthly, causes serious reduction of blood sugar levels in those suffering from type 2 diabetes. But applications go even further, as people struggling with weight loss can experience reduced appetite and lose weight with this same drug. And then it goes even further than that, with some saying this drug can cure non-food based addictions such as alcohol use disorder. Some anecdotal cases can be found online describing GLP-1 patients having spontaneous recoveries from back problems, no longer requiring spinal surgery, thanks to these drugs.

But where does the truth begin and the misinformation of the internet end? Without knowledge of what these drugs and medical conditions are and how they work it can be hard to reason through such claims. This is exactly the kind of reasonable background that so many Americans need to stay

empowered in these public discussions and avoid being manipulated by various forces at play. In this article we hope to do exactly that by giving a very accessible overview of GLP-1s, allowing for a common-sense approach to be then applied. This summary has been researched and presented by properly informed scientists, and providing citations and data to support all claims presented. If you have more of an arts background than science, that is perfectly okay: In fact, we have used one of Shakespeare's famous work as an analogy to help reach across the aisle and make this content relatable to the widest possible range of people.

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#### REGULATION AND POLITICAL CLIMATE

Although we would like to keep everything politically neutral and more scientific and medical in orientation, the current political leadership of the country has a big effect on the pharmaceutical industry through many agencies, particularly the Food and Drug Administration (FDA). The FDA's commissioner is currently Dr Martin Makary, he reports to the Secretary of Health and Human Services, Robert F. Kennedy Jr, often called RFK Jr. for short. This is relevant because RFK is at the head of a populist movement called Make America Healthy Again (MAHA) that is calling for a wide range of reforms to the FDA and HHS more broadly. This movement not only effects government policy, but also public perception of the FDA and pharmaceutical companies in the US, particularly the perception of the trend toward "over-prescription" of medications in the US.



**Image01** – Diagram showing how RFK's "MAHA" movement is one of the pillars of the wider "Trumpism" phenomenon.

Without condemning or condoning, we believe that outlining what we see as possibly positive coming out of this movement and what is potentially negative is necessary in the interests of transparency. We do agree with many of the sentiments that drive this movement but we also disagree with many ideas and policies associated with it as well. Here is a quick pro-con breakdown:

## **Positive Ideas**

- Over Prescribing of Synthetic Medications
- FDA too friendly to Pharma / Corruption
- Synthetic Food Dyes Safety
- Synthetic Drugs Safety (Longitudinal)
- Psychedelic Medicine
- Cannabis Legalization

#### **Negative Ideas**

- Vaccine Skepticism
- "Seed Oil" Conspiracy
- Denial of Needed Medications (e.g. Anti-Depressants)
- Addiction / Rehabilitation Philosophy
- Fluoride / Pediatric Dental Health
- Bacteria / Coliforms / Pathogens
- Anti-Vegan Sentiments (beef tallow, etc)
- Anti-Science / No medical experience
- Recent Funding Cuts (NIH / NSF)

It is also important to note that the MAHA movement is a pillar of a larger political movement under Donald Trump. Although the authors have opinions about Trumpism and the MAGA movement, we feel that sharing them would distract from the goal of this article, which is to engage as wide a range of people in a discussion about the science and business of GLP-1s.

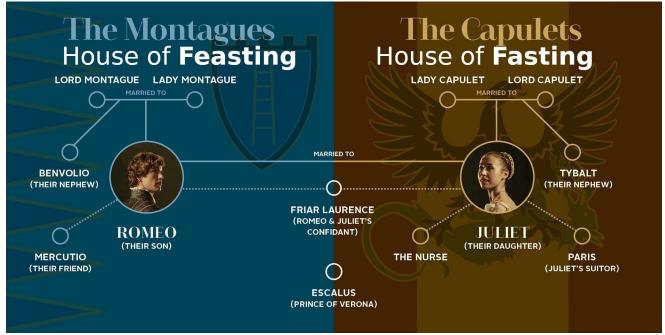
#### MEDICAL SCIENCE OF GLP-1

So now that a quick background of the current FDA leadership is covered, what are these GLP-1s? GLP-1 stands for Glucagon Like Peptide 1. This is an all-natural hormone made by human body that plays a role in regulating digestion and appetite. Technically, the drugs we are discussing are GLP-1RAs: GLP-1 Receptor Agonists. This means it "hits" the same receptor as the natural GLP-1 but is a distinct molecule / substance that is not natural, but engineered by medicinal chemists working under pharmaceutical companies.

The original GLP-1RA is called **semaglutide** brand named Ozempic, Wegovy, and Rybelsus. The newer alternative is **tirzepatide**, under brands Mounjaro and Zepbound. We will be looking at the business aspects of this later in this article, but first we will examine how these molecules work from a medical and scientific perspective. The business side is broken into <u>drug products</u>, <u>social dynamics</u>, and <u>economic forecast</u>, as it has its own complexity separate from the medical science aspects of these drugs.

To understand how it all works scientifically, we need to cover what GLP-1RAs do to the human body. But before we can do that we need to understand natural GLP-1. And yet, before we can do that we need to understand the blood sugar model and glucagon and insulin's role in that. Although this sounds like a lot to cover, it can be done rather quickly as these have a synergy that builds one upon another, like rungs of a ladder. To help make this as accessible as possible, we'll use a model of Montague-Capulet dynamic from Shakespeare.

The Montague-Capulet Dynamic is based on Shakespeare's Romeo & Juliet play about doomed star-crossed lovers. The important part here is that Insulin-Glucagon are going to be polar opposites, like the famous Verona noble merchant families, but in the regulation of blood sugar in human blood. The human body is ultimately controlling itself through systems that help maintain balance in part by directly opposing each other, part of the many negative feedback systems that contributes to **homeostasis**. This is precisely how Prince Escalus ruled Verona by keeping the two noble families in check and preventing either one from dominating city politics.

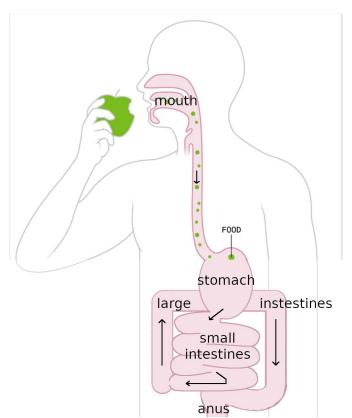


**Image02** – Diagram of the houses of Montague and Capulet and the inter-relationships of the characters.

To follow this analogy, insulin can be thought of as the "House of Feasting", which is stimulated when eating to store absorbed nutrients. The opposing force, glucagon, can be thought of as the "House of Fasting" because it is stimulated when nutrients need to be released from storage and used. How each of these "Noble Houses" exert their control over the body is a bit more complicated, but with an understanding of digestion and the associated blood sugar model, it will appear quite simple.

What is Digestion? Basic model is that we chew food into smaller pieces that we swallow. After that our bodies digest, absorb, and metabolize those foods. GI means **Gastrointestinal** and refers to entire digestive tract. A quick GI Overview can be very helpful here:

- Mouth: teeth → epiglottis → esophagus
- Stomach: pyloric sphincter
- Small Intestines: duodenum → ileum → jejunum
- Large Intestines or colon: ascending → transverse → descending → sigmoid
- Anus



**Image03** – Simplified diagram of the human digestive system. Notice how the illustration follows the bullet points above.

As we chew and swallow a rather intuitive and physical breaking down of large particles into smaller particles is occurring, and rather easy to internalize and comprehend. After this things get a little more complicated and require some understanding of chemistry.

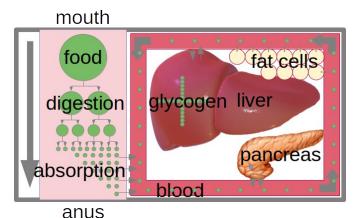
The stomach is largely responsible for breaking polymer chains down. This applies to carbohydrates and proteins, both of which are long chains of molecules called polymers that are made of small repeating units, called monomers. This bond holding the monomers together is typically a

dehydration bond and is broken by a water inserting reaction called hydrolysis. This reaction happens much faster in a strongly acidic environment, which is why the stomach is acidic.

After the stomach food is passed to the small intestines where the next and final breakdown occurs, after which the GI focuses entirely on absorption. Like the stomach breaks down polymer chains of both protein and carbohydrate nature, the intestines break down fat and oil droplets so they can be properly absorbed. This process, of breaking down oil and fat droplets, is called emulsification. This is done through bile salts and other compounds released from the biliary tree, which includes the liver, pancreas, and gallbladder. As they mix with the contents coming from the stomach, called chyme, they both neutralize the acidic pH and solubilize the fats and oils for absorption into the blood.

The rest of the GI, which includes the rest of the small intestines and the all of the large intestines, called the colon, is mostly about absorption. The monomers which were digested in the stomach together with the emulsified fats and oils all get absorbed in the small intestines, and the water invested in breaking down and dissolving these nutrients is largely re-absorbed in the large intestines, leaving only dietary fiber and compounds the body intends to remove through fecal matter, or biliary excretion. The function of water re-absorption at the end of the digestive tract is why most cases of diarrhea have a cause of large intestine dysfunction or inflammation.

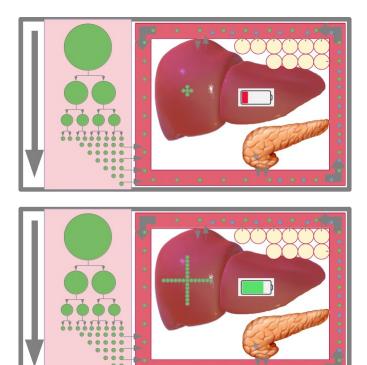
Now that we took a quick tour of the GI tract, from mouth to anus, we can examine "**The Blood Sugar Model**" which is where key concepts like blood sugar will begin to fall into place. This is modeled as glucose molecules in the blood, but it's more complex than that in real body with protein and fat playing key roles. We'll revisit this trichotomy between carbs, protein, and fats/oils later, but for now let's follow the glucose blood sugar model to understand the insulin-glucagon axis.



**Image04** – Diagram of the blood sugar model. This shows the physical GI tract on the left, with the blood stream flowing on the right. Key organs such as liver, pancreas, and fat cells are labeled.

This system will essentially follow those glucose molecules after they get absorbed by the small intestines into the blood. The liver will be acting as a storage facility for extra glucose, and the pancreas will act as an air traffic control tower, regulating movement up or down in terms of blood sugar. Fat cells, or adipocytes, play a role as a run-off storage when the liver is filled to the maximum amount it can hold.

In feasting (or feeding) the blood sugar is high and needs to be stored after a meal. High blood sugar triggers insulin to be released from the pancreas. Insulin causes blood sugar to be first stored in the liver, as glycogen. Insulin causes blood sugar to be secondarily stored in fat cells when the liver is full, where it is converted to fat. This is because fat has a much higher energy density than carbs and so is a better long term storage material, which will be further in the Peptides Section.



**Image05** – Diagram of the blood sugar model. This shows the body in a state of feasting, i.e. digesting food. A battery logo is used to indicate the relative amount of fuel stored in the liver as glycogen. Notice the release of insulin molecules into the blood from the pancreas in **blue**, signaling to the fat and liver to uptake glucose from the blood for storage.

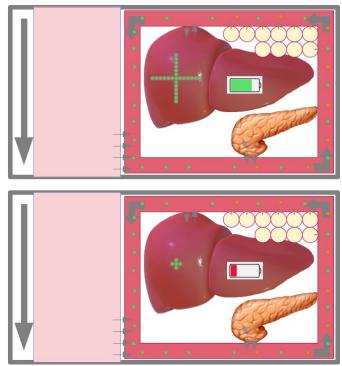
Constant overeating causes constant high insulin levels which lead to insulin resistance, also known as type 2 diabetes. By contrast, type 1 diabetes, typically diagnosed relatively soon after birth, is a genetic condition involving a loss of the pancreas cells that make insulin, called beta cells. Type 2 diabetes differs in that the body is still producing insulin, but the cells have developed a tolerance to it making it less able to store energy and regulate high blood sugar levels. Both have been treated with insulin injections but for type 1 diabetes the injections are much more effective than in type 2 diabetes where changes to diet and exercise are needed in addition to medication.

This insulin side of the axis we call the "House of Feasting" in keeping with our Montague-Capulet analogy. The mechanisms of insulin are counteracted and balanced, in a healthy human, by the opposite effects of glucagon, which we call the "House of Fasting".

In Fasting the blood sugar is low and needs to be released from storage. Low blood sugar triggers glucagon to be released from the pancreas. Glucagon causes blood sugar to be first released by the liver, from glycogen. When the liver is empty of glycogen, the body begins to use fat cells for fuel. The body does this either by burning fat directly, through beta-oxidation lipolysis, or by using the fat together with protein as fuel for making new glucose molecules, a process called gluconeogenesis

Glucagon also causes blood sugar substitutes called ketone bodies to be secondarily synthesized from fatty acids in a process called ketosis. Ketone bodies have other effects on the human body, particularly the brain and mental focus, outside of the metabolic aspects of fat burning and weight loss.

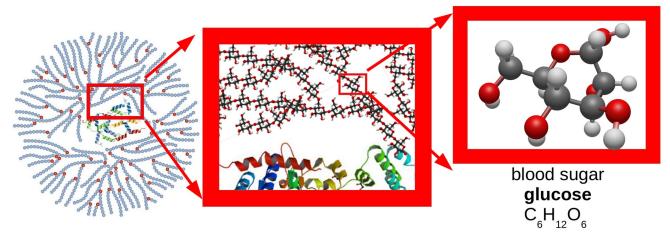
Fasting and aerobic exercise encourages all three metabolic phenomenon: fat burning, gluconeogenesis, and ketosis. Intermittent fasting causes periodic high glucagon and low insulin levels, which leads to insulin re-sensitization, which in turn fights type 2 diabetes more generally through these three metabolic phenomenon. Low carbohydrate diets and endurance exercise regiments can achieve similar results due to their tendency to keep blood sugar and insulin blood levels low.



**Image06** – Diagram of the blood sugar model. This shows the body in a state of fasting. A battery logo is used to indicate the relative amount of fuel stored in the liver as glycogen. Notice the release of glucagon molecules into the blood from the pancreas in **orange**, signaling to the fat and liver to release glucose into the blood for consumption.

For many Americans struggling with weight management and type 2 diabetes, a lack of time spent in this low blood sugar state (in the "House of Fasting") is one of the key causes of their health problems. The other main one being an over abundance of time spent in a feasting state. Restoring balance between these two metabolic states is the clearest perspective many everyday people can adopt to simplify a vastly complex biomedical system. Overly complex systems are more likely to be confusing and thus more prone to manipulation and misinformation, e.g. the overabundance of confusing and dubious diet and exercise trends.

What exactly is glycogen? We've mentioned it multiple times as a critical element of regulating blood sugar, so it merits some explanation. Much like the stomach must breakdown polymerized carbs so they can properly absorbed, the liver much build up polymer chains of glucose to store them and prevent them from remaining dissolved in the blood.

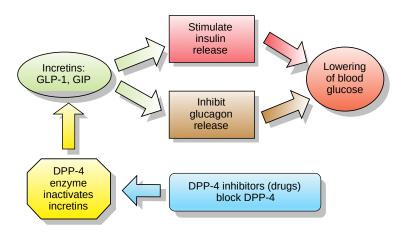


**Image07** – Diagram of the glycogen. This shows the building up of glycogen from individual glucose units, the branching patterns, and the core protein used as a base (colored spiral ribbon).

To make this easier to both quickly build up and break down, a branching pattern is used to create more parallel chains with more exposed endings. The more exposed endings, the more quickly glucose can be added or subtracted. The branching patterns follow the fractal shapes shown by many shapes in nature, particularly things maximizing surface area.

# PHARMACOLOGY AND INTERVENTIONS

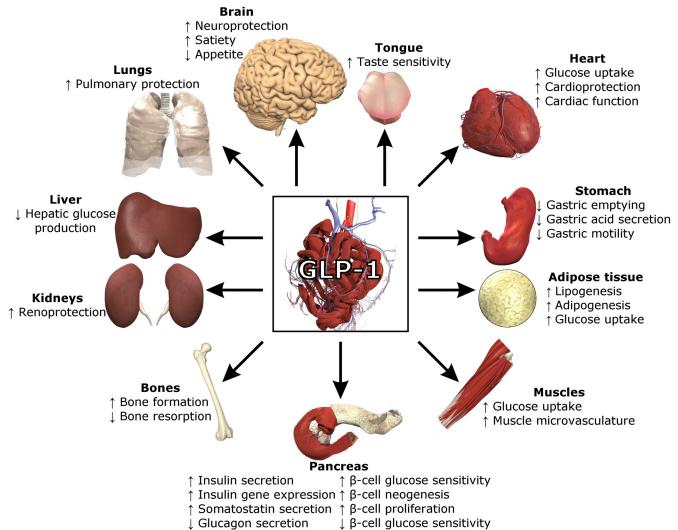
With a solid Insulin-Glucagon axis, where does GLP-1 fit in? GLP-1 stands for Glucagon Like Peptide (-1), but it is not equivalent to glucagon in function. GLP-1 acts more like an anti-glucagon, telling the body to produce less glucagon and more insulin. This alone would help explain why GLP-1s are good at fighting type 2 diabetes, but not weight loss. And yet GLP-1s are effective against both. In fact, this feature is the main reason why GLP-1 focused medications are an improvement over direct insulin injections, which do not have appreciable effect on appetite and food satisfaction. To better understand how GLP-1 can function as a weight loss promoter, the ancillary effects must be examined more closely.



**Image08** – Diagram showing how GLP-1 works on insulin and glucagon, and their net effect on blood glucose. The

older form of drugs before GLP-1RAs, called DDP-4 inhibitors are shown as well.

Looking just at the effect on the pancreas GLP-1 seems equivalent to that of insulin. But looking broadly, particularly in the brain and stomach, it blocks further ingestion (appetite). But looking even more broadly, it helps generate more fat (adipose), so its a complex web of interactions. The effect of GLP-1 on the brain in reducing food intake and/or increasing satisfaction seems to be the main driver of GLP-1 as a weight loss agent, but again this is part of a complex system with many "moving parts" or "balls in the air" to borrow popular turns of phrase.



**Image09** – Diagram showing GLP-1 effect on the wider organ systems of the human body. With this model, a clearer picture of how GLP-1RAs help weight loss starts to emerge.

If synthetic GLP-1RAs are the blockbuster weight loss drugs, then what are those? Well as stated earlier, GLP-1RAs are actually GLP-1 Receptor Antagonists, which means they are drugs that agonize or "hit" the same receptor as the natural GLP-1 produced by the human body. Natural GLP-1 lasts only a few minutes in human blood, meaning it would need to be constantly injected with something resembling an IV drip, which would be wildly impractical. GLP-1RAs offer a longer lasting version appropriate for once monthly injections. One way of summarizing the concept is as an "extended release" or XR formulation, but instead of a formulation of a given drug, its re-engineered to

that confers that XR property on the modified drug.

All GLP-1RAs are synthetic pharmaceuticals made from chemically modified peptides. So what's a peptide? We'll cover that in just a moment in the <u>following section</u>. GLP-1 is a natural peptide: There are two synthetic peptides created by two rival pharma factions:

- 1. Novo Nordisk semaglutide (Ozempic, Wegovy)
- 2. Eli Lilly tirzapatide (Mounjaro, Zepbound)

As mentioned earlier, in the later sections of this paper, we cover the pharmaceutical industry's <u>GLP-1 products</u>, <u>social dynamics</u>, and <u>economics</u>, which are a full topic in their own right separate from the complexities of the medical science. But in this section we want to focus on how the natural GLP-1 made by the human body can be harnessed more effectively *without the use of drugs*.

GLP-1RAs are synthetic but, GLP-1 is natural; how would a person utilize all natural solutions to weight loss involving their body's own GLP-1? All those benefits from GLP-1 we covered do not require synthetic pharmaceuticals. Although natural, GLP-1 has a very short half-life and so must be continuously released for effect. Luckily this is possible with some key lifestyle changes outlined here:

- 1. Fiber: high fiber intake is correlated with weight loss even without diet changes, which is an extraordinary fact! This is because fiber stimulates constant GLP-1 release from large intestine / colon into your blood. For those unfamiliar with dietary fiber supplements, daily tablespoons of psyllium dissolved in water are remarkable effective and relatively convenient Also has profoundly positive effects on bloating, constipation, and general indigestion including heartburn. Traditionalists can keep a high fiber diet but supplements can help compensate for the many rich foods that are served at social functions and in various social contexts.
- 2. Good fats/oils: Olive oil and avocado are the famous ones but there are many healthy oils that boost GLP-1 release (fish, flax, hemp). The list goes on but cow/pig/lamb fat does the opposite because its saturated, whereas these good fats are either mono- or polyunsaturated (in general: unsaturated fats).
- 3. Ketosis / Ketogenic Lifestyle: Changing eating habits so that the body is not constantly in a state of digestion and absorption is essential. This can be simplified into balancing the houses of "fasting" and "feasting" as covered earlier in this article, or put in a context of intermittent fasting, fasting days, meal skipping, or similar. Rehabilitation from snacking addiction is another context to consider this aspect of natural GLP-1 stimulation. In a consumer culture like that proliferating in the United States and many Western nations, this can be a monumental, sometimes Herculean task as it will require opposing certain social trends and for some breaking strongly established habits.

## **PEPTIDES: SOME CONTEXT**

What is a peptide, actually? All of these things are described as peptides, natural GLP-1, synthetic GLP-1RAs, but for those unfamiliar with the term a bit of background is warranted. A peptide is the linear combination of amino acids, and is the basis of all proteins. This linear combination is called a polymer, and it is made out of amino acids, which are its monomer forms (this was covered in the digestion section on the stomach). Some proteins are one big peptide, others are groups of them "attached" to each other, called polypeptides.

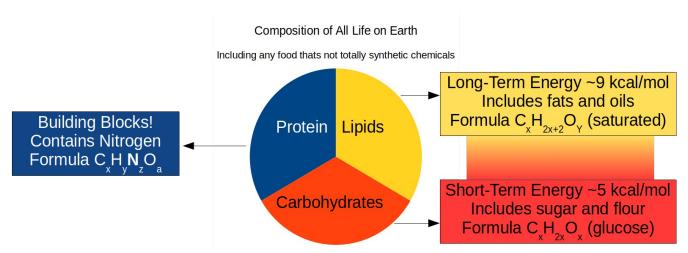
As it can get confusing with so many closely related and subtly different concepts, we thought we would make a simplifying list from a top-down perspective:

• **Protein** – Can be made of one or more peptides. The ones made of more than one are called

- "polypeptides"
- **Peptide** Linear polymers made out of amino acids as its monomer. Always linear, looks like a ribbon with spiral sections and chaotic sections
- **Amino Acid** The monomer that are tied together to make peptides. There are 20 amino acids, many of which are about the size of a glucose molecule.

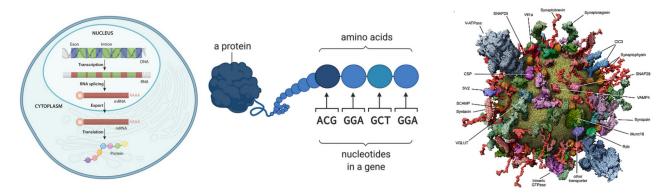
To put this information in proper context, all life follows three major categories of chemical composition (i.e. what makes it up):

- 1. **Protein** large peptides or polypeptides. All are polymers of amino acids. Responsible for all non-energy storage functions in a cell, including structure, catalysis (controlling chemical reactions), as well as being a source of energy when other sources are finished i.e. gluconeogenesis.
- 2. **Lipid** fats and oils, high density energy storage that is slow to access but gives a lot of energy once it gets warmed up.
- 3. **Carbohydrate** sugars and starches, low density energy that is quick to access but can run out rather easily without deeper energy reserves behind them (lipids <u>are</u> those deeper energy reserves). All carbohydrates are polymers (**poly**saccharides) of simple sugars (**mono**saccharides).



**Image10** – Diagram showing the division of all living matter into the three major categories of protein, lipid, and carbohydrate.

What is a peptide, actually? Technical talk is important, but so is the context of a human narrative. Proteins are <u>essentially</u> everything: They are the only part of of life that differentiate living cells by their DNA. What does that mean? If not for the differences in our proteins, a bacteria, a spider, a tree, and a human would all be the same life form, which obviously they are not. The differences in DNA sequences (genotype) only have an effect in the real world (phenotype) because they are translated into protein sequences, and manifest as different proteins. The other parts, lipids and carbohydrates, are just energy and **are the same in all living cells**, especially compared to proteins.



**Image11** – Diagram showing the concepts behind peptides / protein, and their derivation from DNA. The left diagram shows a cell, with the pathway from DNA to protein illustrated through transcription and translation. The central diagram shows how the protein is first broken down into a linear sequence, and that linear sequence is derived from the linear sequence of DNA (i.e. nucleotides in a gene). The right shows some examples of surface proteins displayed on a vesicle in a synapse between neurons, mostly to show the broad diversity that protein function can have.

Essentially proteins are the expression of our DNA and genes. They give us our hair color, eye color, but also our personality and temperament, our eczema and asthma, our allergy to peanuts and shellfish. This is the core dogma of modern molecular biology that every biology undergraduate must learn: DNA > RNA > protein as the core function of the cell. A version of this focused on anatomy components looks very similar: nucleus > RNA polyermase > ribosome. Inevitably, this language extends beyond the popular lexicon, but it is the scientific language used to describe our modern exquisitely validated theory of genetic inheritance of traits.

Also proteins are the differentiation between family members, who share DNA but have critical differences. The difference in DNA between a human and a plant is higher than between a human and a mammal, such as a dog. But the difference between a human and a dog is larger than between a human and a chimpanzee. Some studies cite the DNA difference between human and chimpanzee at 3%, making 97% identical (modern studies think the true difference is closer to 1.2%). And the difference between you and your parents is even smaller, <1% leaving >99% identical. Proteins are the carriers of this difference, as the other 2/3 biochemical components (lipids and carbohydrates) are not directly affected by DNA and can therefore be thought of as more universal between lifeforms. The eerie similarity between identical twins you observe is due to a very high DNA overlap, but what you are seeing is the downstream similarity in their proteins. They are DNA's manifestation.

So now that we know what peptides are, we can cover GLP-1RA pharmaceuticals. They are essentially peptides that mimic your natural GLP-1 with key chemical modifications. These are not just rival molecules that we will cover, but rival factions in the pharmaceutical oligopoly, one of the most powerful industries on the planet at this time.

## THE GLP-1 PRODUCTS ON THE MARKET

Okay, now that we have taken the long road of being properly informed on the scientific background of this hot topic, let's get into the actual drugs on the market. We will look at semaglutide, and tirzepatide, and a brief glance at the new oral version orforglipron, which is technically not a peptide in chemical structure.

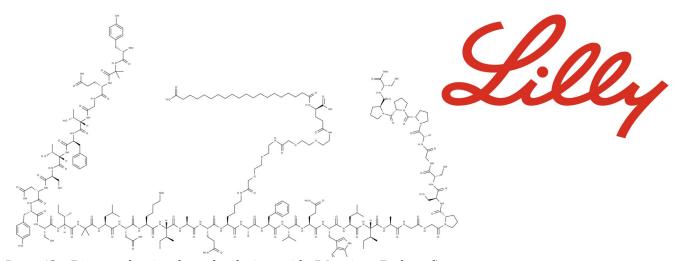
What is semaglutide? It is also known as Ozempic, Wegovy for type 2 diabetes and weight loss respectively. We have illustrated the molecular diagram, but for those not familiar with this notation, what this GLP-1RA contains is a modification on amino acid residues #2 and #20. The #2 gets a

dimethyl instead of the regular single methyl present on the amino acid alanine, and the #20 gets a long polymer chain added to a lysine amino acid.

This molecule does not exist in nature, and it is the active ingredient in these injections, and is patent-able (with the USPTO). So besides profit, why else would the medicinal chemists make these modifications to GLP-1, thereby making semaglutide? A clear reason is because natural GLP-1 has a half-life of mere minutes, designed to be continually released as part of natural feed-back loops. This compound lasts weeks and works for monthly injections.

Image12 – Diagram showing the molecule semaglutide (Ozempic, Wegovy).

Now let us look at the other major pharmaceutical GLP-1RA, tirzepatide (Mounjaro, Zepbound). Like semaglutide covered just before, here we see modifications to the amino acid residues #2 and #20. Essentially the same modifications too, with a doubling of the methyl on #2 and a very similar long chain added to the lysine on #20. This molecule is very similar in structure to the previous, but was awarded a separate USPTO patent, making it a separate profitable pharmaceutical with protected intellectual property associated with it.



**Image13** – Diagram showing the molecule <u>tirzepatide</u> (Mounjaro, Zepbound).

Are there critical differences between semaglutide and tirzepatide? Clinically there is very limited statistical evidence that these medications have significant differences in side effects. But the financial incentive to make two separate small molecules with separate patents is clearly very strong. And although it is largely driven by the profit motive for each company, it goes further than that: Our whole economic system is designed to promote competition and so the philosophy that rival products

need to be competing for consumers is imposed, whether it is medically appropriate or not. Although this philosophy originally protected American consumers from price gouging monopolies, the FDA-pharmaceutical industry complex is built around monopoly-esque market advantages (i.e. exclusive patents, R&D for new exclusive drugs, "blockbuster" drugs, etc). See the following section "Economics of Pharma Industry" for more details on these economic phenomenon and the impact they have on American's health.

**Image14** – Diagram showing the molecule behind <u>orforglipron</u>.

As of yesterday (August 7<sup>th</sup>, 2025) Eli Lilly made a earnings report following that of competitor Novo Nordisk about a week earlier. Novo Nordisk reported earnings under-projections and blamed "compounding pharmacies" for the loss of revenue, as well as big pharma competitors such as Eli Lilly. Part of the response of Eli Lilly was to advertise a yet-unapproved oral version of GLP-1RA which it calls orforglipron (brand name TBD). Because this molecule is not a peptide, it is not vulnerable to the polymer digestion of the stomach which targets dehydration bonds between monomers with hydrolysis (see section Science of GLP-1 for review of stomach, and wider, digestion). This allows the injectable drugs of semaglutide and tirzepatide to be converted to an oral pill form, which is believed to "overcome" one of the market barriers to a wider market share. This molecule, like the peptides above, is a GLP-1RA, meaning it hits the GLP-1 receptor in the human body. But what makes it different besides the different chemical class allowing a bypass of injection, is the far smaller size, with a molecular mass of 883, versus 4,814 (tirzepatide) and 4,114 (semaglutide), making it about1/5th the size of these larger "macromolecules" and classifying it in the "small molecule" class. Small molecules include aspirin, Tylenol, cocaine, heroin, Zoloft, metformin, and nearly all widely known pharmaceutical compounds.

## **MOTIVE AND PROFITS**

Dr Kessler, Former head of FDA, says in his May 2025 New York Times article: "In era of addictive foods, we <u>need</u> GLP-1s". This statement was actually the impetus for this whole article, as it triggered a fear that the unnatural aspects of the food industry was creating an equally unnatural aspect of the pharmaceutical industry. This would mean that through financial incentives, each industry fed each other revenue at the expense of the public health. <u>Comments</u>, in response to this article, from everyday Americans are all over the road from supportive to combative, innovative to paranoid, and informed to ignorant. After having reviewed several key comments which we have reproduced screenshots of in the appendix, we have organized them into six major categories:

1. **RFK** / **Trump supporting comments**. Many of them may surprise you because they don't necessarily seem to be coming from classically conservative mindsets, but because they are

- critical of "establishment" types, such as former regulators of large corporations, they show explicit support for the MAHA / MAGA movement generally.
- 2. Anti-big business comments with emphasis on pharmaceutical and agriculture industries. In particular the emphasis that the link between the two is profitable to both and exponentially more detrimental to public health than either in isolation. Generally though, these are unified behind calls for proper regulations of big business, with a focus on food and drug industries as egregious examples of under-regulated industries in the US. Privatized healthcare and the myriad of issues it brings, largely through misaligned incentives between finance and public health, is a secondary but critical theme as well.
- 3. **Anti-shame comments / complaint of low empathy for weight struggles**. This dovetails with a greater progressive movement to address body image issues in society at large and is connected with clinical data showing eating disorders have been rising rapidly in recent years, more than doubling in less than two decades and rapidly approaching 10% of the US population.
- 4. **Anti-addictions comments, which the team behind this article is very much sympathetic to**. Food has been engineered in the US to be "the new cigarette" and yet lawsuits against the big business entities responsible for and profiting from this are not mirroring what happened with big tobacco years ago.
- 5. **Anti-meat / vegan comments, also much sympathy from the authors, although some vegan activist show a tendency to a myopic worldview on these issues**. Also just because many of these are coming from a genuinely good place, doesn't make them scientifically informed in all cases.
- 6. Pro-GLP-1RA comments that say things like "the war against obesity via behavior modification is lost, and what 'actually works' needs to be championed." Comments such as this show a demographic that is aware of, but has given up on, an ideal practice of medicine and regulation of the industry thereof. Very similar to category 2 above, but with more of an emphasis on clinical necessity and practical considerations, rather than an big business or industrial economic look.

Please feel free to review the comments in the appendix to see the examples we have provided to give some social context to this discussion. What is remarkable is the theme of complaint in these comments about corruption and essentially collusion between the large business interests of the food industry, sometimes called "Big Ag" or "Big Food", and those of the pharmaceutical industry, known widely as "Big Pharma".

What the narrative essentially describes is a Big Ag that has engineered the most profitable food products imaginable, and now Big Pharma can create a very lucrative market fixing the obesity that this creates. Many call for the FDA to "do something" about this collusion between Big Ag and Big Pharma, which in turn reveals a diverse array of parties to blame for the current public health crisis. Some blame business-as-usual FDA attitudes that are too friendly with big business to check their interests and properly and fairly regulate their industries as a result. This blame can be seen to be blamed on the outgoing Biden administration, particularly by those championing RFK or Trump, although this practice largely resembled previous administrations, and so was not really a uniquely Biden, or Democrat, issue. Other more apparently left leaning comments blame excessive capitalism and under regulation for these issues and seem to be calling for a social democrat style philosophy of more stringent regulation and taxation for causes designed to address the negative effects on public health.

Regardless of blame that is assigned by the public, the history of the FDA and how it arrived at its current state of regulation is very interesting. As many studied in high school US history class, "The

Jungle" by Upton Sinclair, was an early investigative journalism exposé into abuses in the food industry. This revealed practices such as dust from red bricks being used to adulterate ground cinnamon, which was of great concern (and the relatable, almost contagious, human emotion "disgust") to the public once they became aware. This created a climate in which the modern FDA started being created, approximately between 1900-1940 with a series of laws strengthening its powers until the passage of the landmark 1970 Controlled Substance Act and creation of enforcement division known as the DEA (Drug Enforcement Administration).

Although it is less commonly seen in populist online comments, those with some insight into how modern FDA regulation of pharmaceutical companies work have pointed out that approximately half of the FDA budget comes not from taxpayer funds from congress, but rather from "user fees". In this context, the "user" is not the patient taking the drug, but the pharma company applying for approval of a new drug. On the surface it can seem like a clever way of making the pharma industry that profits from these drugs pay for a greater share of the industry regulation, letting society at large to be taxed less for the cost of this highly specialized regulation. But over time this makes the federal agency beholden to the finances of the pharma companies and indirectly dependent on their cashflow and profitability to fund their own regulatory activities. For example, shutting down one of the biggest pharma giants would result in the loss of the "user fees" from that very large company, which may represent a significant fraction of the FDA's budget. Subtle financial incentives such as this, over time, can motivate the regulators to keep cash flowing through the existing parties, which can limit the extent of regulatory limits imposed and enforcement actions taken by the FDA.

A few examples of the FDA's ability to steer food and drug norms in the United States may merit mentioning for context of how this agency's power and influence are exerted. American cheese is the most obvious example, made through a process involving chemicals such as sodium citrate. This process allows for a more consistent looking cheese with better "meltability" (less separation during cooking) and most profitable of all, a longer shelf life. This was patented by James L. Kraft in 1916 in the US and made available as Kraft Singles in 1950. What this has created since is a whole industry of "cheese products" which are legally distinct from natural cheese. Whereas natural cheese is a regulated food product, "cheese products" are unregulated and can contain less than 51% natural cheese in their ingredients. This has created a unregulated pocket within the greater dairy industry for ultra-processed and highly profitable products which have become increasingly normalized in the American diet.

Another example is the rise of anti-depressant class known as SSRI (selective serotonin uptake inhibitor). Because there are so many SSRIs now we will focus on the first, brand name Prozac (fluoxetine). This was developed in the 70's by one of the big pharma companies we are examining for GLP-1 drugs, Eli Lilly. While development of the drug took until the mid 80's, in 1987 the drug went on the US market and grew to \$350 million in sales in the first year and peaked at \$2.6 billion years later, which represents a very rapid rise of a new product and a new medical market for treatment of depression. When the patent on this drug expired in 2001 and let other companies compete with generic versions of the drug, sales dropped an astonishing 70%. What this blockbuster drug did was create not only a wave of generic drugs of this molecule, but similar and competing molecules that would come with a patent.

The irony of the anti-depressant narrative is that after the first SSRIs, no patent would ever be as profitable as that first one again, despite the market for SSRIs growing because it is now sub-divided into market shares between the big pharma companies. But the financial incentives of each company still drove the changes to medical and clinical practice in the US, with six major SSRIs currently very popular including the original Prozac: Citalopram (Celexa), escitalopram (Lexapro), fluvoxamine (Luvox), paroxetine (Paxil), and sertraline (Zoloft). This has created a "drugs first" pattern in the treatment of depression among US psychiatrists where these drugs which were originally used for

treatment resistant depression due to unpleasant side effects are quickly becoming a line of first response for all patients, often with a period of cycling between these drugs to find the "right fit" for a patient based on side effects and symptom management. Compare this to EU standard medical practice which is to use behavioral interventions first (exercise, diet, lifestyle), followed by natural remedies (lemon oil, St. John's wort, etc), and only third "harsher" synthetic pharmaceuticals. In the US the triage seems to work backwards with pharmaceutical products being given first and "alternative medicine" only being pursued by patients who continue to experience issues with depression symptoms or side effects. Although this is not beneficial for patient health, it is very lucrative for the pharmaceutical companies and distributes a fair amount of cash to prescribing psychiatrists, pharmacies, and many other ancillary services that are paid in conjunction with the drug maker. Aside from contributing to the high cost of drug prices and inaccessibility of healthcare, this pattern also leaves millions of Americans struggling with SSRI withdrawal years after their battle with depression has ended.

The important thing in this case study is the regulatory aspects and how we can learn about them in our thinking on the GLP-1 drugs. Is it the FDA's jurisdiction to create prescribing guidelines for doctors, or is that more the role of the AMA (American Medical Association) or APA (American Psychological Association)? Well its a complex area because the FDA's jurisdiction includes what the drug is and is not approved to treat, but things such as "first line of response vs. treatment resistant cases only" are not squarely in the FDA's purview and start to stray into AMA / APA territory. But the pattern of profitable drugs driving the treatment options available to patients is clearly seen here, and that process, of what drugs are approved and for what disorders, is more squarely in the jurisdiction of the FDA.

## THE ECONOMICS OF THE PHARMACEUTICAL INDUSTRY

The profits of these companies that produce these drugs are also a critical aspect of this phenomenon to examine closely. Every time there is an approval of GLP-1RAs by the FDA, this correlates with stock price bump for pharma company in anticipation of massive revenue stream and subsequent windfall profits. But why is there is expectation of windfall profits, where do these numbers come from? With some simple arithmetic we can help outline numbers for anyone:

All number use the US population as an estimate at 300,000,000 (300M) Americans
All %number are derived as such: 10% of Americans = 300,000,000 x 10% = 30,000,000

- 1.  $\sim$ \$1,000.00 USD per injection / month =  $\sim$ \$12,000.00 USD/year/patient.
  - 1. Obese Americans ~ 40% of USA  $\rightarrow$  \$12,000 x 120,000,000 patients = \$1.44 trillion /year
  - 2. Severely Obese Americans ~ 18% of USA  $\rightarrow$  \$12,000 x 54,000,000 patients = \$648 billion /year
  - 3. Type2-Diabetes Americans ~ 12% of USA  $\rightarrow$  \$12,000 x 36,000,000 patients = \$432 billion /year

These numbers are obviously very rough approximations, but that is enough to give a sense of scale, sometimes called "order of magnitude". What this means is even if these estimates we are generating here are off by 20%, 50%, or even 70%, they give a ballpark sense of what kind of quantities we are talking about. Ozempic in 2024 was popularly known for going for \$1,200/month instead of our estimate for \$1,000.

Who will will pay for these services and the associated pharma profits? Currently insurance is known to pay for type2 diabetes cases but not obesity cases, but this norm may change as the medical insurance industry, the medical industry, and other aspects of society shift in the coming years. Given

that these limits are relatively arbitrary (i.e. obesity leads to type 2 diabetes), the landscape between the trichotomy of out-of-pocket, private, and public insurance coverage are a constantly shifting desert landscape:

- Out-of-pocket: The wealthy can purchase the drug easily, see 2024 "South Park" special.
- Private insurance: Premiums and co-pays will pay for these profits by raising rates on all.
- Public insurance (Medicaid / Medicare): Taxes and federal withholding will pay for these profits, by raising taxes on all.

Regardless of how these drugs are paid for, they will be paid for by raising a fee on a wider community. To further this drug cost debate, the phenomenon of compounding pharmacies buying the cheap active ingredient, the peptides we have been discussing, and formulating them into injectables themselves has saved massive amounts from the consumer facing price of these drugs. This led to an explosion of compounding pharmacy GLP-1 drugs (GLP-1RAs) among consumers because cost savings were so significant. This also means that part of the cost structure that brand drugs like Ozempic and Zepbound patients are paying for is not just the drug itself, but a large mark-up on the brand name. When 3<sup>rd</sup> parties who had the resources to compound the injectable but not make the active drug realized this, they made a tidy profit off the of the difference, which cut into the profit margins of the large pharmaceutical companies. This led to a reaction in 2024 where compounding pharmacies producing more affordable GLP-1s were systematically shut down, by the FDA, at Novo Nordisk and Eli Lilly's "request" (substantive lobbying efforts).

# **MISINFORMATION (GENERALLY)**

As we reach the end of our GLP-1 discussion, some readers will continue to research many aspects of this topic, from the medical science of how it works, the pharmaceutical history of the products and the market conditions they are motivated by and operate under, and wider information about health, wellness, and weight management. What we felt is necessary in an age with escalating misinformation is a small bit about misinformation and its manifestations in historical context, to best equip our readers to find good, solid, and reliable information when researching and how to identify information of questionable accuracy.

Although misinformation is part of what supports the GLP-1 "revolution", it is far more widespread, and intertwined, with this single subject. Many examples exist of Trumpism affecting health and medical aspects of America, particularly in the RFK vein of "wellness influencers". We have covered this in the previous section about the public comments on the NYT article by Dr Kessler, but here we extend this phenomenon out of the populist support to the establishment narrative by public figures. In particular Governor Bobby Jindal's Article on Food Transparency and GRAS, which follows RFK's attack on food dyes and synthetic substances. To help give an example of why Gov Jindal's article should be treated with skepticism include his political motivation for the article, the lack of scientific or medical credentials to speak effectively on the matter, and the political opportunism or "trend surfing" nature of the narrative.

Additionally much scientific evidence has started to emerge to suggest that weight regain after GLP-1 treatment cessation is very common, and often has a net self-defeating effect on patients who used these drugs for less than a continual, lifetime prescription. This information fits with the concern that the profit-driven philosophy of big business idealizes an addictive product that causes long-term dependency, guaranteeing future revenue (Wilding 2022).

Corporate disinformation campaigns are widespread in recent history. The authors have compiled a brief list of recent notable examples, but countless more exist. It is important to at least be

aware of the dynamics of these known corporate disinformation campaigns:

# 1. McDonalds Migraine "Hack" → Today.com article

This particularly troubling article points to a popular "hack" for migraine headaches, suggesting a big mac with fries and a large Coke is a "cure-all" for these debilitating and painful headaches. Though there may be some science to some aspects of this, namely that certain key stimulus such as the chemicals in the food may interrupt the cycle at the beginning of the headache, sometimes known as the "aura", articles like this are an opportunity for spreading misinformation as the untested theory of medical nuance may be misconstrued by large numbers of readers established fact, all to the benefit of McDonald's. Notice that competing brands are not included in this article, and relationships between corporate interests of McDonald and Today's parent company NBC-Universal are highly likely.

#### 2. Tobacco

This one is particularly troubling because it led not to more reversible conditions like obesity but rather emphysema and lung cancer. Despite the medical evidence being very clear about cigarettes and lung cancer, the interference of the tobacco companies created a "public debate" full of misinformation and intentional disinformation to delay restrictions on the tobacco industry.

#### 3. Sugar

Directly connected to the issues in the GLP-1 topic, the sugar industry has been running disinformation campaigns for a long time. The push for "fat-free" snacks in the 90's was the maturation of a disinformation campaign started in the 1950's blaming fats for rising rates of heart disease in the industrialized world. Modern medical studies show that excessive sugar causes AGE (advanced glycation end-products) which drives the inflammation that causes heart disease, high blood pressure, stroke, atherosclerosis, and more.

# 4. Wellness Supplements

Wellness supplement manufacturers have recently found financial success using marketing of unproven medical claims and is a great example of "trend surfing". Using social media and influencer culture to create an apparatus for "customer education" to make any and all health problems seem curable by their supplement. Often these come with barely noticed warnings of "claims not evaluated by the FDA". In some cases the supplement may well have many medical legitimate benefits, such as CBD from cannabis, which rapidly becomes exploited by salesman and profiteers to generate a consumer trend bubble to drive sales, often damaging the credibility of a new compound that can genuinely improve people's health. Other times this is used to push damaging and toxic substances onto an unsuspecting consuming public, such as tianeptine, often called "gas station heroin" and sold under brand's such as "Neptune's Treasure". Or synthetic cannabinoids that were popular about 10 years ago under brand names such as "K2" and "Spice", advertising a safe and legal alternative to cannabis when the truth is that natural cannabis is one of the safest substances known and these products were exceptionally dangerous compounds (many of which have now been banned as a result of the deaths and severe injury done to consumers). RFK's popular support in the "health" space is largely from this industry and community called "wellness influencers".

## 5. Global Warming / Oil Companies

The most consequential of all disinformation campaigns is the huge one performed by the great "Seven Sisters" of the oil and gas industry, themselves children of the break-up of Rockefeller Standard Oil Company by the US Government in the early 20<sup>th</sup> century. They had proof of global warming as soon as the 1970's and yet began a campaign of disinformation that continues to this day to sow doubt in the public's mind about the link between carbon emissions and global warming. The death toll from this campaign may ultimately make all the combined deaths by lung cancer caused by smoking seem small.

Public disinformation campaigns are widespread too. These are different from misinformation, which does not necessarily have a deceptive intent, and corporate / government misinformation campaigns, which always come from a institution's interests (sometimes called "top-down"). These campaigns are spontaneously generated from the public, and are more "bottom-up" in structure. They seem more motivated not by conspiracies to optimize profits or control, but rather the psychological gratification of individuals who internalize the message of the campaign and become spreaders or boosters of the message. We have a brief list of these spontaneous and public origin disinformation campaigns below:

- 1. Anti-VAX
- 2. Seed Oil
- 3. 5G

In conclusion, the advent of weight loss drugs poses many philosophical and moral questions which society at large seems to be increasingly struggling to address let alone resolve. Weight loss drugs have existed in the past, but GLP-1RAs create a new era of convenience and populism behind them which raises questions about human lifestyle and corporate synergy working against consumer interests. Perhaps the model of helping people struggling with their health is not as compatible with the model of blockbuster drugs and profitable junk foods as some economic theorists have put forth. Perhaps robust and human-focused regulation is being slowly eroded as "inconvenient" to the business community, and its gradual loss leaves the human health care industry as a dystopian hellscape.

## **CITATIONS**

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#### **APPENDIX**

