Milk Bioactive Peptides

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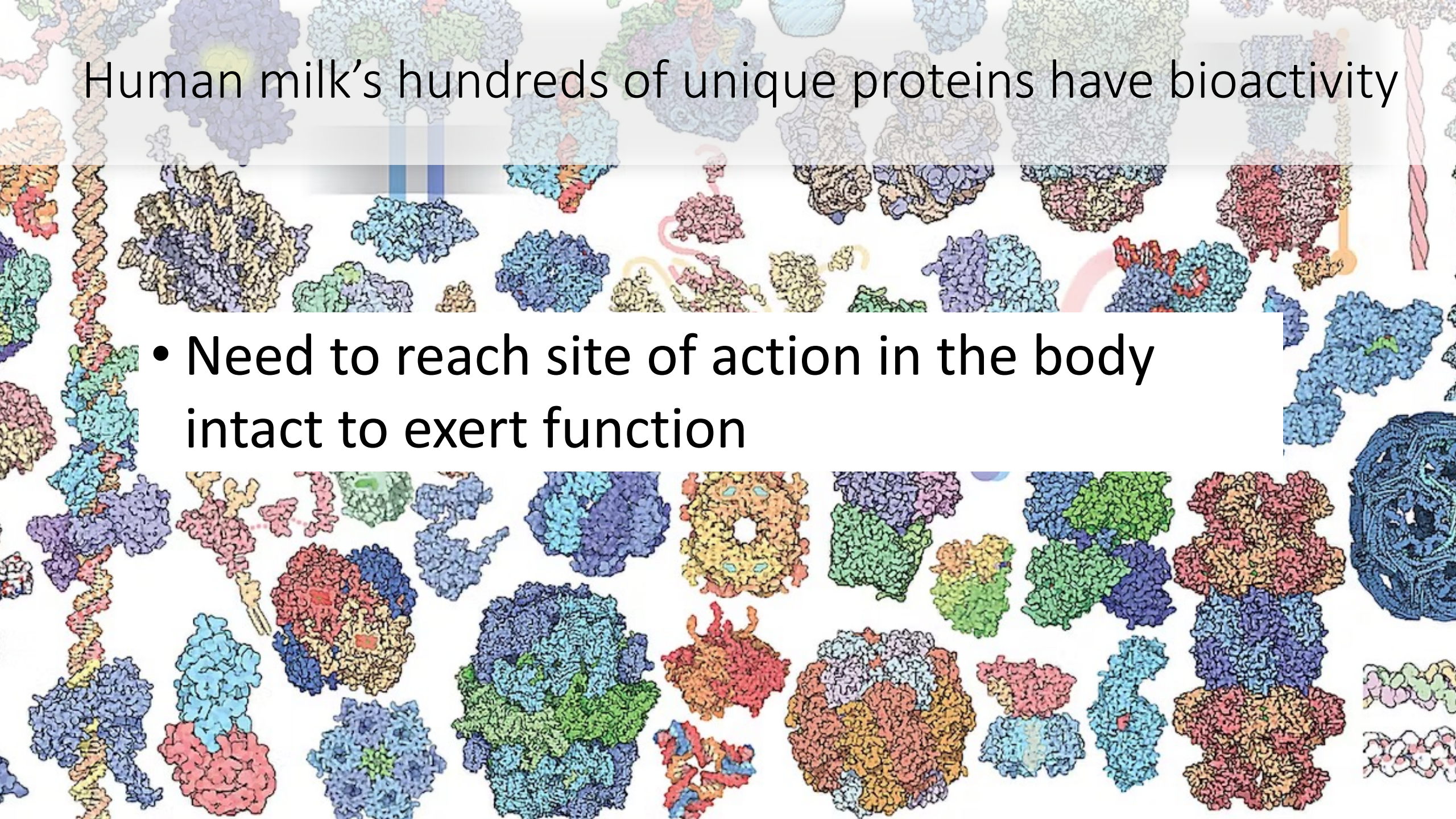
Milk has evolved over more than 250 million years

- Each compound must benefit the infant
- Milk evolved to a complete nourishment system for suckling neonates: both basic nutrients and bioactives

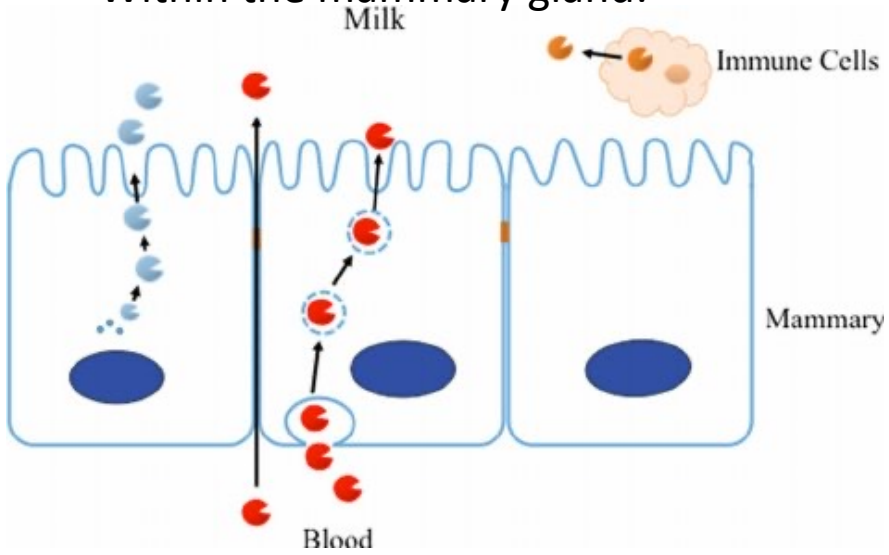
Human milk's hundreds of unique proteins have bioactivity



- Need to reach site of action in the body intact to exert function

Milk proteins can be digested to peptides

Within the mammary gland:

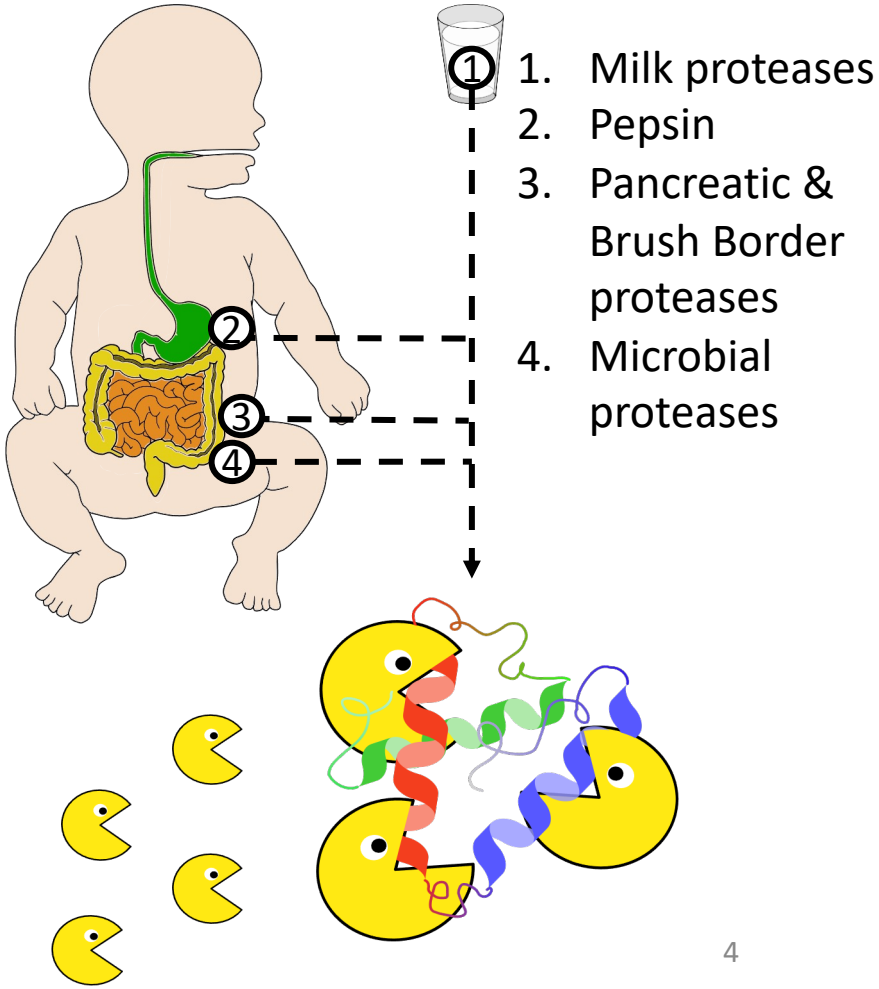


Intact Milk Proteins

Peptides

During fermentation:

Across digestion:



1. Milk proteases
2. Pepsin
3. Pancreatic & Brush Border proteases
4. Microbial proteases

Hundreds of bioactive milk peptides have been discovered

Milk Bioactive Peptide Database

MBPDB Search

MBPDB multiple search

MBPDB add single entry

MBPDB add multiple entries

MBPDB add proteins

MBPDB help

Contact Us

Dallas Lab Peptide Tools

Remove Domains

Auto Skyline output enhancement

Homology Search

PepEx

Data by: Søren Drud Nielsen, Robert L. Beverly, Yunyao Qu, David C. Dallas (www.dallaslab.org)

Web development by: Nikhil Joshi & Adam Schaal (UC Davis Bioinformatics Core), Søren Drud Nielsen

The database is SQLite 3.7.17 on a CentOS 7.1.1503 server. The front-end of the site was developed using HTML, Python 2.7.5 and Django 1.9.7 and is served by Apache 2.4.6. The back-end scripts were written in PERL and Python and use Blast+ 2.5.0.

admin

Milk Bioactive Peptide Database

MBPDB Search

If you are using this database please cite:
Nielsen, Søren Drud, Robert L. Beverly, Yunyao Qu, and David C. Dallas. 2017. "Milk Bioactive Peptide Database: A Comprehensive Database of Milk Protein-Derived Bioactive Peptides and Novel Visualization." *Food Chemistry 232 (October)*. Elsevier: 673–82.

Latest Peptides Added to Database

Time Approved	Peptide	Protein ID	Functions
May 23, 2018, 3:25 a.m.	ILDKEGIDY	P00710	DPP-IV Inhibitory
May 23, 2018, 3:25 a.m.	ILELA	O97943	DPP-IV Inhibitory
May 23, 2018, 3:25 a.m.	LLQLEAIR	O97943	DPP-IV Inhibitory

Search Milk Bioactive Peptide database

Single Peptide Sequence

If sequence is empty (and no file is chosen below), then it will search all sequences and search options will be ignored.

OR file with multiple peptides (Example):

Choose File No file chosen

A simple text file with one column of peptides.

Search type: Sequence Truncated Precursor

Similarity threshold: 100% Scoring matrix: Identity

Get extra output?

Protein ID

If protein ID is empty, then it will search all protein IDs.

Function (choose from dropdown or type in your own)

If function is empty, then it will search all functions.

Species (choose from dropdown or type in your own)

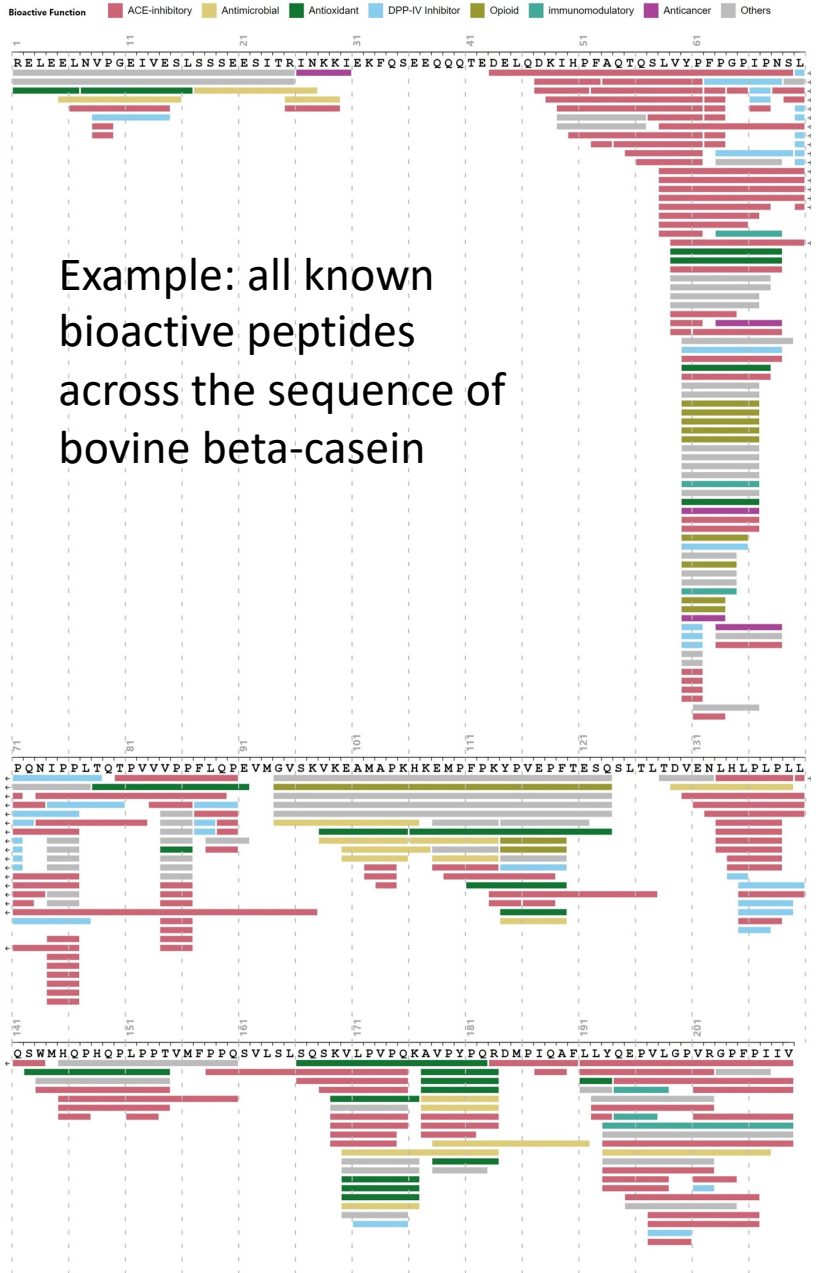
If species is empty, then it will search all species.

Category

If category is empty, then it will search all categories.

Download results (Tab-separated values file)

Search DB

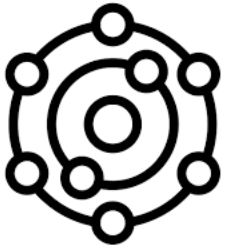


Example: all known bioactive peptides across the sequence of bovine beta-casein

Milk peptides have many different functions

Blood pressure control

Antimicrobial



Anti-oxidant

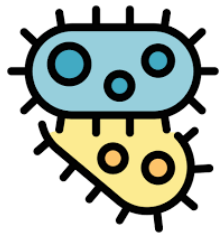
Glucose control

Immune defense

Opioid (regulating gut function)

Anti-cancer

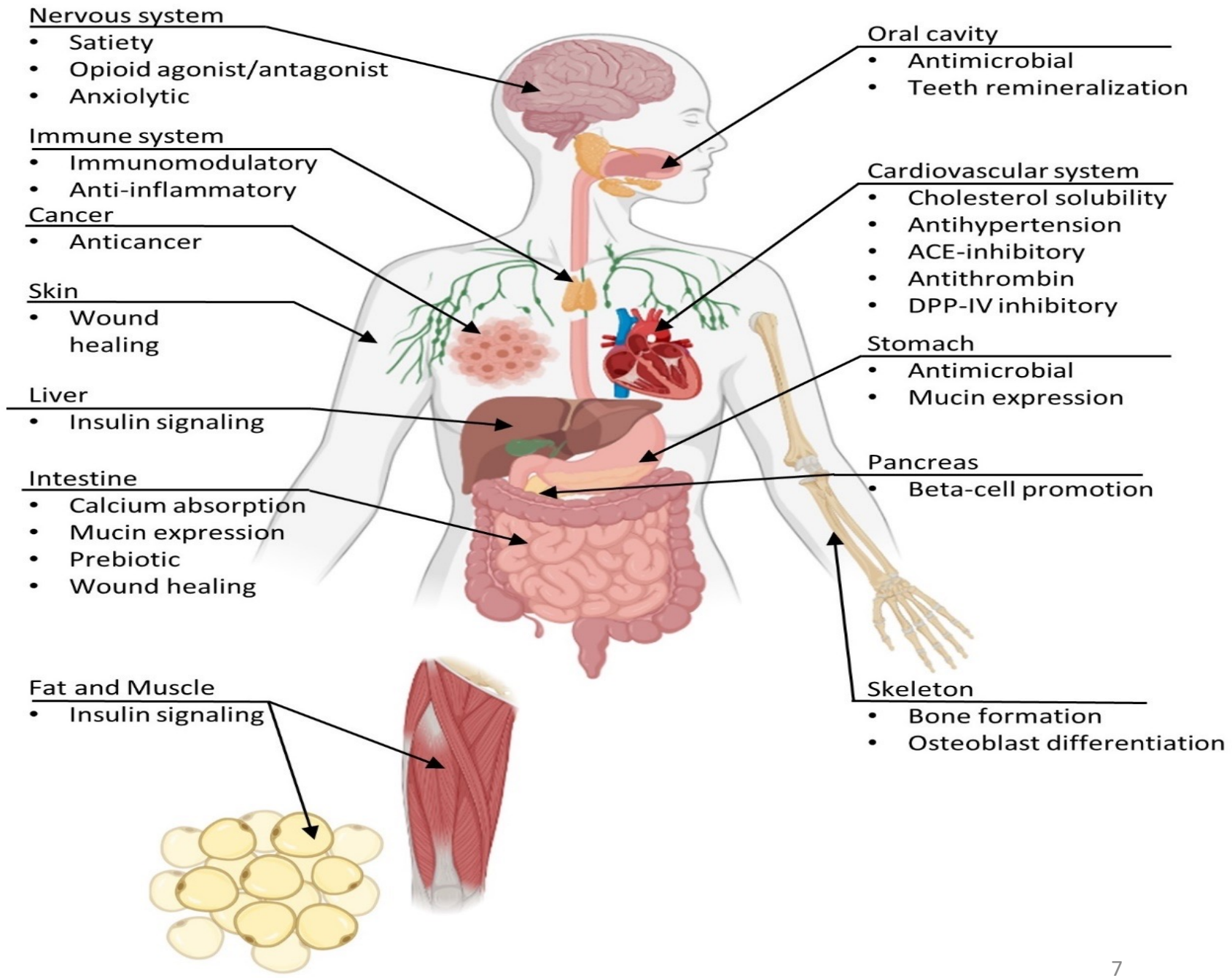
Calcium absorption



Prebiotic

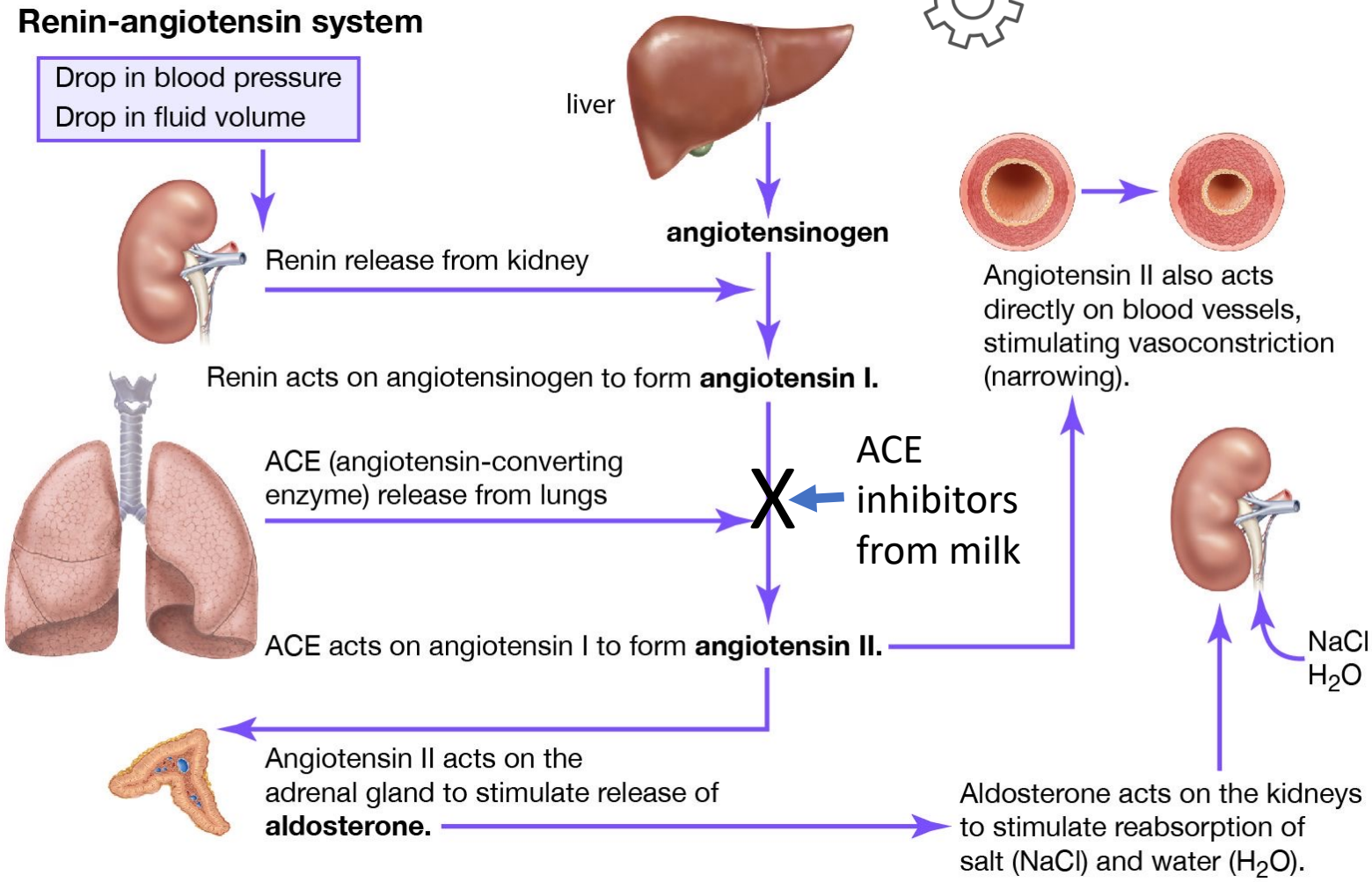
Milk peptides could affect many parts of the body

- Milk peptide function depends on whether each can reach sites of action in the body
  - E.g., blood pressure-regulating peptides would need to reach the bloodstream



Blood pressure control peptides (angiotensin-converting enzyme (ACE) inhibitors)

Mechanism of action:



High blood pressure common, increases risk of cardiovascular disease

355 milk peptides known to inhibit angiotensin-converting enzyme (ACE)

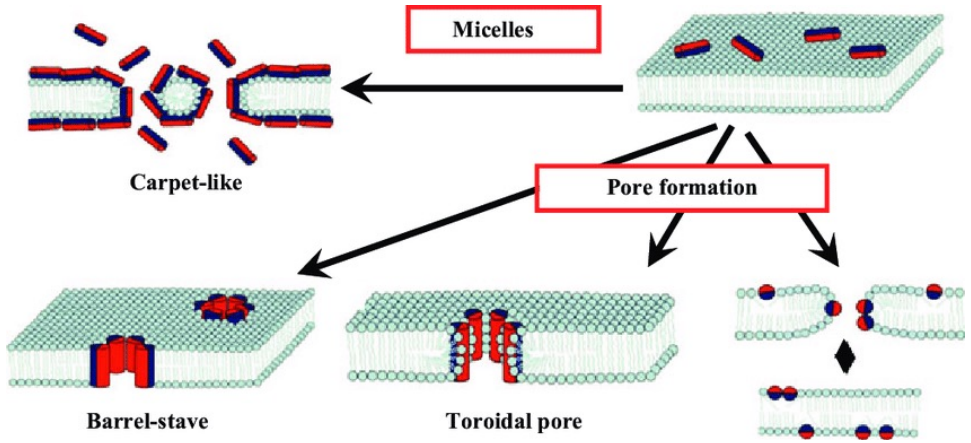
Some milk peptides can lower blood pressure in rodents

Some milk peptides can lower blood pressure in humans

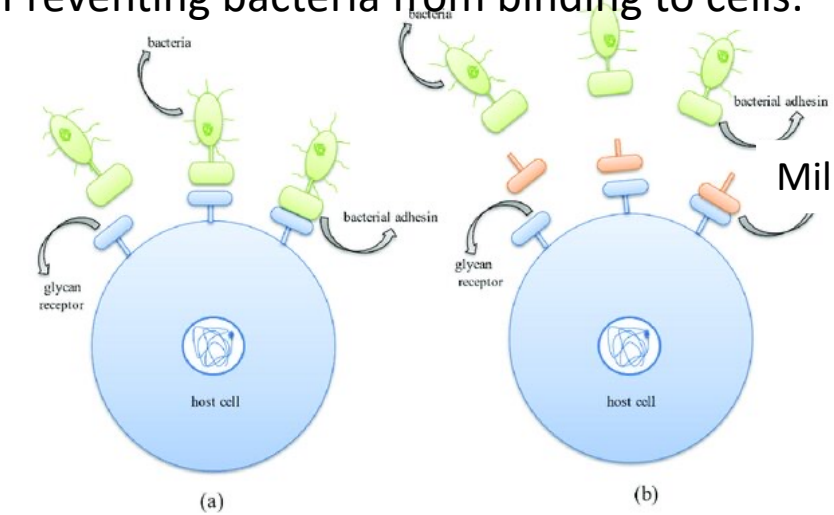
- E.g., Isoleucine-proline-proline (IPP) and valine-proline-proline (VPP) from casein

Antimicrobial peptides

Destroying bacterial membranes:



Preventing bacteria from binding to cells:



Milk peptide

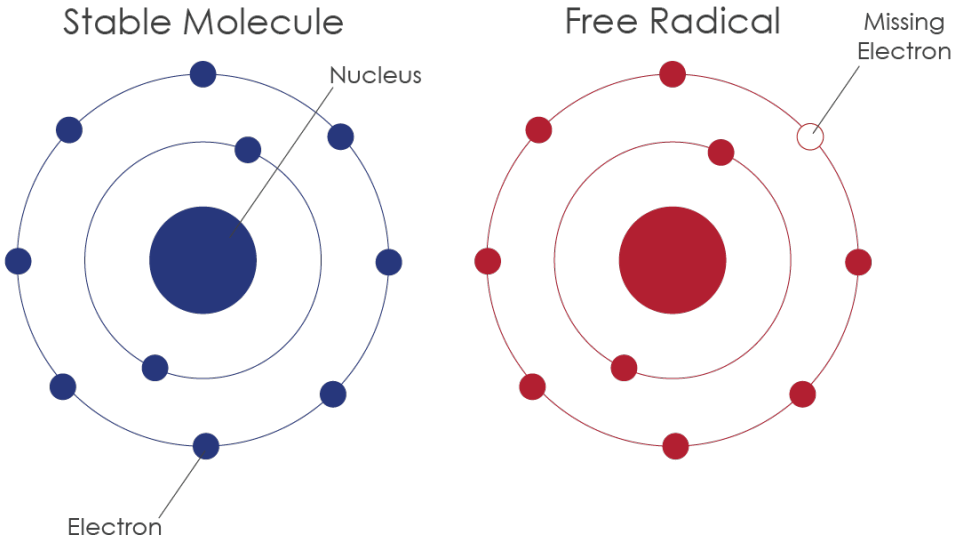
Growing need for novel antibiotics.
Protection from infection.

186 milk peptides

Feeding kappa-casein glycomacropeptide to piglets reduced E. coli adherence to intestinal villi

Clinical studies needed!

Antioxidant peptides



Excessive oxidation associated with cardiovascular disease, gut inflammation

Peptides scavenge free radicals or up-regulate antioxidant enzymes in cells

91 milk peptides can exert antioxidant activity in vitro

Some animal studies show reduction of oxidative stress

No direct evidence in humans, but whey protein supplementation shown to increase plasma antioxidant capacity.
Need more clinical studies!

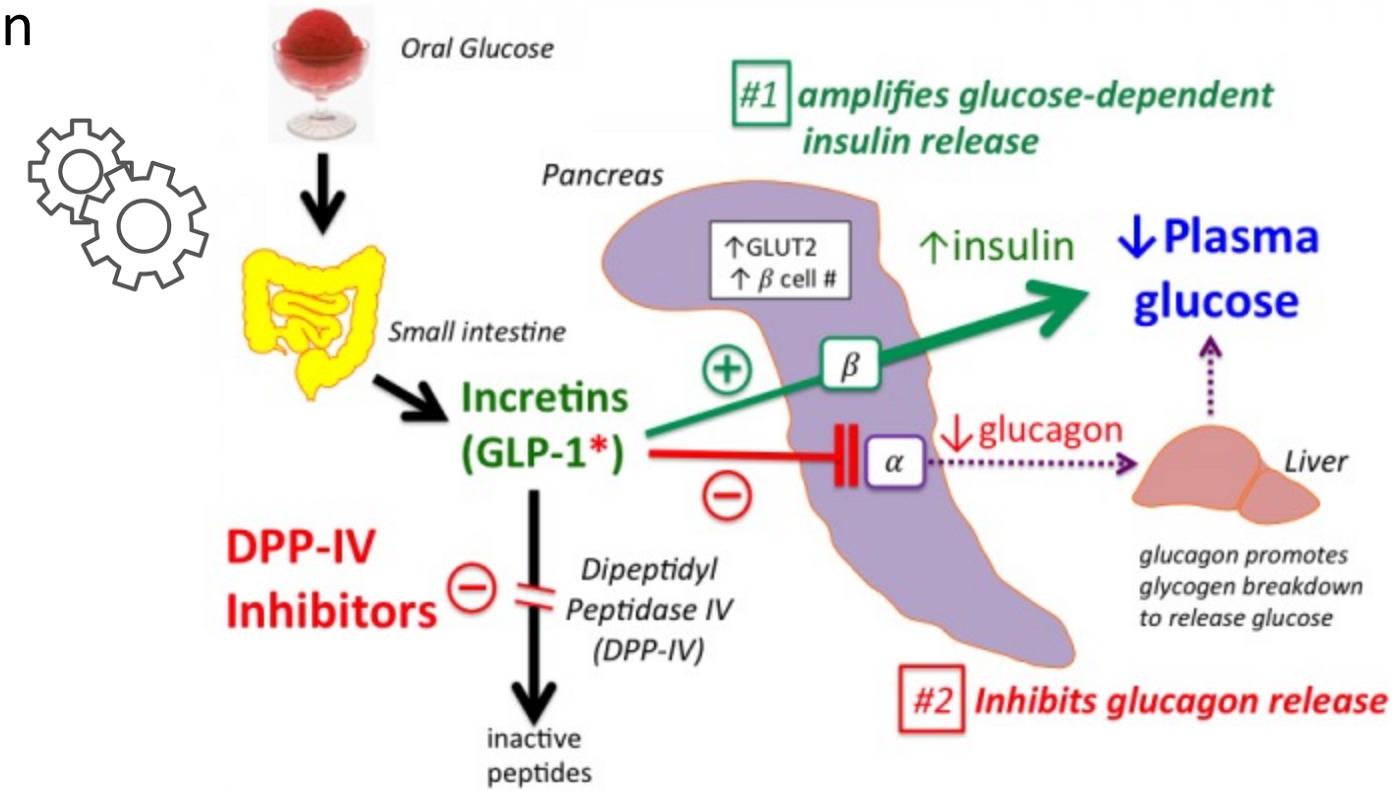
Blood glucose control peptides

Poor blood glucose regulation is key component of type II diabetes, can damage tissues

79 milk peptides inhibit dipeptidyl peptidase IV (DPP-IV)

Feeding a milk DPP-IV-inhibitory peptide to rats lowered blood glucose in response to a glucose tolerance test

Clinical studies needed!



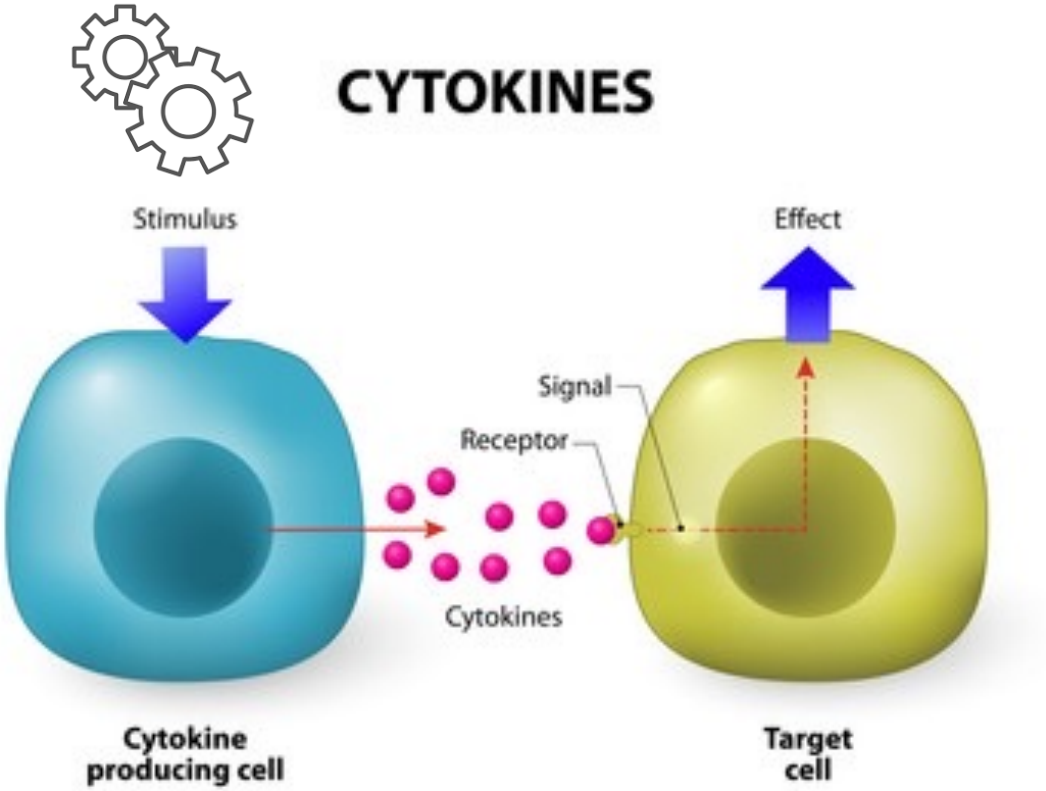
Immune system-regulating peptides

Underactive immune response increases risk of infection. Overactive immune response increases risk for autoimmune diseases and allergy

46 milk peptides modulate immune cell function

Several peptides fed to rodents inhibited inhibited inflammation

Clinical studies needed!



Opioid peptides

Gastrointestinal transit time affects nutrient absorption and gut comfort. Mucin helps protect from infections. Analgesics are used for pain relief.

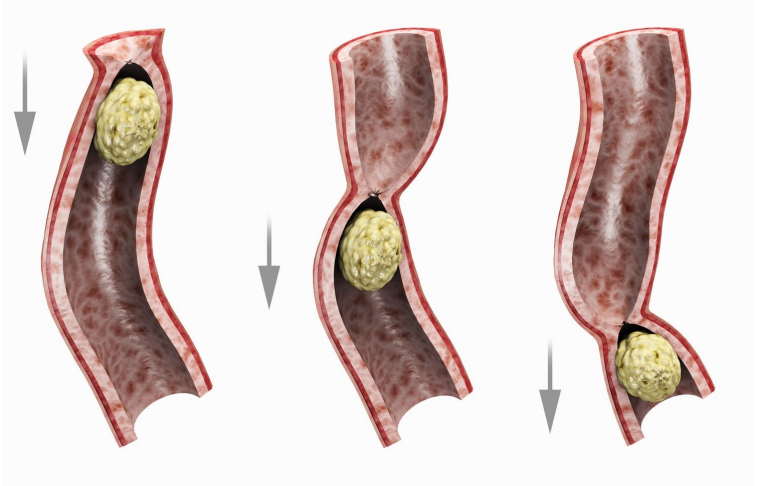
26 milk-derived opioid peptides

Indirect support that milk opioid peptides alter gastrointestinal transit time.
Opioid peptide can increase mucus secretion.
No studies found on analgesic effect.

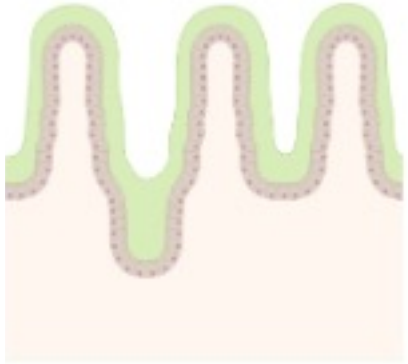
Indirect support that milk opioid peptides alter gastrointestinal transit time. Need more clinical studies!
No clinical studies examining milk opioid peptide effects on mucin secretion
No clinical studies found on analgesic effects.

Opioid binds to opioid receptor
In the gut, this triggers:

1. Changes in rate of gut motility



2. Mucin secretion



In the brain, could trigger pain relief

Anti-cancer peptides

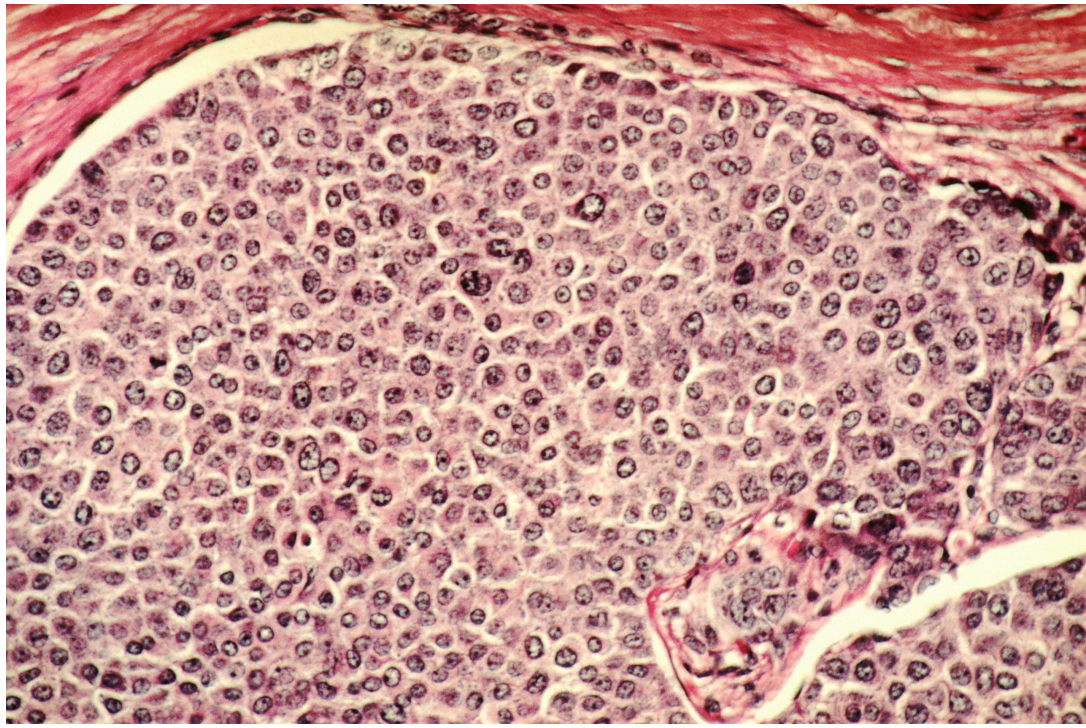
Novel treatments are needed for cancers

Varied, understudied

18 milk peptides have anti-cancer activity

In mice, some injected milk peptides can decrease tumor growth

Clinical studies needed



Cancer cells

Calcium absorption peptides

Calcium supports healthy bones and teeth. Increasing calcium absorption could help prevent osteoporosis and cavities.

Phosphorylated amino acids on peptides bind to calcium ions, keeping them soluble, enhancing absorption

5 known milk calcium absorption-enhancing peptides in vitro

In mice, feeding a calcium-binding milk peptide from milk for 7 weeks increased serum calcium, femur length and femur calcium levels

Equivocal results from using milk calcium phosphopeptides for teeth remineralization and cavity protection in humans
No clinical studies evaluating the impact of milk peptides on bone growth or structure

Prebiotic peptides

Enhancing the growth of beneficial bacteria in the gut improve gut health

Likely: chains of sugar (glycosylation) attached to peptides feed these bacteria (which have specific enzymes to break them down)

3 milk peptides known to promote growth of commensal bacteria in vitro

No direct animal studies

Clinical studies needed

Bifidobacteria

Summary and next steps

- Large array of bioactive peptides in milk that may help improve human health
- Opportunities for product development and marketing
- Need research:
  - Determine where peptides survive to and their bioactive potential
  - Animal and clinical testing
- Further research can help enhance perceived value of milk products and enhance consumer health

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Questions?

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