

Bioactive Peptides – a new tool in the feed technology toolbox

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South African Feedlot Association Conference

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Man's quest for tools ...

+

Man's "exponential" increase
in technological capabilities ...



LIVE 1.8M views

SPEED 78 KM/H
ALTITUDE 0 KM
LOX
CH4



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STARSHIP FLIGHT TEST



SPEED 16573 KM/H
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Why the quest for
new tools ?

The perpetual need for improvement ...

- Production
 - Growth rate
 - Feed efficiency
 - Slaughter %
 - Carcass weight
- Product quality
- Animal wellbeing
- Environmental sustainability
- Return on investment

The perpetual need for improvement ...

- Production
 - Growth rate ... **ADG = 1.65 kg; carcass ADG = 1.22 kg**
 - Feed efficiency ... **5.5 (DM basis); 7.5 carcass FCR**
 - Slaughter % ... **58.8**
 - Carcass weight ... **285 kg (CCW)**
- Product quality
- Animal wellbeing
- Environmental sustainability
- Return on investment

Two notable champions from the past

- First: Ionophores
 - Monensin (Rumensin™)
 - Late 1970s
- Second: Beta-agonists
 - Zilpaterol hydrochloride (Zilmax™)
 - Mid 1990s
- Next: Bioactive peptides ???

The ~~Bermuda~~ feedlot triangle

- Weaner calf price
- Feed cost ... nutrition → → →
- Carcass price

→ → → Profit

Importance of nutrition

- Purpose:
 - Supply nutrients – energy, protein (amino acids), minerals, vitamins
- Affects:
 - Rate of production (ADG_{carcass}) and efficiency of production (FE_{carcass})
- Primary cost item
- Often the only thing that the feedlot operator can control/manipulate...

Feed additives

- Feed additives are non-nutritive substances added to feed to improve the conversion of feed → meat & milk
- Examples: ionophores, buffers, probiotics, beta-agonists ...
- Now a “new” player looking in on this (rather crowded) stage:

Bioactive peptides

Objective of this presentation

Bioactive Peptides

- What are they?
- How do they work?
- Where do they fit in?
- Can they become a tool in the feedlot?
- **Will** they ... ???

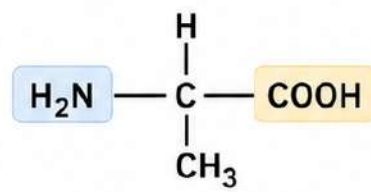
The story starts with ***proteins*** ...

- A familiar entity ... a key nutrient
- Billions of individual proteins across all living organisms
- Ruminant feedstuffs contain thousands of specific proteins
- A **protein** is a macromolecule composed of one or more polypeptide chains of **amino acids** linked by peptide bonds, folded into a distinct 3-dimensional conformation that dictates its biological or structural function
- Typically contains **16% nitrogen** (the basis for the 6.25 multiplier used in crude protein analysis)

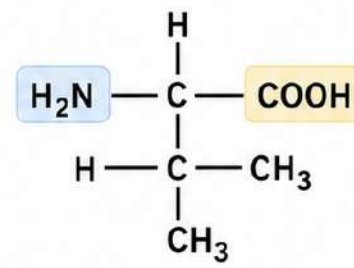


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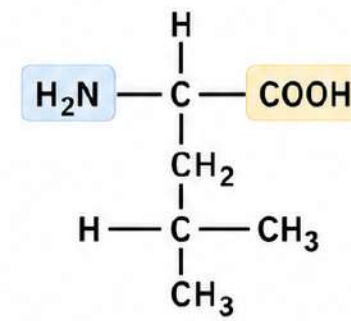
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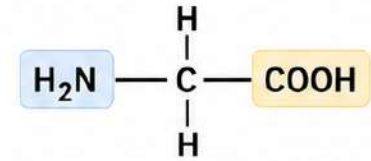
alanine
(Ala., A)



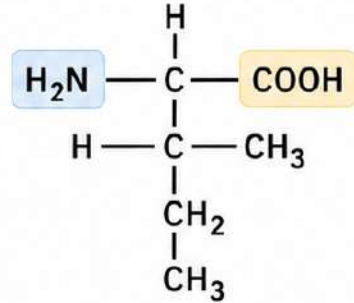
valine
(Val., V)



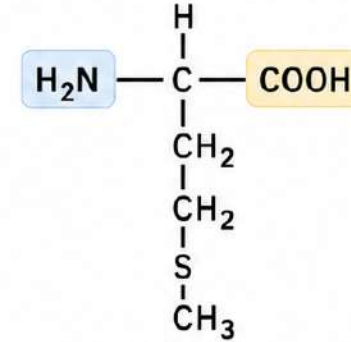
leucine
(Leu., L)



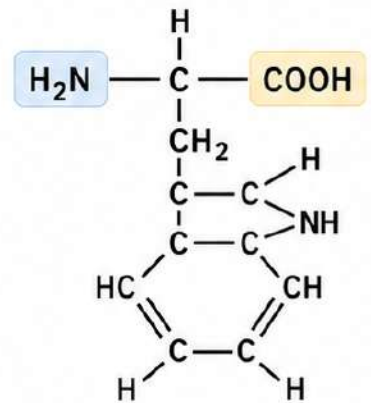
glycine
(Gly., G)



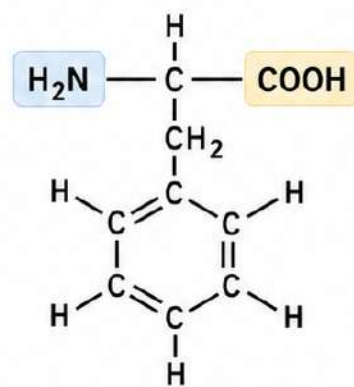
isoleucine
(Ile., I)



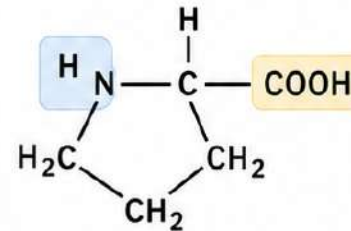
methionine
(Met., M)



tryptophan
(Try or Trp., W)



phenylalanine
(Phe., F)



proline
(Pro., P)
an amino acid

The 20 standard (“natural”) amino acids

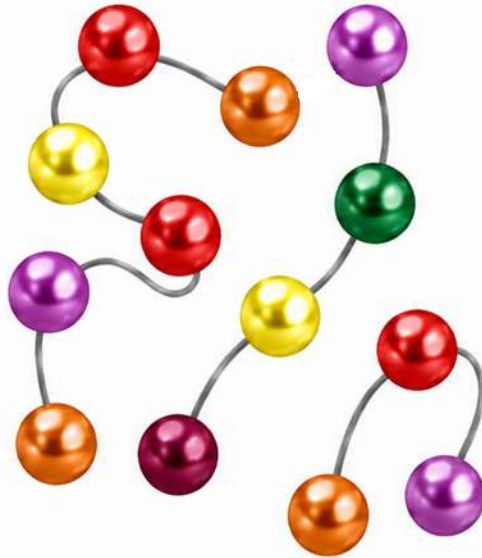
Amino acid	Three-letter	One-letter
Alanine	Ala	A
Arginine	Arg	R
Asparagine	Asn	N
Aspartic acid	Asp	D
Cysteine	Cys	C
Glutamine	Gln	Q
Glutamic acid	Glu	E
Glycine	Gly	G
Histidine	His	H
Isoleucine	Ile	I

Amino acid	Three-letter	One-letter
Leucine	Leu	L
Lysine	Lys	K
Methionine	Met	M
Phenylalanine	Phe	F
Proline	Pro	P
Serine	Ser	S
Threonine	Thr	T
Tryptophan	Trp	W
Tyrosine	Tyr	Y
Valine	Val	V

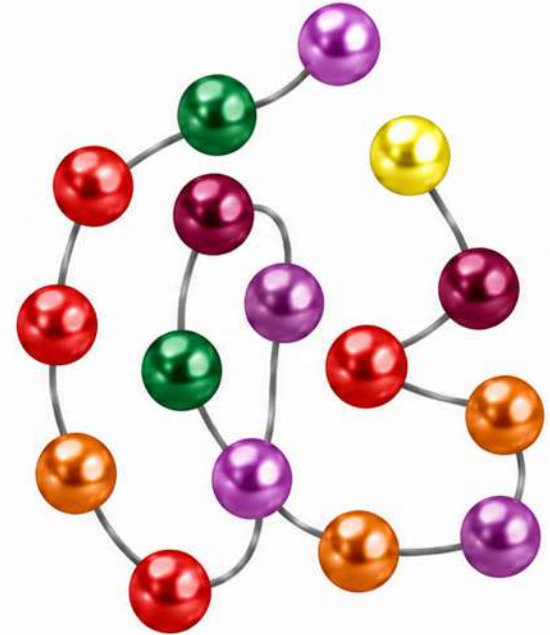
Amino Acid to Protein



Amino acids

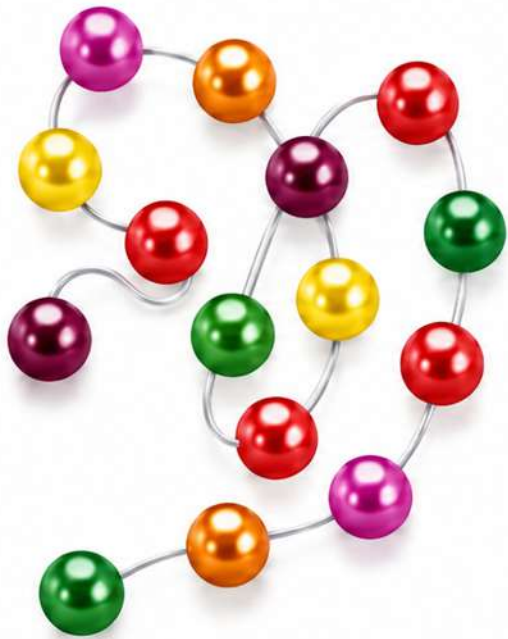


Peptides



Protein

Protein Digestion



Protein



Peptides



Amino acids

Protein Structure

**PRIMARY
STRUCTURE**



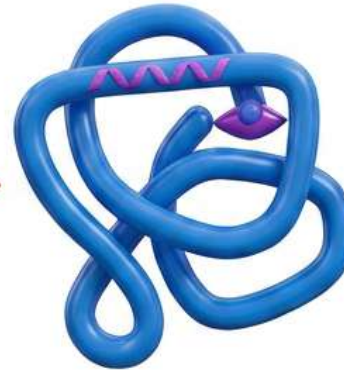
Amino Acid

**SECONDARY
STRUCTURE**



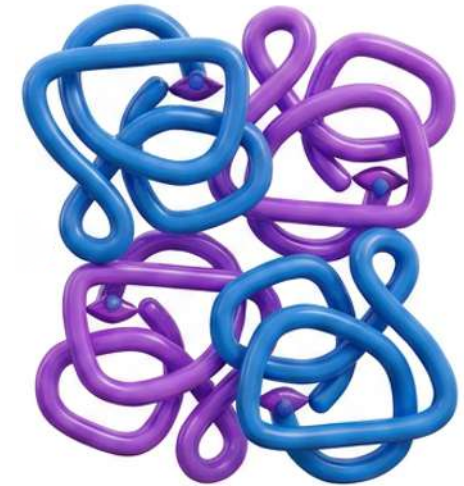
Helix

**TERTIARY
STRUCTURE**



Polypeptide Chain

**QUATERNARY
STRUCTURE**



Assembled Subunits

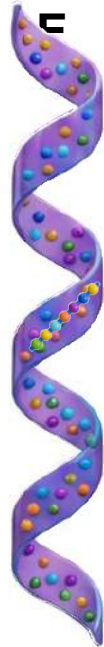
Protein Structure

**PRIMARY
STRUCTURE**



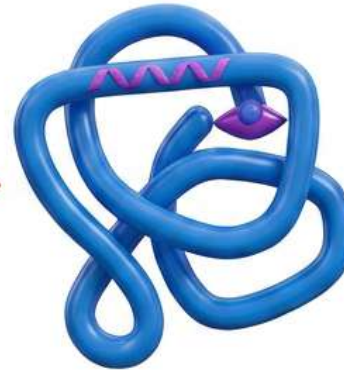
Amino Acid

**SECONDARY
STRUCTURE**



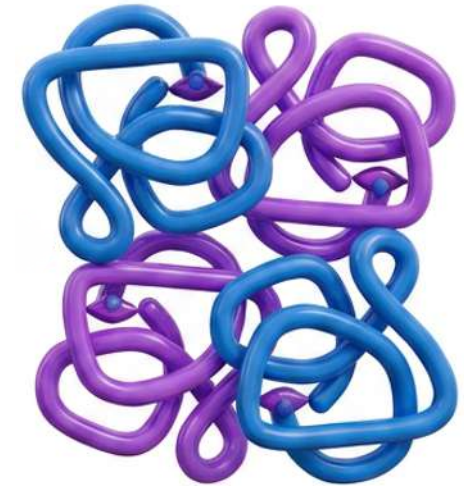
Helix

**TERTIARY
STRUCTURE**



Polypeptide Chain

**QUATERNARY
STRUCTURE**



Assembled Subunits

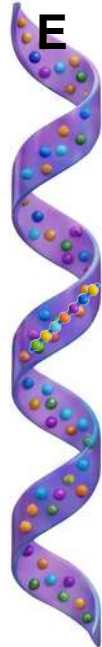
Protein Structure

**PRIMARY
STRUCTURE**



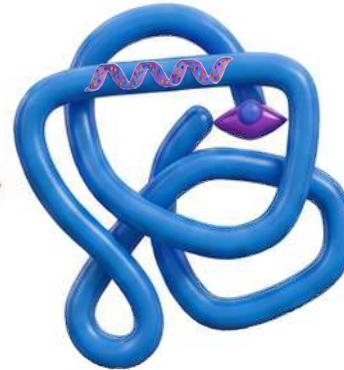
Amino Acid

**SECONDARY
STRUCTURE**



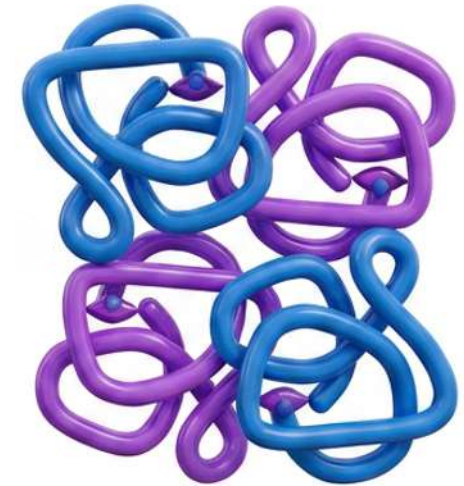
Helix

**TERTIARY
STRUCTURE**



Polypeptide Chain

**QUATERNARY
STRUCTURE**



Assembled Subunits

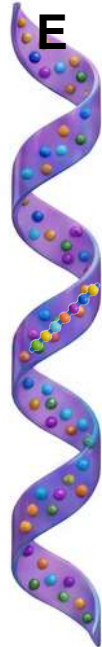
Protein Structure

**PRIMARY
STRUCTURE**



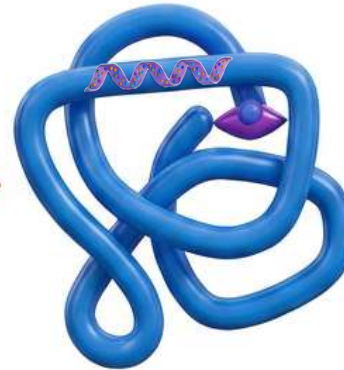
Amino Acid

**SECONDARY
STRUCTURE**



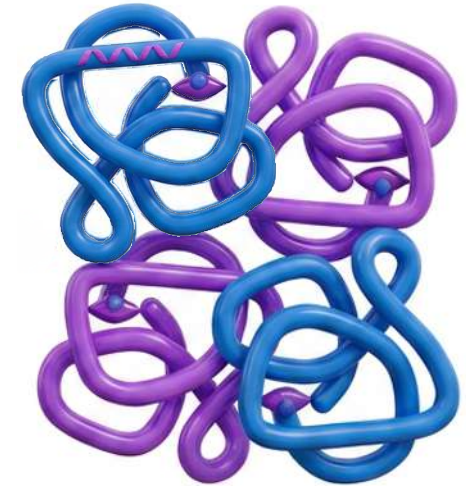
Helix

**TERTIARY
STRUCTURE**



Polypeptide Chain

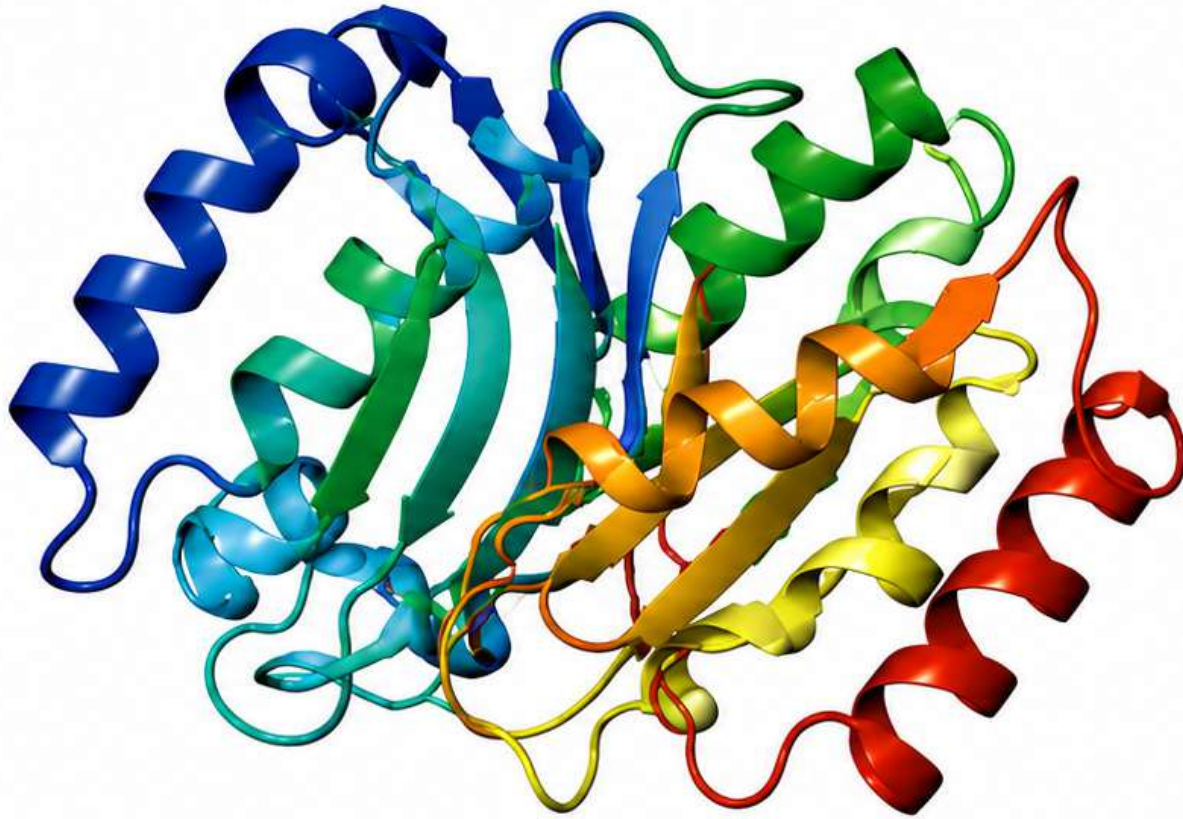
**QUATERNARY
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Assembled Subunits

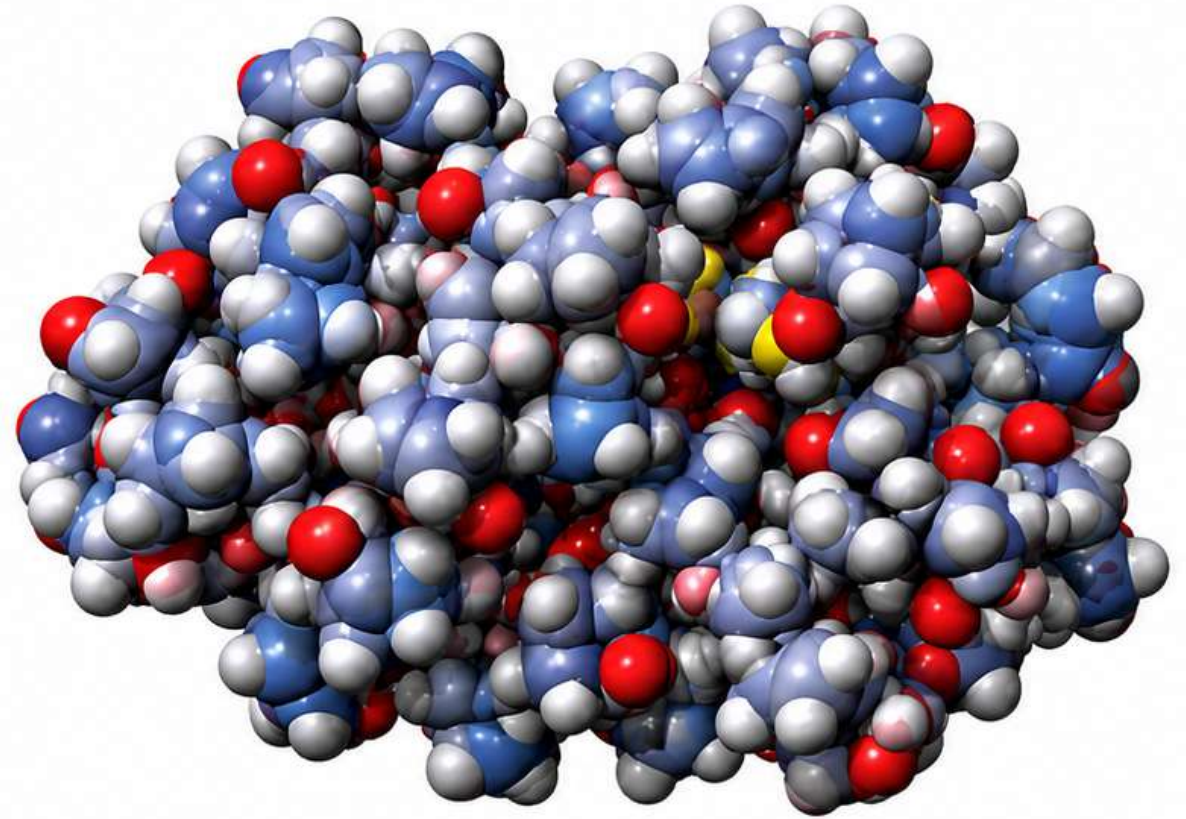
The Same Protein Shown in Two Representations

Ribbon (cartoon) representation

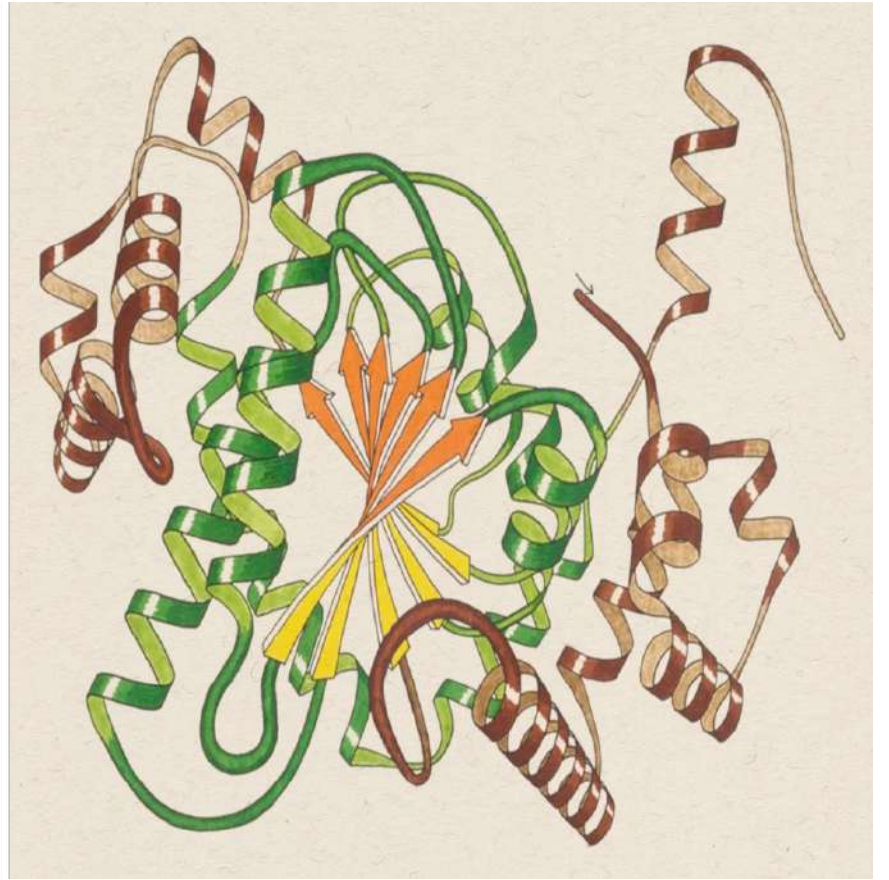
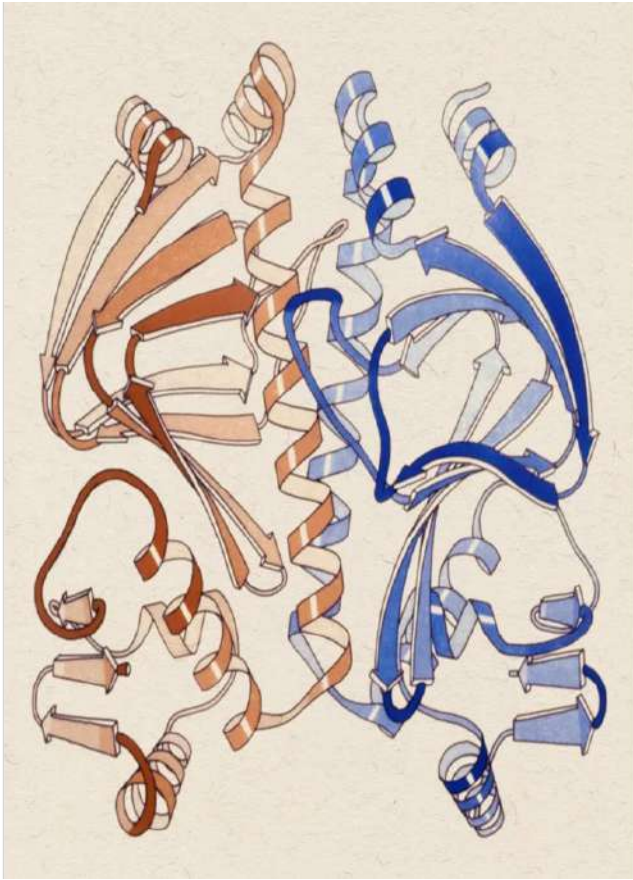


Secondary structure elements (α -helices, β -strands and loops) are visible.

Space-filling representation

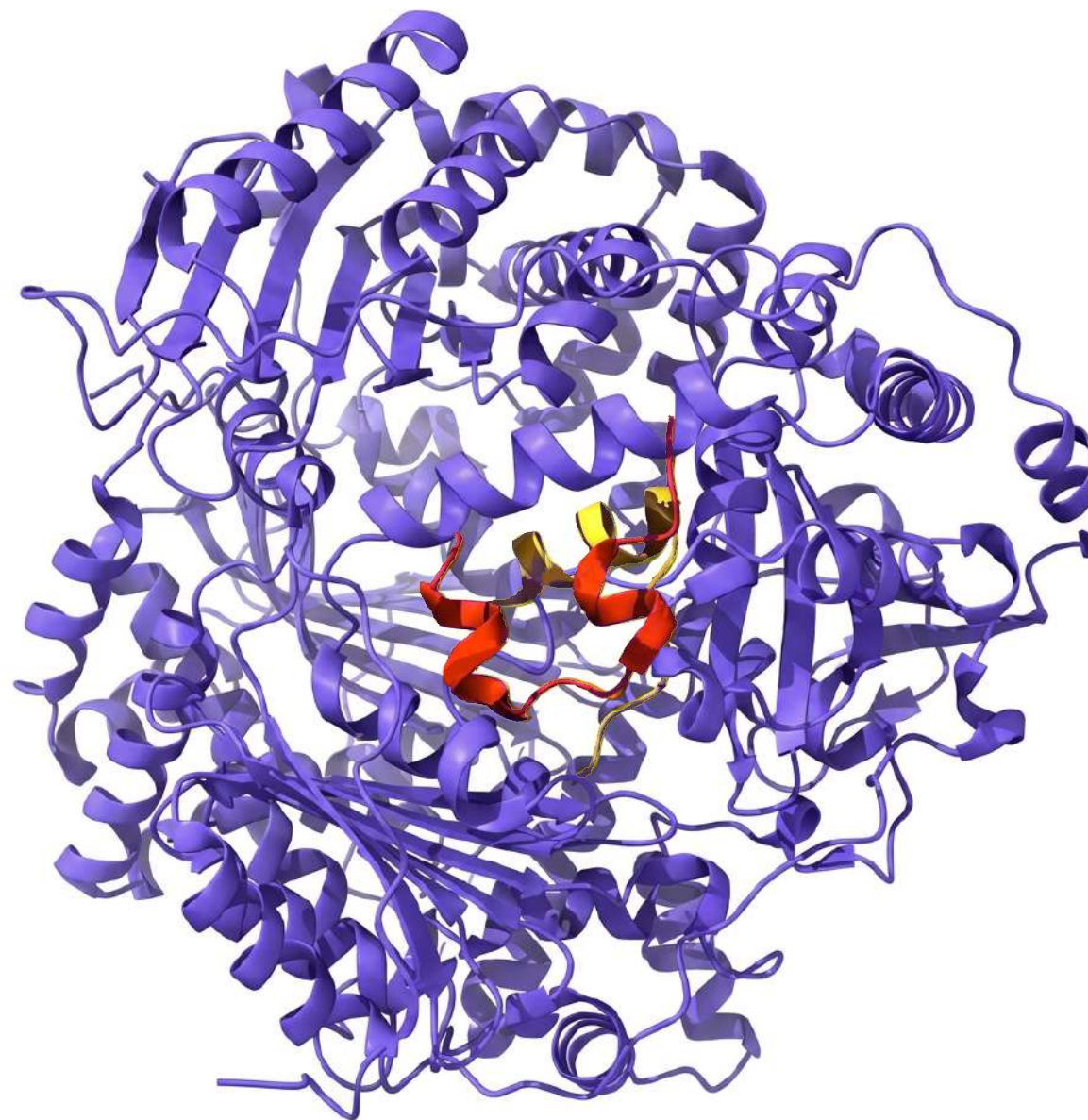


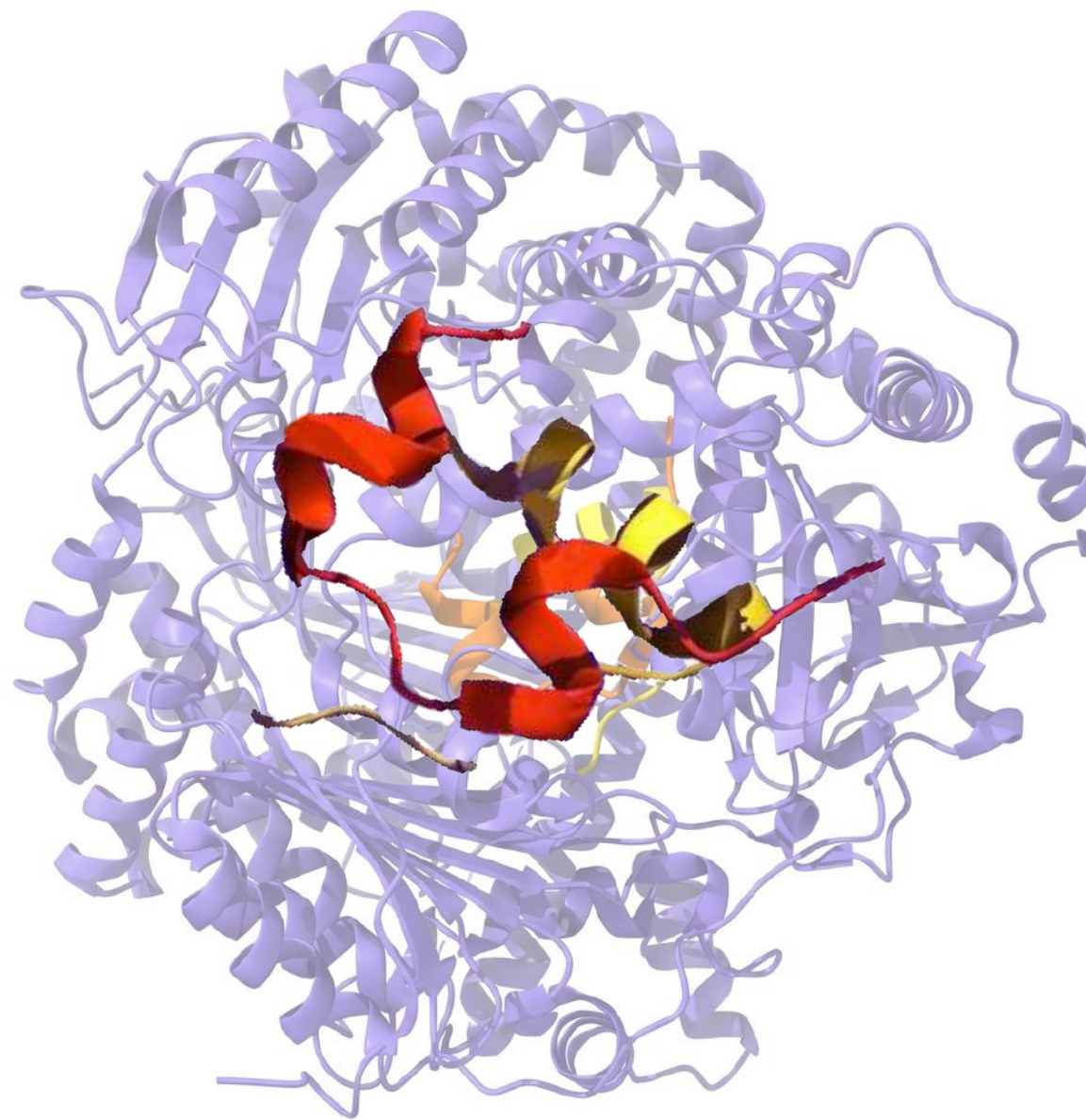
All atoms are shown as spheres, giving a sense of the protein's overall shape and surface.



What is a *Bioactive Peptide (BP)*?

- **A short chain of amino acids** (typically 2 – 20, sometimes up to 50 amino acids)
- **Hidden ("encrypted") within a larger protein**
- **Inactive while part of the intact protein**
- **Released** by enzymatic hydrolysis (digestion, fermentation, or food processing)
- Once released, it can **interact with specific receptors or enzymes**
- Can influence **physiology beyond simple nutrition**





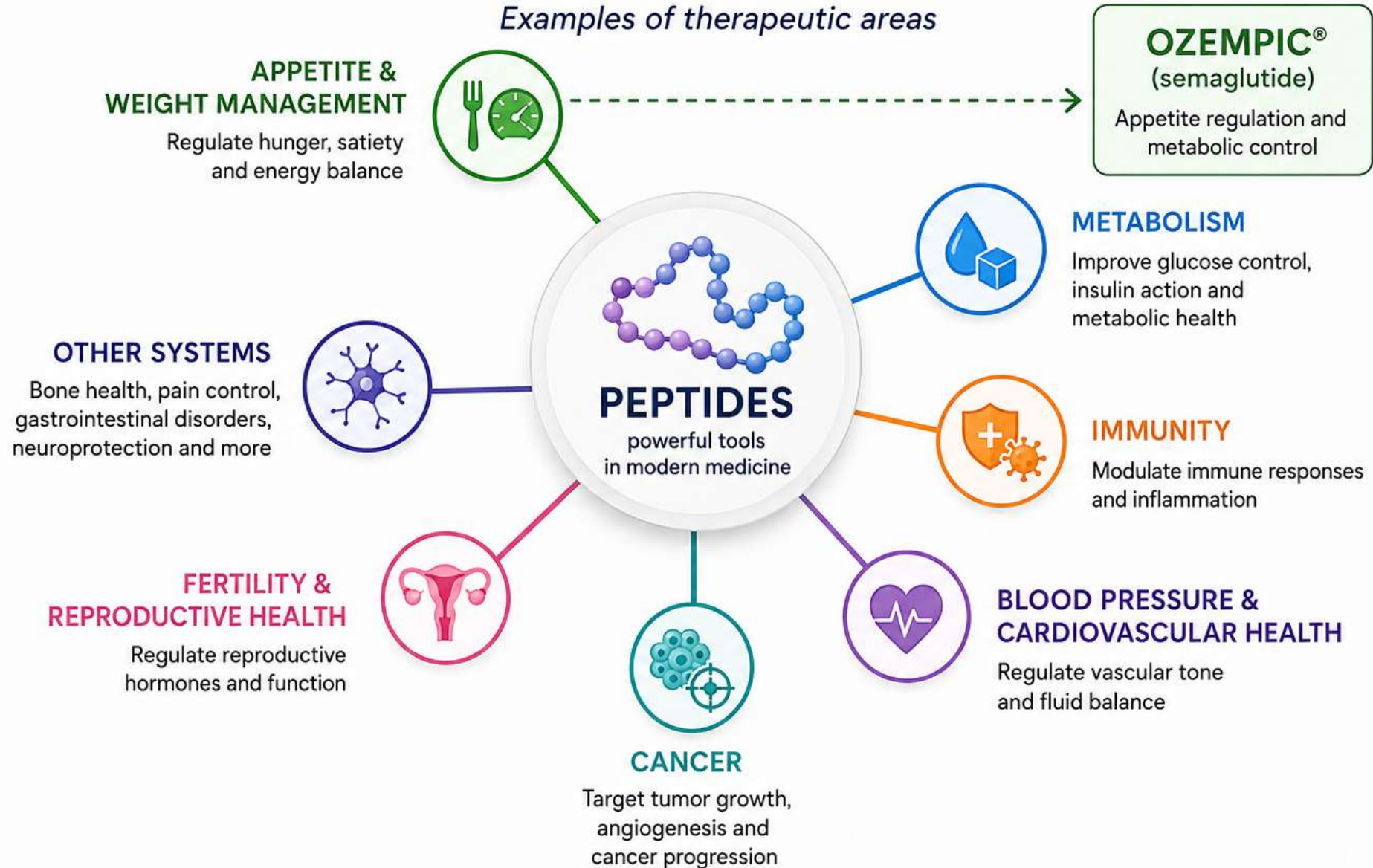


BP: from discovery to modern therapeutic

- **1921 – Insulin:** the first peptide used successfully as a medicine
- **Following decades,** many naturally occurring peptides were discovered
- **Today,** peptides are used as ***biological signalling molecules*** to target appetite, metabolism, immunity, blood pressure, fertility, cancer and many other physiological systems ... in humans
- **One of the best-known examples today:**

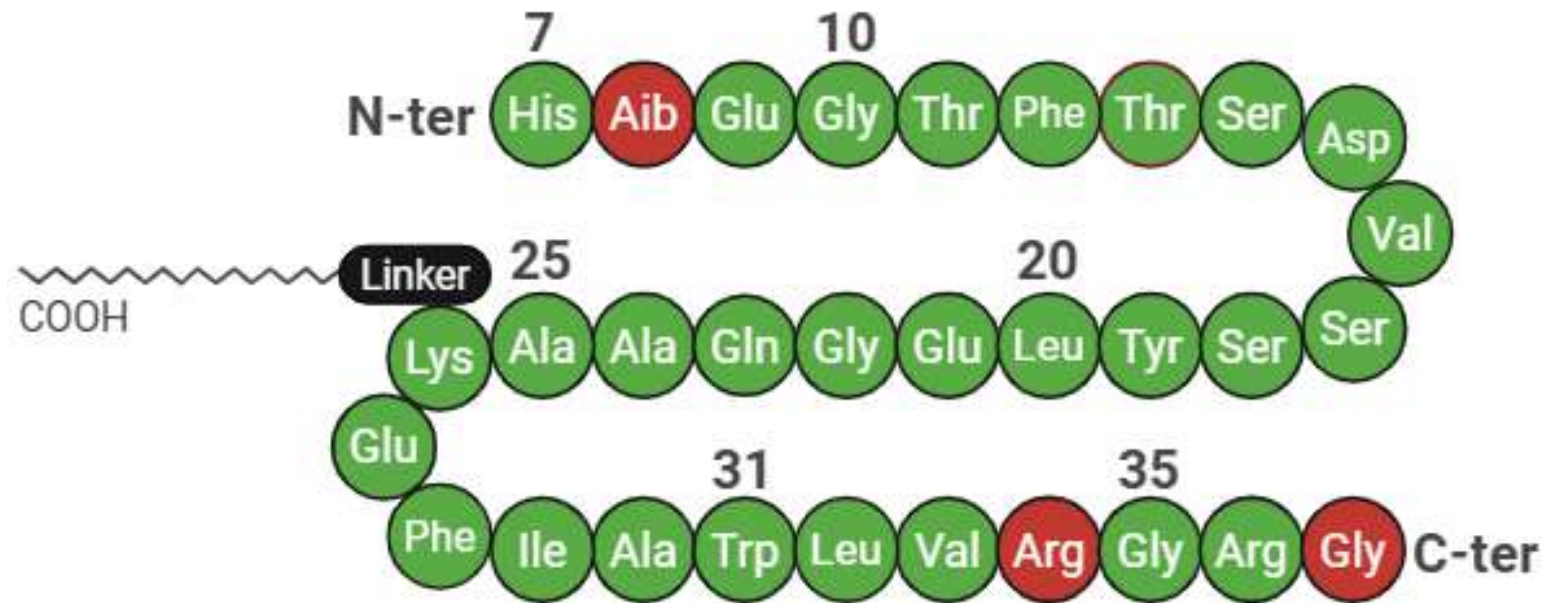
Peptides are used to target many physiological systems

Examples of therapeutic areas

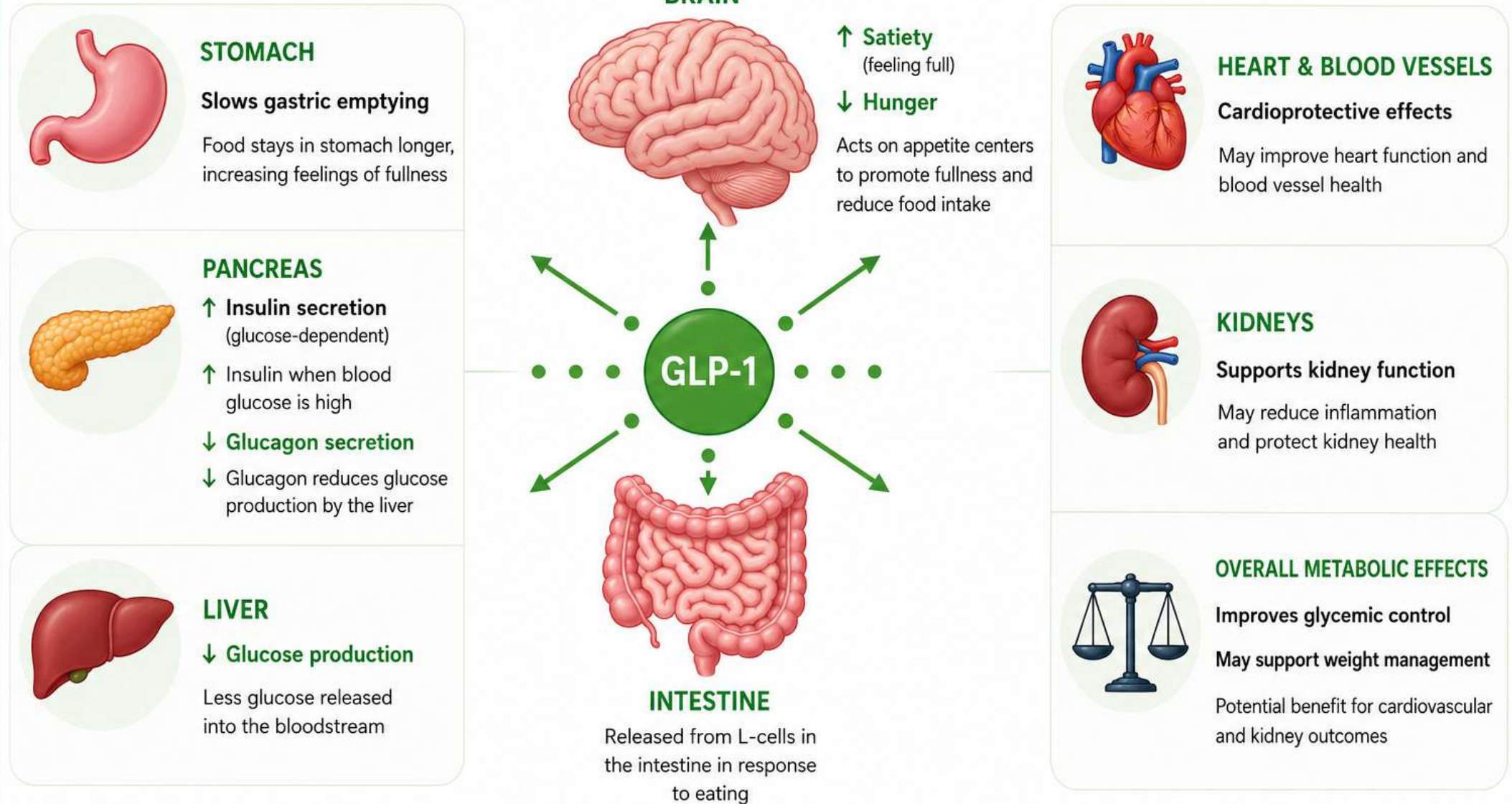




***Ozempic* is a peptide ... a bioactive peptide:**

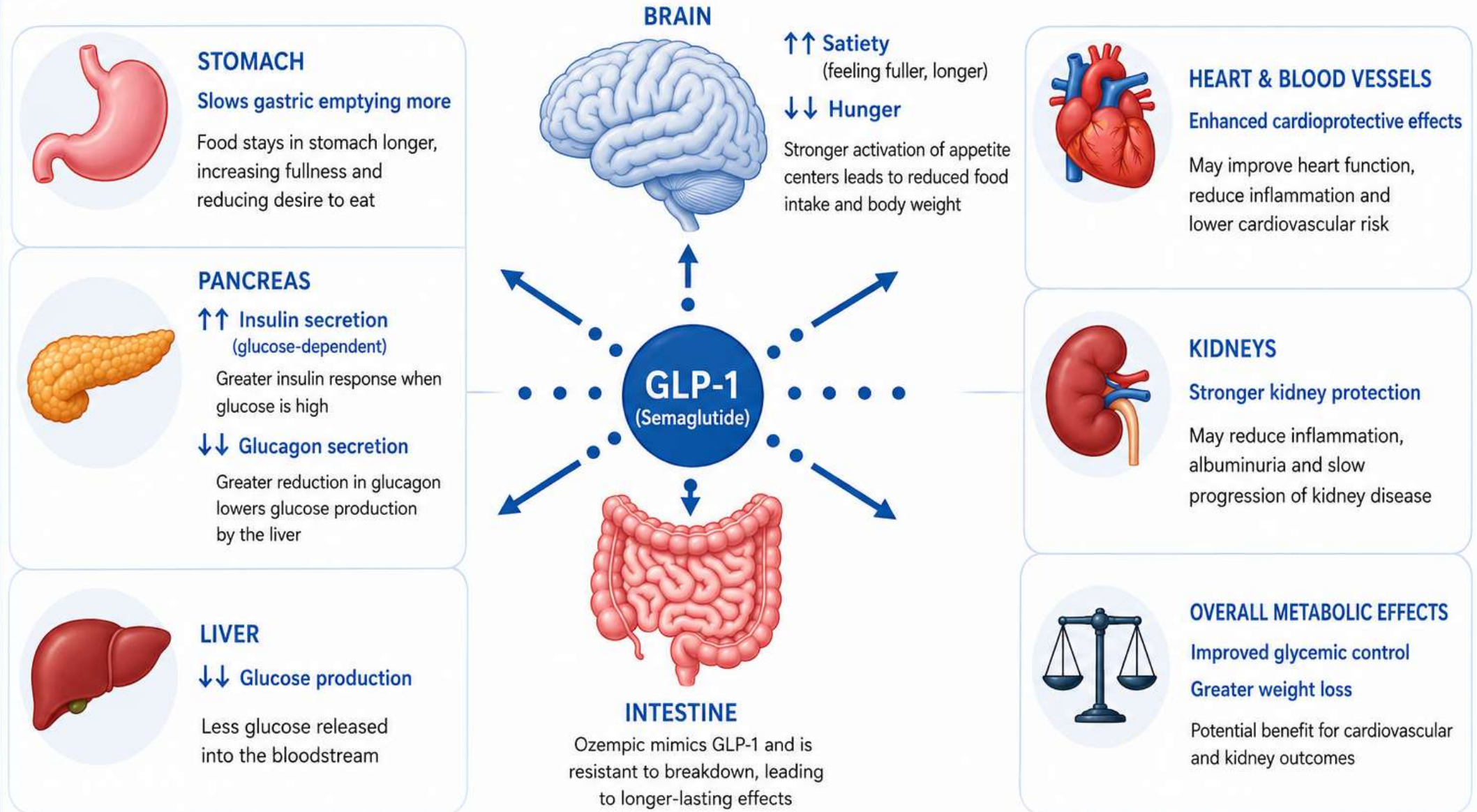


NORMAL GLP-1: HUNGER & SATIETY AND OTHER EFFECTS



Note: Individual responses may vary. Ozempic is a prescription medication used with diet and exercise.

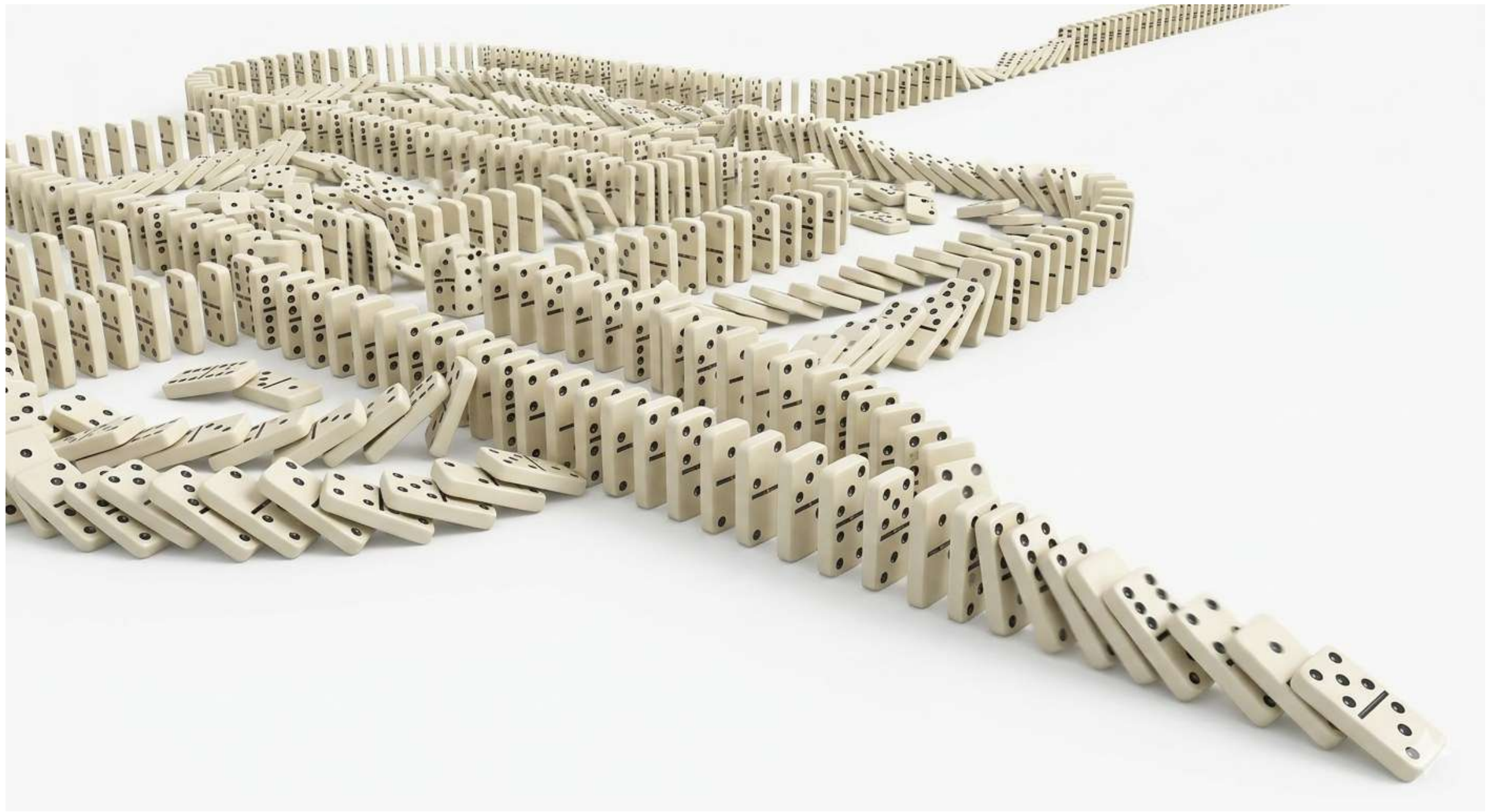
GLP-1 WITH OZEMPIC (SEMAGLUTIDE): ENHANCED EFFECTS



Note: Individual responses may vary. Ozempic is a prescription medication used with diet and exercise.

How can *milligrams* make such a big difference?

- Dose size: 1.0 mg per week
- Bioactive peptides act as signals – not as nutrients
- Many bioactive peptides act as signalling molecules; they produce biological effects at very low doses because their signals are amplified inside cells.
- The secret: **signal amplification**
 - ... through a cellular cascade ... “domino effect”



What do we want in the feedlot?

- Exactly the opposite!
- We're looking for:
 - Appetite ↑
 - Weight gain ↑
- And while we're at it:
 - More protein, less fat – in gain
 - Improved feed efficiency ...

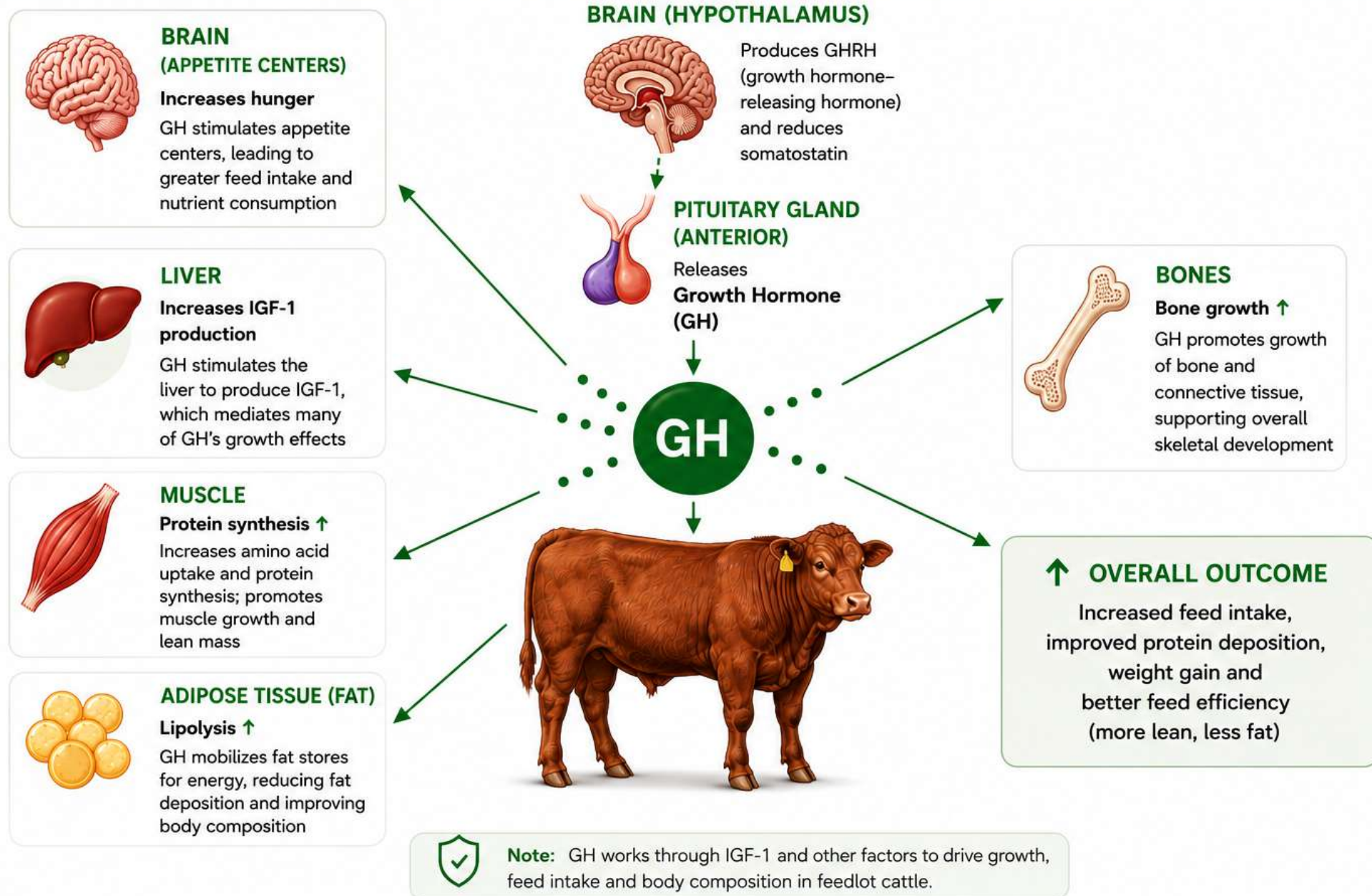
So, let's consider a hypothetical alternative:

- Suppose we have a peptide, similar to *Ozempic*, but working in “the opposite direction” ...
- ... affecting **growth hormone** ... growth hormone ↑

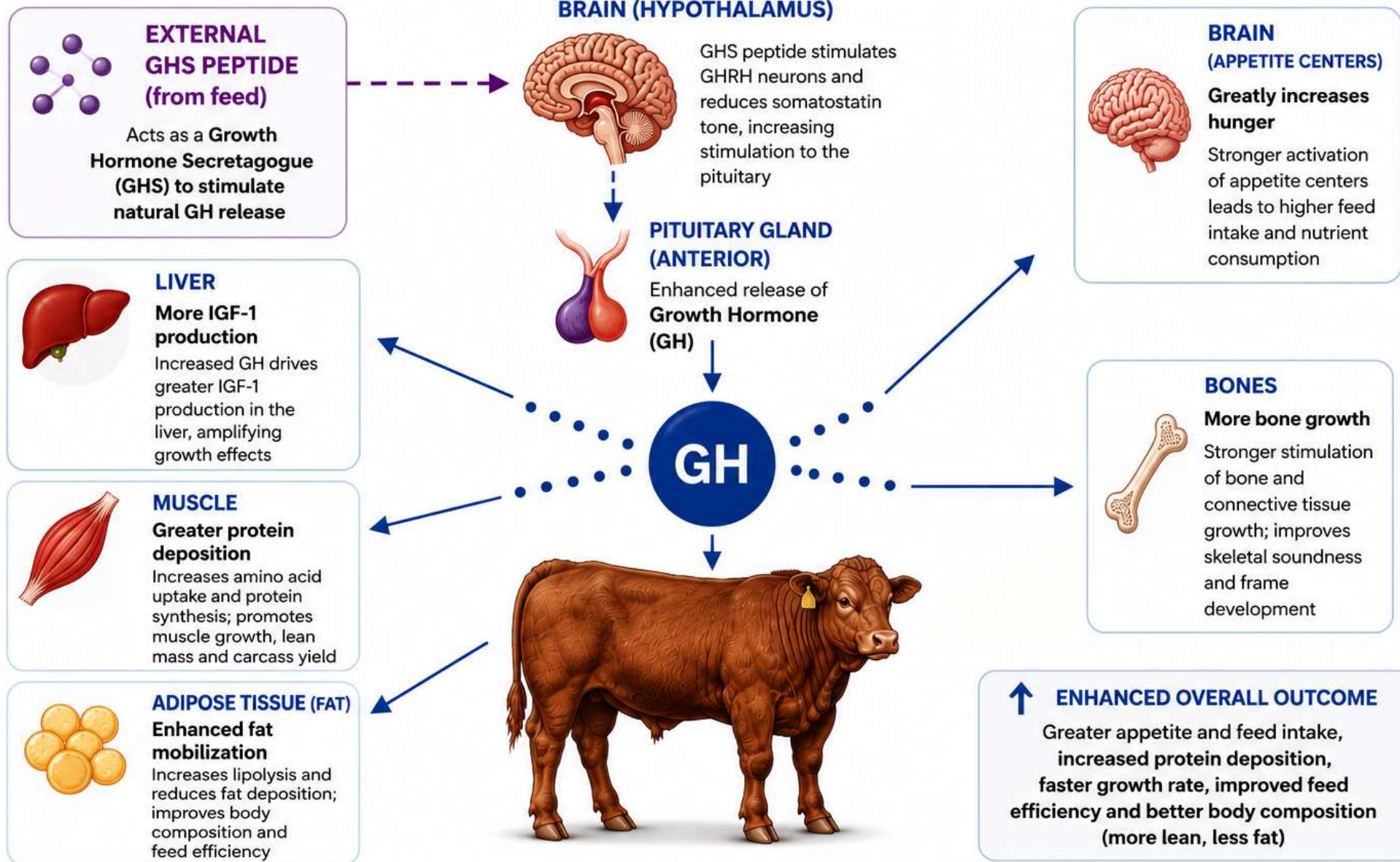


- Growth hormone secretagogue (GHS)

NORMAL GROWTH HORMONE (GH): HOW IT WORKS IN A FEEDLOT STEER



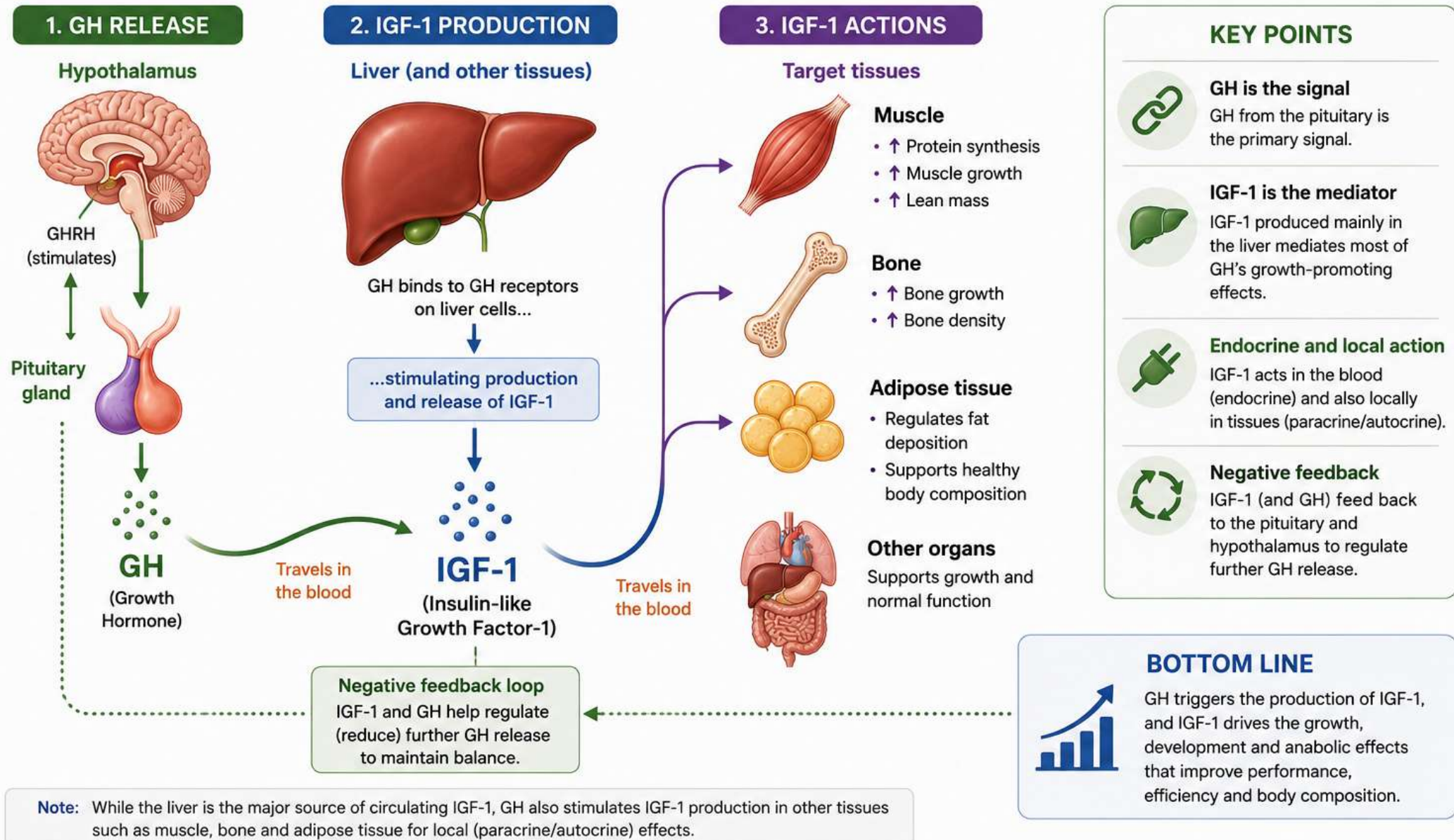
EXTERNAL GHS PEPTIDE SUPPLY: ENHANCED GROWTH AND PERFORMANCE IN A FEEDLOT STEER



Note: External GHS peptide acts by stimulating the natural release of Growth Hormone (GH). Responses may vary with dose, genetics, nutrition, health and management.

THE RELATIONSHIP BETWEEN GROWTH HORMONE (GH) AND IGF-1

*GH stimulates the liver and other tissues to produce IGF-1.
IGF-1 mediates most of the growth-promoting effects of GH.*



Bioactive Peptides: Many Possible Biological Targets

Influencing More Than Just Growth



RUMEN FERMENTATION

- Modulate microbial populations
- Improve fermentation efficiency
- Influence VFA production
- Support rumen wall health



IMMUNITY

- Modulate innate and adaptive immune responses
- Enhance disease resistance
- Support immune balance



GUT HEALTH

- Strengthen gut barrier function
- Enhance nutrient absorption
- Support gut repair
- Promote overall gut health



INFLAMMATION

- Regulate cytokine signaling
- Reduce excessive inflammation
- Support tissue recovery



ANTIOXIDANT DEFENSE

- Neutralize reactive oxygen species
- Reduce oxidative stress
- Support cells during heat stress or disease



STRESS RESILIENCE

- Improve resilience to physiological stress
- Support adaptation to heat, transport and other stressors



Bioactive peptides may influence multiple physiological systems—not just growth.

The specific response depends on the peptide, its target receptor, dose, delivery and bioavailability.

Finding a *useful* bioactive peptide

- Billions of unique proteins in nature
- Proteins contain, on average, **300 to 400 amino acids (AAs)**, ranging from about **20** to over **3,000 AAs**
- How are useful bioactive peptides discovered?

Approach 1 – Discovery (Bottom-up)

Protein source



Enzymatic hydrolysis



Hundreds or thousands of peptides



Screen for biological activity



Identify the active peptide(s)



Approach 1 – Discovery (Bottom-up)

Advantages

- Unbiased
- Can discover completely unexpected BPs

Limitations

- Slow
- Many false leads
- Difficult to identify the active peptide

Approach 2 – Targeted Design (Top-down)

Identify a physiological target



Identify the receptor or pathway



Design or search for peptides predicted to interact with it



Test and optimise



Approach 2 – Targeted Design (Top-down)

Advantages

- More focused
- Higher probability of success

Limitations

- Requires detailed biological knowledge
- Biology is often more complex than expected

Table 1. Published works on bioactive peptides extracted from different natural resources.

Activity	Sequence	Mechanism	Study Model	Source	Reference
Antioxidant	YFMVLVVMLFHR	Free radical scavenging	<i>In vitro</i>	<i>Hermetiaillucens</i>	[125]
Antioxidant	APPPLQHQ	Free radical scavenging	<i>In vitro</i>	<i>Izmir Tulum cheeses</i>	[126]
Antioxidant	LEQQVDDLEGSLEQEKK	Free radical scavenging	<i>In vitro, in silico</i>	<i>Hams</i>	[127]
Antioxidant	GKHQQEEENE ⁺ GSI, VNPESQQGSPR, IGINAENNQRN, FVDAQPQQKEEG.	Free radical scavenging	<i>In vitro</i>	<i>Soymilk</i>	[128]
Antioxidant	AKCAKFQRNMKKVVRG-NH ₂	Free radical scavenging	<i>In vitro</i>	<i>Milk proteins</i>	[129]
Antioxidant	IVVE	-	<i>In vitro</i>	<i>Chlorella (Chlorellavulgaris)</i>	[130]
Antioxidant	YWDAW	ROS Scavenging	<i>In vitro, in vivo</i> (Rat)	<i>Fish</i>	[131]
Antioxidant	MVVACVLPEA	Free radical scavenging	<i>In vitro</i>	<i>saltedjellyfish (Rhopilema hispidum)</i>	[132]
Antioxidant	EMPFPK, PYPQ, PQSV, YFYPE	Free radical scavenging	<i>In silico</i>	<i>Milk</i>	[133]
Antioxidant	VDPP, SSGE, DGEA, NQDK, WTP	Free radical scavenging	<i>In vitro</i>	<i>Salmo salar</i>	[134]
Antioxidant	LLGDV, NLDSS	Free radical scavenging	<i>In vitro</i>	<i>Rice wine</i>	[135]
Antioxidant	LPFR, WGFKPK, PFDLR, FPGEL	Free radical scavenging, tyrosinase inhibitory	<i>In vitro, in silico</i>	<i>Camelliaoleifera</i>	[136]
Antioxidant	FWENHDPTQGMR, SPFEKPGAPGKPTTT, AVGISKPSMPSKPE, SPFEKPGAPGKPTITA, STGISVPGPMGPGSPR, PEEERPKPSRPVVPPLIPPK, HPSDFGADAQAAMSK	Free radical scavenging	<i>In vitro</i>	<i>Freshbeef tripe</i>	[137]
Antihypertensive	IAE	ACE-inhibitory	<i>In vitro</i>	<i>Spirulina (Arthrospira platensis)</i>	[130]
Antihypertensive	YPDLPYH	ACE Inhibitory	<i>In vitro</i>	<i>YellowSilkCocoons</i>	[138]
Antihypertensive	VPP, IPP	ACE inhibitory	<i>In silico</i>	<i>Fermented sour milk</i>	[133]

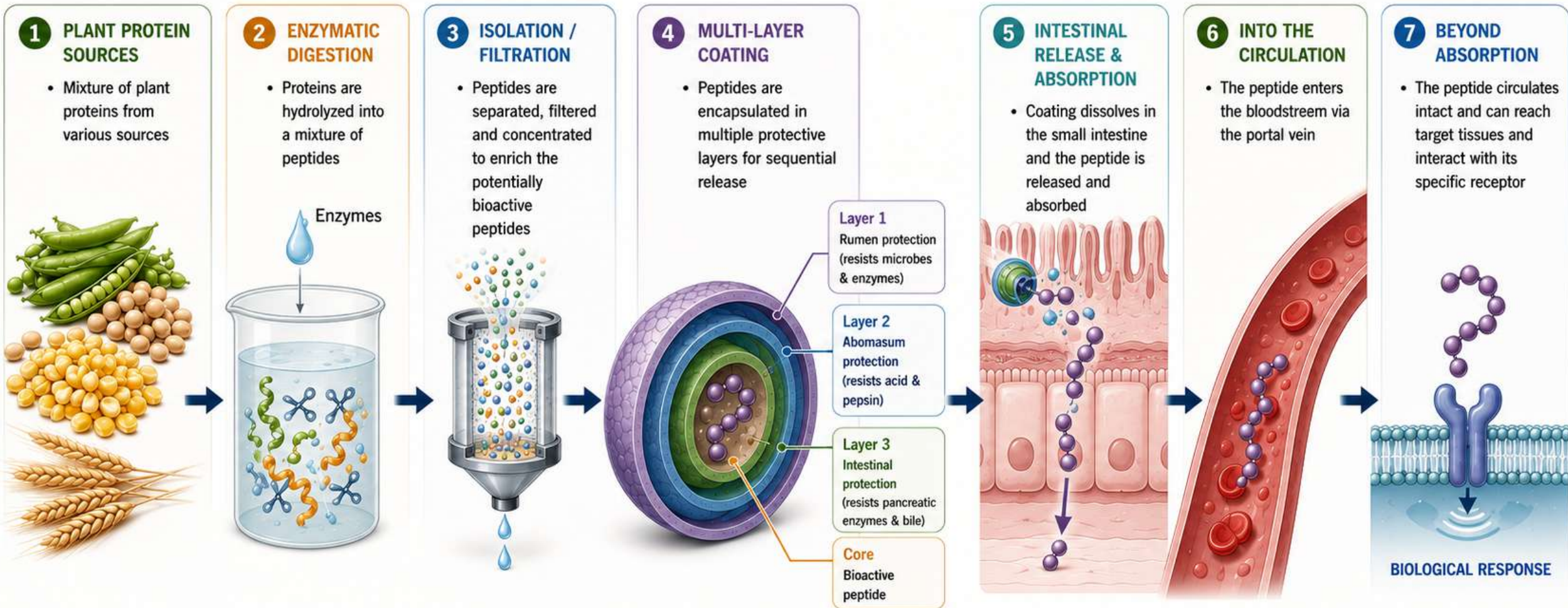
Summary of Bioactive Peptides (Adapted from Table 1)

Rodríguez-Cabello et al. (2026)

Biological activity	Main mechanism	Typical study model	Examples of natural sources
Antioxidant	Free-radical (ROS) scavenging	In vitro, in silico, rodents	<u>Common:</u> Milk; Fish; Soy; Cereal grains; Spirulina; Salmo salar; Microalgae <u>Interesting:</u> Salted jellyfish; Yellow silk cocoons; Cicada chrysalis; Fresh beef tripe; Rice wine; Snake venom; Fly larvae; Frogs; Turkish cheese
Antihypertensive	ACE inhibition	In vitro, in silico, rodents	
Antithrombotic	Inhibition of platelet aggregation	In vitro, rodents	
Antimicrobial	Inhibition of bacterial growth	In vitro, in silico	
Antidiabetic	DPP-IV inhibition; α -glucosidase inhibition	In vitro, in silico	
Anticancer	Cancer cell elimination / growth inhibition	In vitro	
Osteoprotective	Suppression of inflammation	In silico	

From Plant Proteins to Bioactive Peptide in the Circulation

The journey of a bioactive peptide



Designed to withstand the harsh conditions of the rumen



Protects against acid and pepsin in the abomasum



Protects against pancreatic enzymes and bile in the small intestine



Releases where absorption occurs for maximum peptide recovery



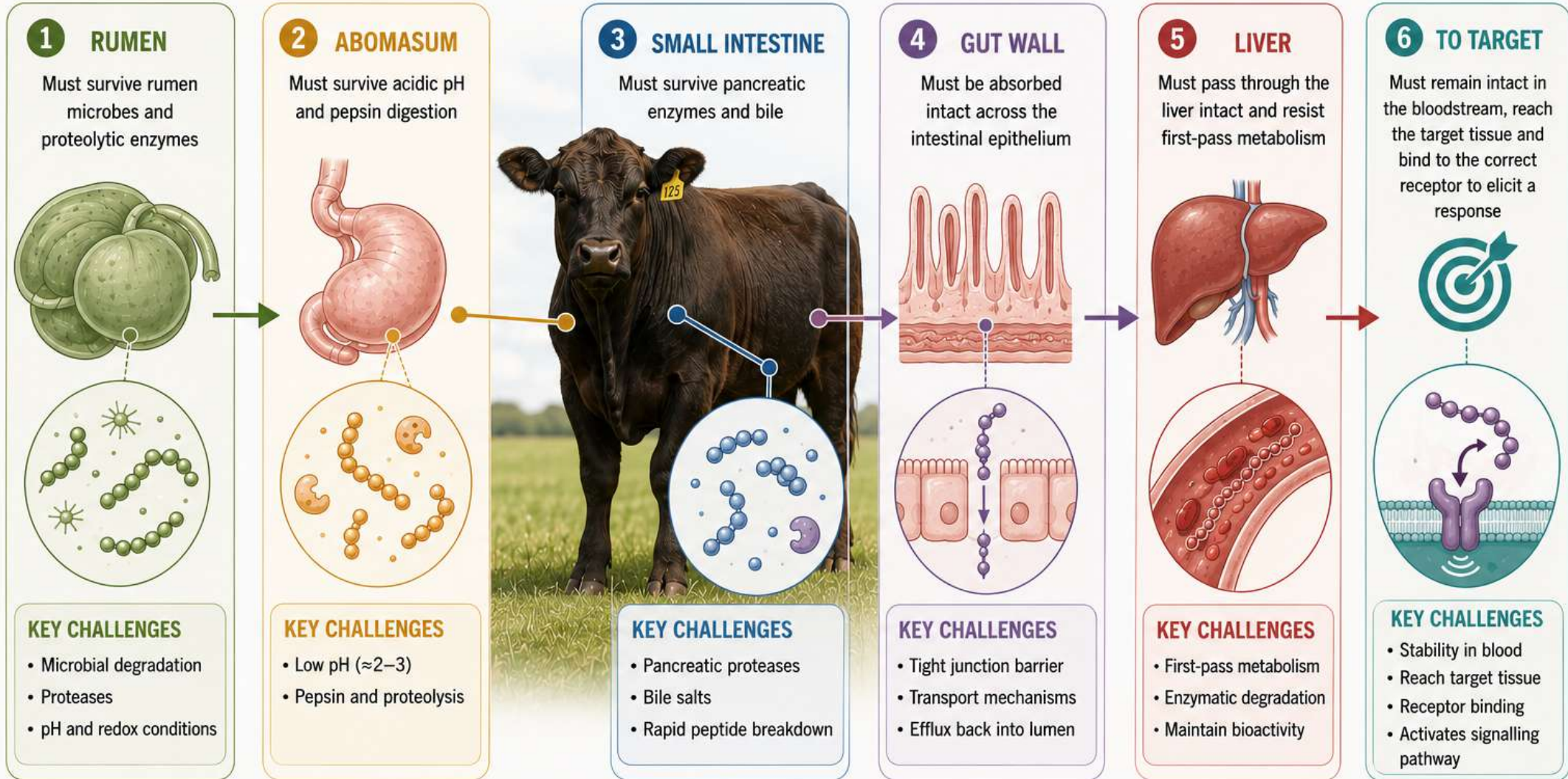
Delivers the peptide intact into the circulation



Enables the peptide to reach target tissues and exert its physiological effect

The Journey of a Bioactive Peptide in a Ruminant

Overcoming barriers from feed to target tissue



A bioactive peptide must survive every step of this journey to reach its target and exert a biological effect.

Bioavailability is the greatest challenge in ruminants.

There are really **three stages** in the BP story:

1. Discovery

1. Which proteins contain interesting peptide sequences?
2. Bioinformatics, databases, AI, and laboratory screening all play a role.

2. Release

1. How do we liberate those peptides from the parent protein?
2. This is where enzyme selection, pH, temperature, reaction time, etc., become critical. **Bioactive Peptide Engineering**

3. Delivery

1. Once you have the peptide, how do you get it through the rumen, stomach, and intestine intact and absorbed into the bloodstream?
2. This is where encapsulation and delivery technology become important.

Supporting data?!

- ... "There is a paucity of empirical data regarding the use of bioactive peptides in feedlot and dairy cattle"
- Reasons:
 - BPs for ruminants is a rather novel field
 - The rumen is a challenging obstacle
 - ... not many peptides get through it intact
- Some data from Brazil
 - Demonstrative purposes, rather than supporting evidence

Feedlot pen trial

- 224 yearling Nelore cattle
- 16 pens; 14 animals per pen
- Feeding period: 101 days
- Treatments:
 - Control
 - 1 gram BP product per kg feed DM
 - 2 grams BP product per kg feed DM
 - 3 grams BP product per kg feed DM

Feedlot pen trial

Variable	Treatment (g BP product/kg feed DM)				Ctrl vs Trt
	Control	1	2	3	
Initial BW (kg)	376	377	376	377	
Feed intake (kg/d)	11.1	11.4	11.0	11.3	0.56
ADG (kg)	1.710	1.850	1.790	1.820	0.03
FE (gain: feed)	0.157	0.165	0.170	0.160	0.26
Cold carcass weight (kg)	300	309	307	304	0.03

ADG: 140 grams ↑

Cold carcass weight: 9 kg

↑

Feedlot individual-pen trial

- 40 yearling Nelore cattle
- Individual pens
- Feeding period: 79 days
- Treatments:
 - Control
 - 1 gram BP product per kg feed DM

Feedlot individual pen trial

Variable	Control	BP product	P-value
Initial BW (kg)	435	432	0.656
Feed intake (kg/d)	9.00	9.76	0.086
ADG (kg)	1.49	1.62	0.251
Dressing %	56.3	57.0	0.188
Cold carcass weight (kg)	311.3	320.8	0.071

Cold carcass weight: 9.5 kg ↑

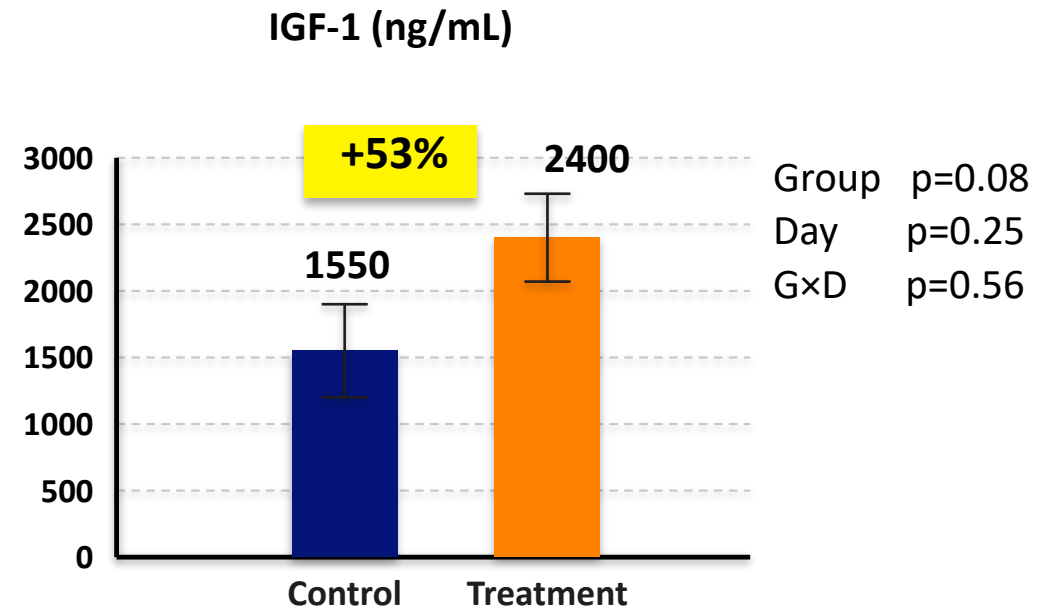
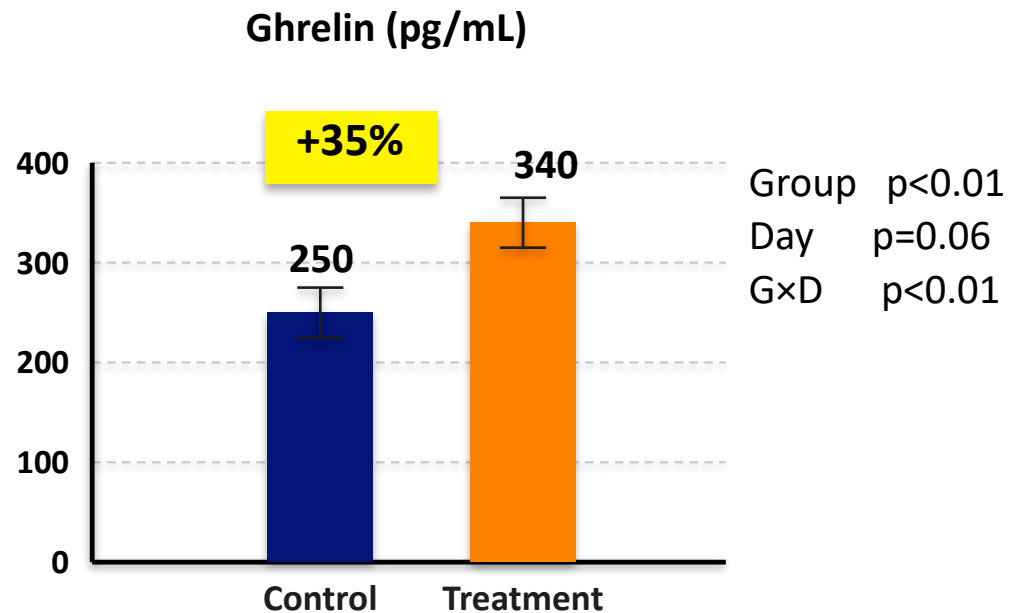
Dairy cow trial 1 (Correia *et al*, 2024)

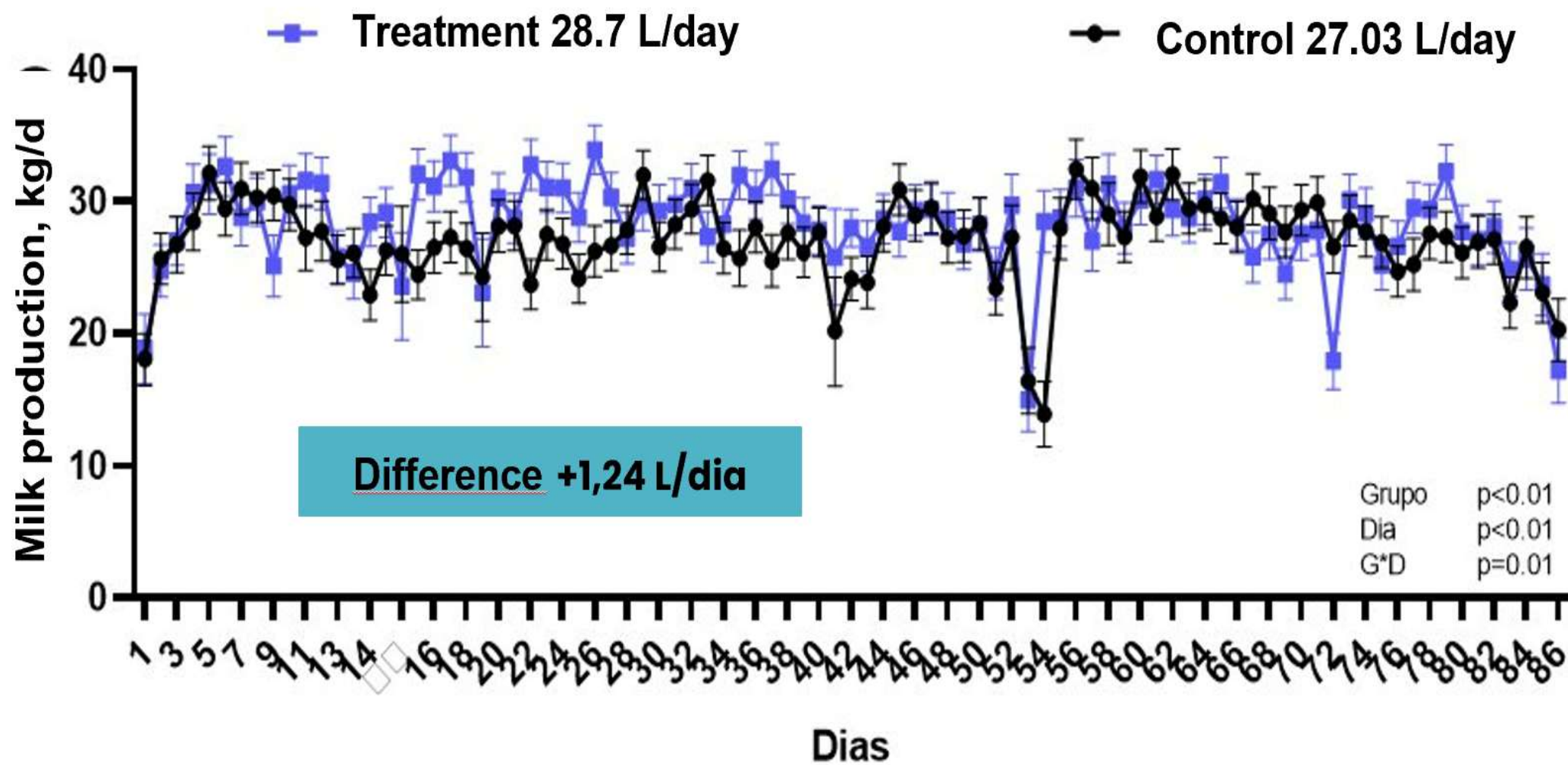
Federal University of Pelotas (Brazil)

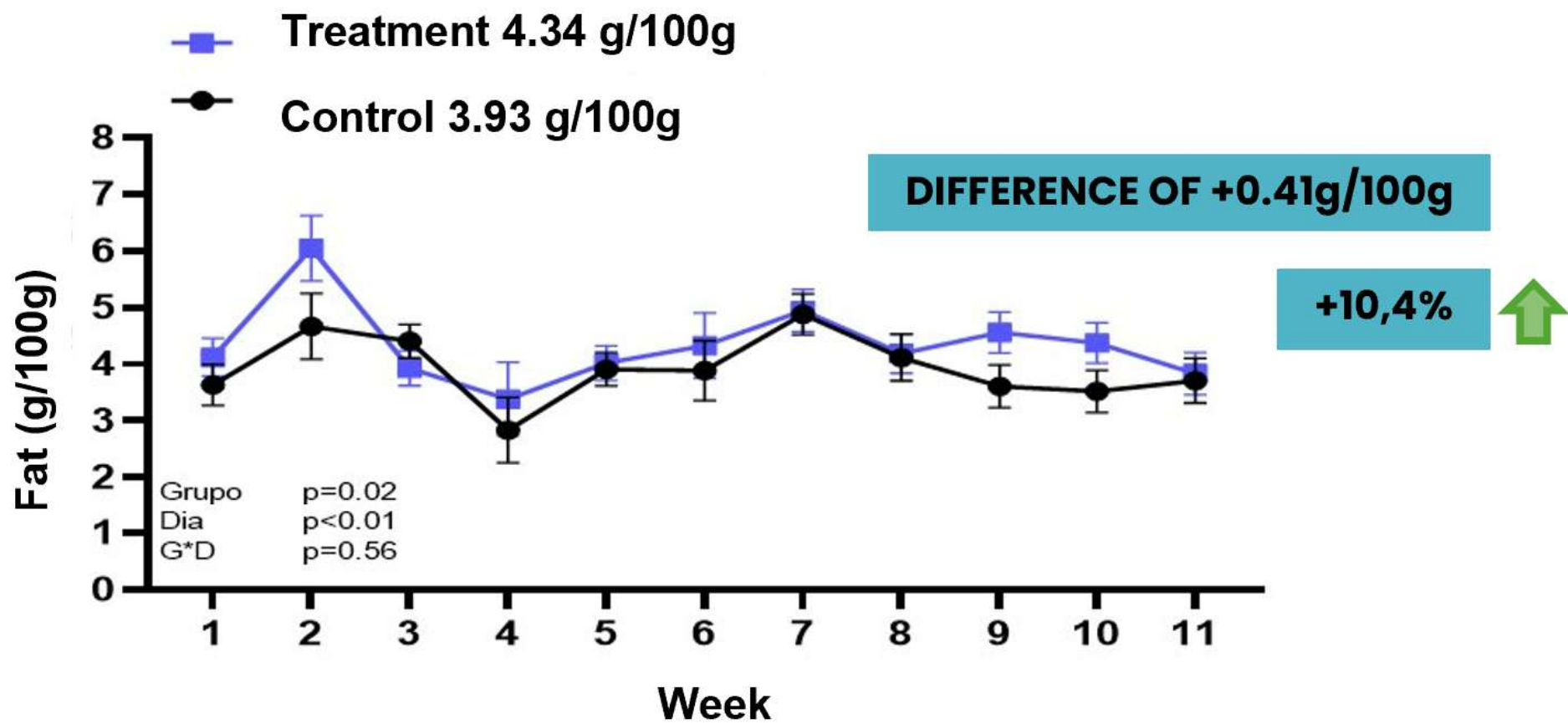
NUPEEC-HUB – Center for Research, Education and Extension in Livestock Production

- 37 Holstein cows
- 36 months of age (avg)
- Primiparous
- 60 to 150 DIM
- 1 g BP product per kg of TMR DM vs Control (no BP product)
- Fed ad lib; daily DMI *ca* 23 kg
- Milked twice daily
- Blood samples collected on Days 0, 7, 14, 21, 28, 35, 42, 60, 75, and 90

BP product increased *ghrelin* production and tended to increase *IGF-1* levels







Dairy cow trial 2 (Nehme Marinho *et al*, 2024)

University of Florida

- 18 Holstein cows
- 3 x 3 Latin square; 28d experimental periods
- Multiparous
- From 68 DIM
- 0, 1, or 2 g BP product per kg of TMR DM
- Milked thrice daily

+2,1 kg

+4,41%

+130g

+8,66%

Table. Effect of supplemental bioactive peptides on performance of Holstein cows

Item	Treatment			SEM	P-value	
	T0	T1	T2		Linear	Quadratic
DMI, kg/d	26.8	26.7	26.8	0.6	0.96	0.85
Milk, kg/d	52.3	52.8	52.5	0.9	0.70	0.21
ECM, kg/d	47.6	49.7	49.6	1.0	0.02	0.09
ECM/DMI, kg/kg	1.80	1.89	1.86	0.06	0.32	0.25
Fat, %	2.91	3.07	3.13	0.14	0.01	0.41
Fat, kg/d	1.50	1.63	1.63	0.06	0.01	0.12
Fatty acids, kg/d						
< 16 C	0.38	0.41	0.41	0.02	0.01	0.10
16 C	0.51	0.56	0.56	0.02	0.02	0.09
> 16 C	0.46	0.50	0.51	0.02	0.004	0.19
Protein, %	2.77	2.80	2.80	0.04	0.20	0.37
Protein, kg/d	1.45	1.48	1.47	0.04	0.14	0.08

Dairy cow, bioactive peptides, production

Concluding remarks

- For humans, BPs have arrived – it is the new bandwagon
- For ruminants?
 - Makes sense; holds promise
 - Faces challenges
 - *(Will BPs make it to the feedlot and the dairy?)* ***cost : benefit ?***
- With the rapid growth in technology (including AI), expect to see bioactive peptides in the feed technology toolbox sooner rather than later ***keep a lookout for it ...***
- **Bioactive Peptides** may well be the next ***champion!***

THANK YOU!

