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Fatty Bacteria in the Intestine and Collagen Bacteria (Dominio: Bacteria Woese, Kandler & Wheelis 1990): Therapies and Biotechnology

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Abstract: Recent evidence has suggested that the intestinal microbiota is involved in energy regulation and the inflammatory process, an environmental factor related to the pathophysiology of obesity. The microbiota contains a variety of living microorganisms that colonize the intestine, and its development occurs throughout the life cycle from birth to adulthood. Collagen is one of these ingredients with functional characteristics. It is a protein of animal origin, whose function in the body is to contribute to the structural integrity of the tissues in which it is present. However, with the onset of adulthood, collagen deficiency begins to be noticed, as the body reduces its production, making its supplementation necessary. This review aims to study fatty bacteria in the intestine and collagen bacteria. Data were collected using a quantitative and descriptive approach, through books and the following databases: SciVerse Scopus, Scientific Electronic Library Online (SciELO), the Academic Search Tool (Scholar Google), Academia.edu., Researchgate, Library of Medicine and National Institute of Health (USA), (PubMed) and Scientific, Latin American Literature in Health Sciences (LILACS). The search was developed using the subject descriptor, mosquito, diseases, filaria, hosts, transmission, diagnosis, and treatment referred to in periodicals, through a literature review. In the initial search, the titles and abstracts of the articles were considered for the broad selection of likely works of interest, with the abstracts being highlighted.

Keywords: Genes, Gut, Inflammatory, Microbiota, Obesity.

Research Paper

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1. INTRODUCTION

1.1. Bacteria

Are organisms formed by a single unicellular cell and can occur isolated or in groups. It is also worth mentioning that bacterial cells are smaller than eukaryotic cells. Bacteria are prokaryotic beings, that is, they do not have a defined nucleus, and their genetic material is concentrated in a region that is not surrounded by a membrane. This region is called the nucleoid. In addition to the genetic material present in the nucleoid, small circular DNA molecules called plasmids can be observed in bacteria, which replicate independently (Santos, 2008; World Health Organization, 2024).

Bacterial cells also lack cellular organelles, structures surrounded by membranes suspended in eukaryotic cells' cytosol. Ribosomes are present in this type of cell; however, they are different from those observed in eukaryotic cells, being smaller and with differences in protein and RNA content. Bacterial cells have a cell wall located outside the plasma membrane. The function of the cell wall is to ensure that the cell's shape is maintained and to protect it. Many species of bacteria rely on flagella to move (Santos, 2008; World Health Organization, 2024).

These structures can occur across the entire cell surface or be concentrated at the ends. Bacteria can also have fimbriae, filamentous, hair-like structures these organisms use to adhere to the substrate. Another appendage found in bacteria is pili, which are structures that hold cells together during DNA transfer. Some authors use pili and fimbria as synonyms, indicating that sexual pili are appendages related to the transfer of genetic material (Santos, 2008; World Health Organization, 2023).

1.2. Objective

This review aims to study fatty bacteria in the intestine and collagen bacteria.

2.0. METHODS

Data were collected using a quantitative and descriptive approach, through books and the following databases: SciVerse Scopus, Scientific Electronic Library Online (SciELO), the Academic Search Tool

(Scholar Google), Academia.edu., Researchgate, Library of Medicine and National Institute of Health (USA), (PubMed) and Scientific, Latin American Literature in Health Sciences (LILACS). The search was developed using the subject descriptor, mosquito, diseases, filaria, hosts, transmission, diagnosis, and treatment referred to in periodicals, through a literature review. In the initial search, the titles and abstracts of the articles were considered for the broad selection of likely works of interest, with the abstracts being highlighted.

3. FATTY BACTERIA IN THE INTESTINE

3.1. The Microbiota in Energy Regulation and the Inflammatory

Recent evidence has suggested the involvement of the intestinal microbiota in energy regulation and the inflammatory process, being an environmental factor related to the pathophysiology of obesity. The microbiota contains a variety of living microorganisms that colonize the intestine, and its development occurs throughout the life cycle from birth to adulthood. The interaction between genetic factors determines the amount and type of food ingested, lifestyle, and the use of antibiotics (Borges *et al.*, 2014).

At the last International Congress on the Human Microbiome, in Vancouver, Martin Blaser, from New York University, presented a paper comparing two groups of mice raised in comparable conditions: the first received low doses of antibiotics daily, while the second was not medicated. Ultimately, the mice fed antibiotics had less diverse intestinal flora than the others, weighed 15% more, and accumulated 25% more fat in the liver hepatic steatosis (Figure 1) (Nieuwdorp *et al.,* 2013; Borges *et al.,* 2014).

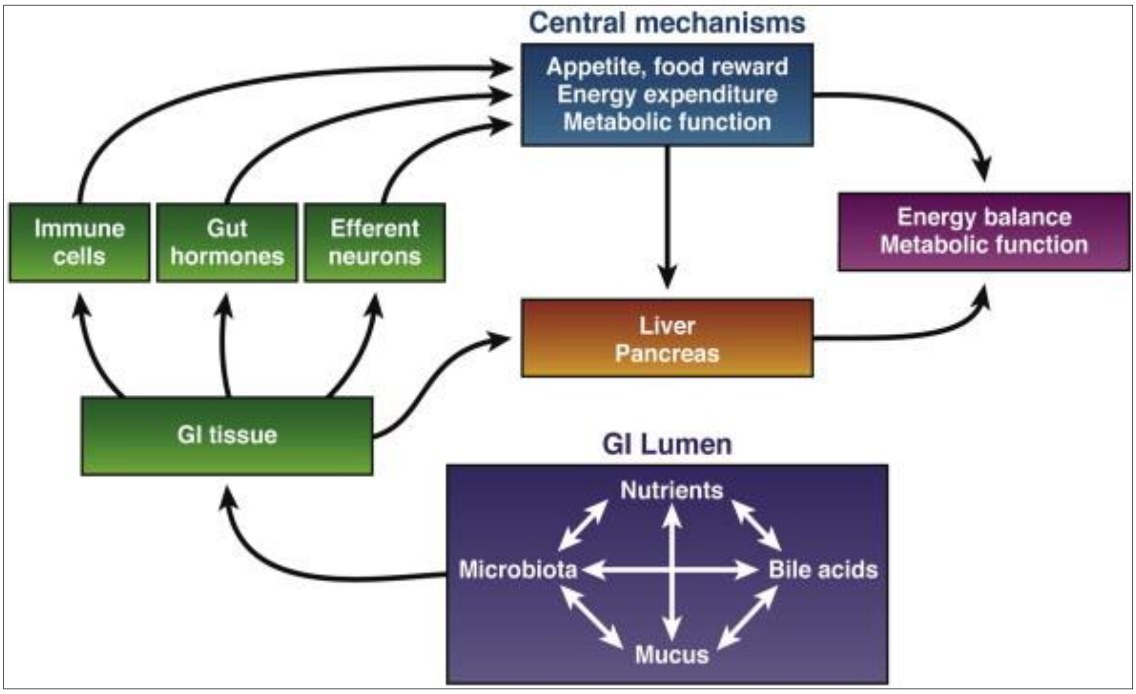

Figure 1: Three major pathways via which intestinal microbiota can affect human metabolism. Host metabolism and energy balance are influenced by an interplay of nutrients, bile acids, intestinal microbiota, and the composition of the epithelial mucus layer. The processes in the intestinal lumen exert their effects systematically on metabolism via the production of gut hormones, affecting (para)sympathetic tone and regulation of immune cell action. GI, gastrointestinal

Source: Doi: org/10.1053/j.gastro.2014.02.008

Researchers from the Meta-HIT consortium, dedicated to investigating the relationship between health conditions and bacterial genes in the human intestine, compared the genes of bacteria in the feces of 177 lean Danes with those detected in 122 obese or overweight compatriots. While the feces of most participants contained around 600,000 different bacterial genes, at least a third of the obese ones had around 360,000, indicating less biodiversity (Lenharo, 2011; Varella, 2011; Andrade, 2015; Vieira and Zaramel, 2022; Flório *et al.,* 2024).

Six species of bacteria were identified, and their presence or absence made it possible to predict, in more than 80% of cases, whether they belonged to the intestinal flora of a thin or fat person. In contrast, the analysis of genetic factors predisposing to obesity made it possible to predict correctly only 58% of the time. Gut bacteria may play a role in weight gain, according to a study from the University of Copenhagen published in the scientific Journal Microbiome. According to the researchers, some bacteria in the gut microbiome are more efficient at extracting energy from food than others, which explains why some people gain weight more easily, even when following a healthy diet. The researchers analyzed fecal samples from 85 people (Figure 2) (Delzenne and Cani, 2007; Dibaise *et al.*, 2008; Conde and Borges, 2011; Silva *et al.*, 2013).

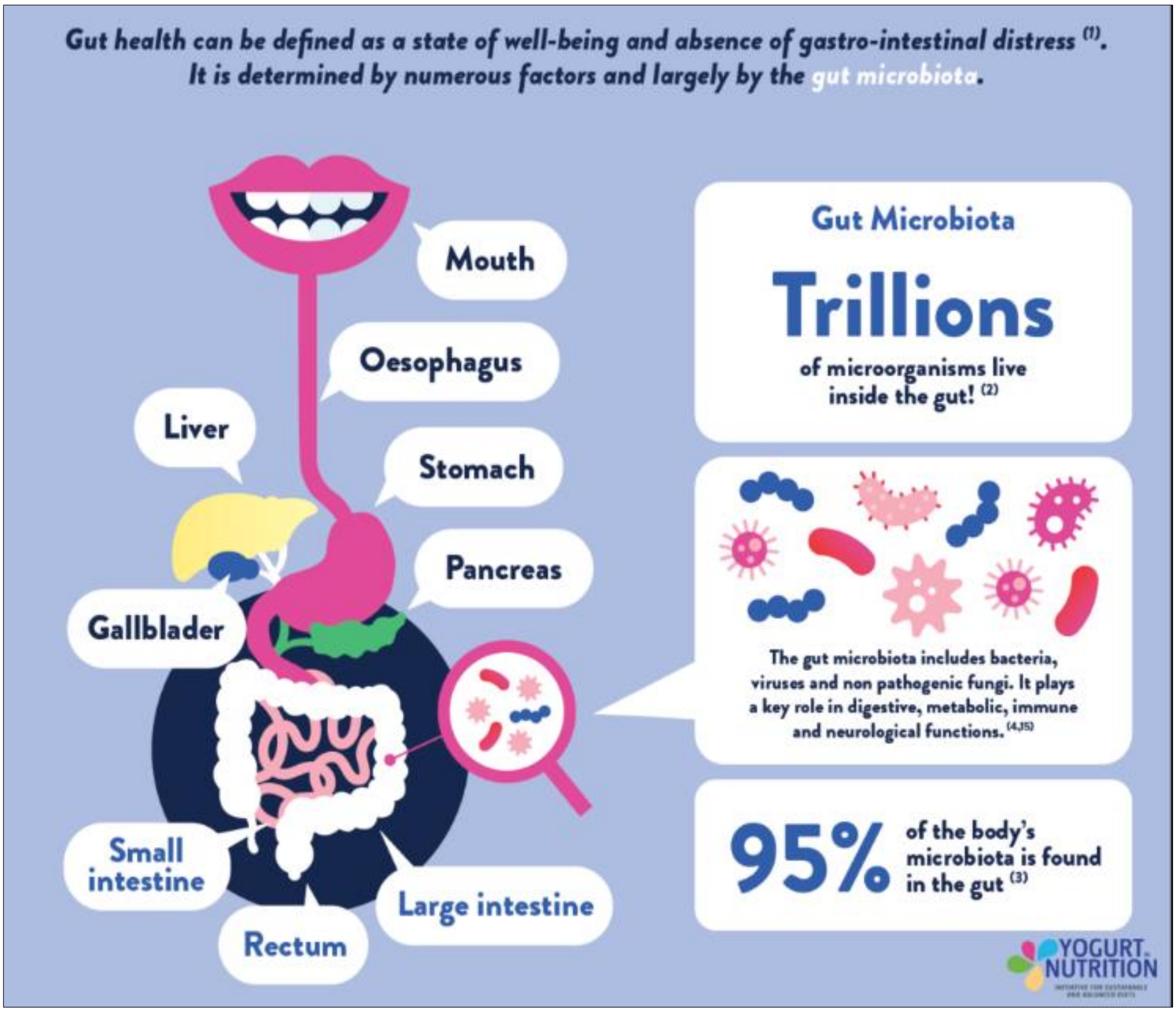

Figure 2: The gut microbiome or gut microbiota is the ecosystem living in our gut. It is estimated that our gut hosts trillions of microorganisms
Source: https://www.yogurtinnutrition.com/tag/gut-microbiota/

When they separated the participants into two groups one with those who showed they extracted more energy from food and the other with those who extracted less scientists observed that members of the group that extracted more energy from this process weighed 10 percent more than members of the other group, an average difference of 20 pounds. In addition to the microbiome, the group also studied intestinal transit time, which also showed an important role in weight gain: a shorter intestinal transit time can result in more energy (Bervoets *et al.*, 2013; Shen, 2013).

"We thought that a longer digestive journey time would allow more energy to be extracted, but we see those participants with type B gut bacteria, which extract more energy, may also have a faster passage through the gastrointestinal system," the study authors say. According to the team, our gut bacteria are great at extracting energy from food, which is good because the process provides extra energy. However, if we consume more than we burn, the extra energy the bacteria provide increases the risk of weight gain [Researchers from the University of Copenhagen] (Park *et al.*, 2006; Almeida *et al.*, 2009; Rodrigues, 2011; Bervoets *et al.*, 2013; Shen, 2013).

3.2. Calories Consumed and the Energy Spent on Physical Activities or Genetic Inheritance

Gaining weight does not depend solely on the balance between the number of calories consumed and the energy spent on physical activities or genetic inheritance. This equation can include at least three other variables, such as the type of bacteria that a person has in their intestinal flora, the degree of exposure to toxic substances, and the amount of calcium they ingest. The number of bacteria inhabiting our intestines is 10 times greater than the number of cells in our body. Therefore, to think that they do not play any relevant role in diseases is naive", he analyzes. According to him, bacteria present in the intestines of obese individuals are different from those observed in the intestines of thin individuals, both in rats and in humans (Figure 3) (Almeida *et al.*, 2009; Bervoets *et al.*, 2013; Shen, 2013).

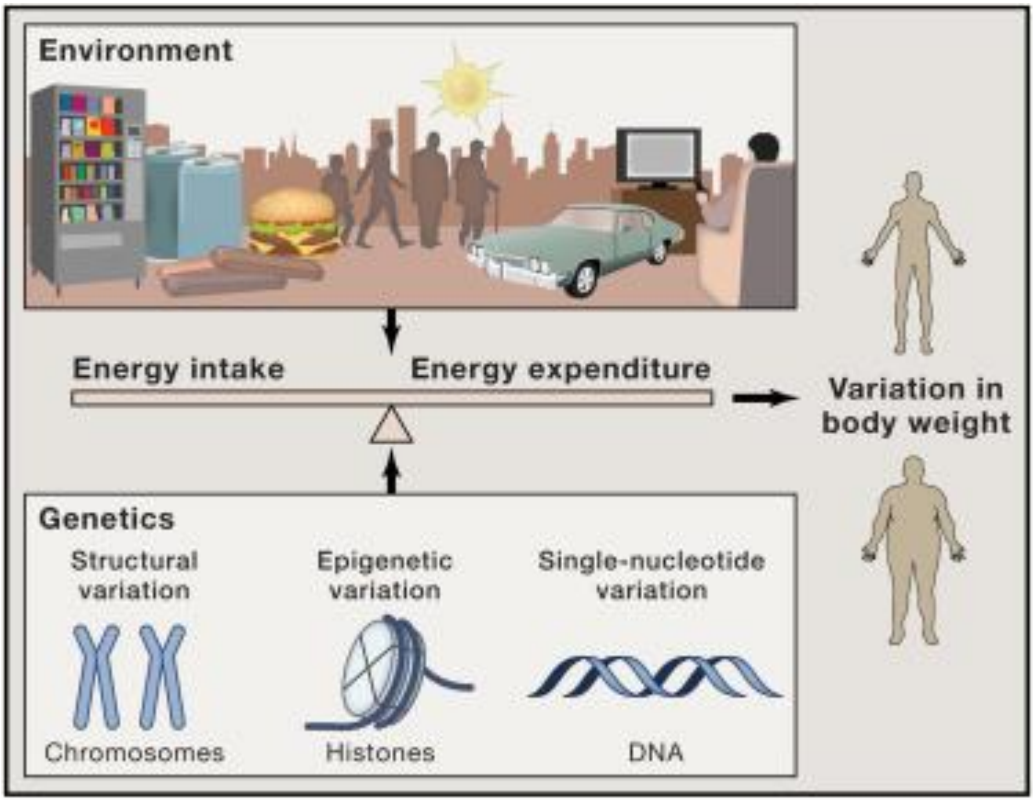

Figure 3: Contribution of genes and environmental factors to weight gain
Source: http://dx.doi.org/10.1016/j.cell.2015.03.00

Now, scientists are investigating how these bacteria interfere with body fat. One possibility is that some types of bacteria, more frequent in the intestinal tract of obese individuals, extract energy from food and pass it on to the individual's body, inducing weight gain. Meanwhile, other bacteria, more common in the intestines of thin people, extract and consume this energy, which helps maintain a slim body. The research aims to create an obesity treatment based on the mechanism of action of intestinal bacteria (Fleissner *et al.*, 2010; Bervoets *et al.*, 2013; Shen, 2013).

"We just need to be careful not to see 'miracle workers' offering treatments with antibiotics or probiotics that promise the end of obesity," [Mário José Abdalla Saad, professor of Clinical Medicine at the Faculty of Medical Sciences at Unicamp]. He explains that the "efficiency" of bacteria varies from person to person and that, today, studies are still sequencing the DNA of these microorganisms to understand the process better (Fleissner *et al.*, 2010; Schwiertz *et al.*, 2010; Bervoets *et al.*, 2013; Shen, 2013).

3.3. Firmicutes Bacteria

A diet rich in fats contributes to the growth of Firmicutes bacteria, which contributes to weight gain, in the same way that reducing fatty foods in the diet causes the opposite result, that is, it increases Bacteroidetes, which aid in weight loss. There are still no reports in the literature on the incidence and prevalence of this condition, which makes it difficult to understand its magnitude as a public health problem and guide clinical practice (Figure 4) (Backhed *et al.*, 2004; Ley *et al.*, 2005; Spezia *et al.*, 2009a; De *et al.*, 2010; Tilg and Kaser, 2011).

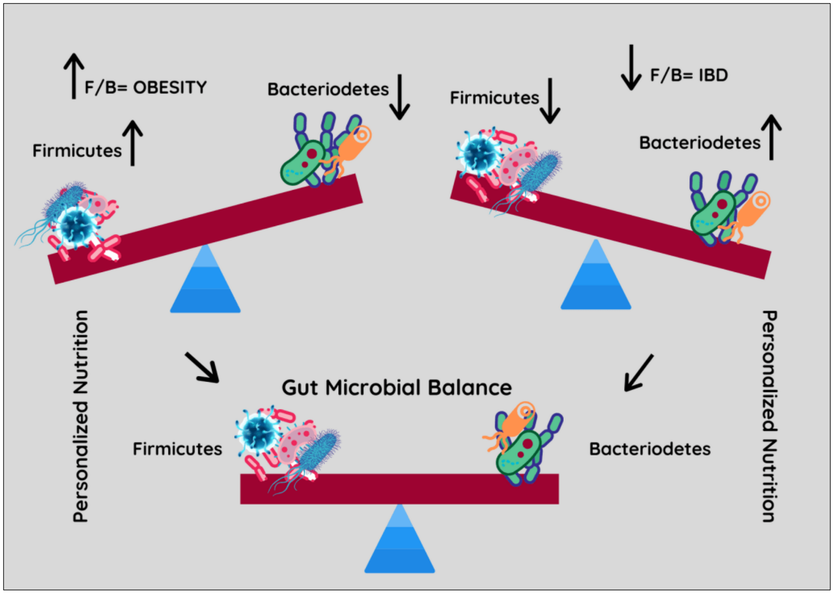

Figure 4: The Firmicutes includes Gram-positive bacteria that are predominantly from the genera *Bacillus, Clostridium, Enterococcus, Lactobacillus,* and *Ruminococcus* while phylum bacteroidetes consist of 7000 different species of Gram-negative bacteria that are predominantly from the genera *Bacteroides, Alistipes, Parabacteroides,* and *Prevotella*. When it comes to irritable bowel disease, phylum Proteobacteria plays a dominant role since it is correlated with the decrease in firmicutes
Source: https://genefitletics.com/2021/05/07/firmicutes-to-bacteroidetes-ratio-relevant-biomarker-for-obesity-irritable-bowel-disorders/

Two gut bacteria are linked to preventing weight gain and are often found in thin individuals: *Akkermansia muciniphila* Derrien *et al.,* 2004 (Verrucomicrobiales: Akkermansiaceae) and *Christensenella minuta* Morotomi *et al.,* 2012 (Christensenella: Christensenellaceae). *Akkermansia muciniphila* is an abundant bacterium in the human intestinal tract. It is the only intestinal representative of the Verrucamicrobia in human feces and is depleted in adults who are overweight, have diabetes, and several other diseases. AKK muciniphila is known to play a key role in maintaining intestinal health and in the metabolic modulation of the host. Interestingly, it has been shown that AKK muciniphila levels are correlated with several disorders that share a systemic inflammatory background and compromised intestinal barrier (Figures 5-6) (Tilg and Kaser, 2011; Silva *et al.,* 2013; Vieira and Zaramel, 2022; Flório *et al.,* 2024).

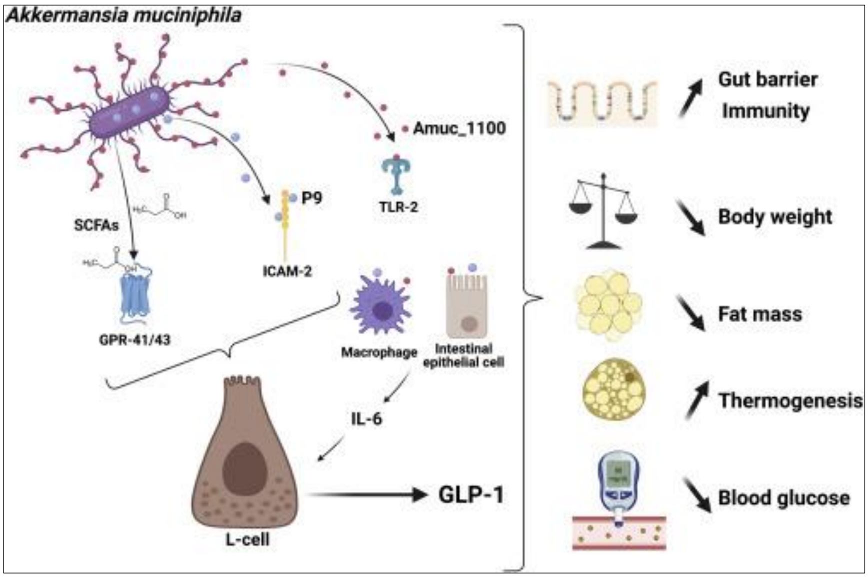

Figure 5: Specific biomolecules produced by *Akkermansia muciniphila* Derrien et al. 2004 (Verrucomicrobiales: Akkermansiaceae) and their mechanisms of action
Source: https://doi.org/10.1016/j.cmet.2021.05.004

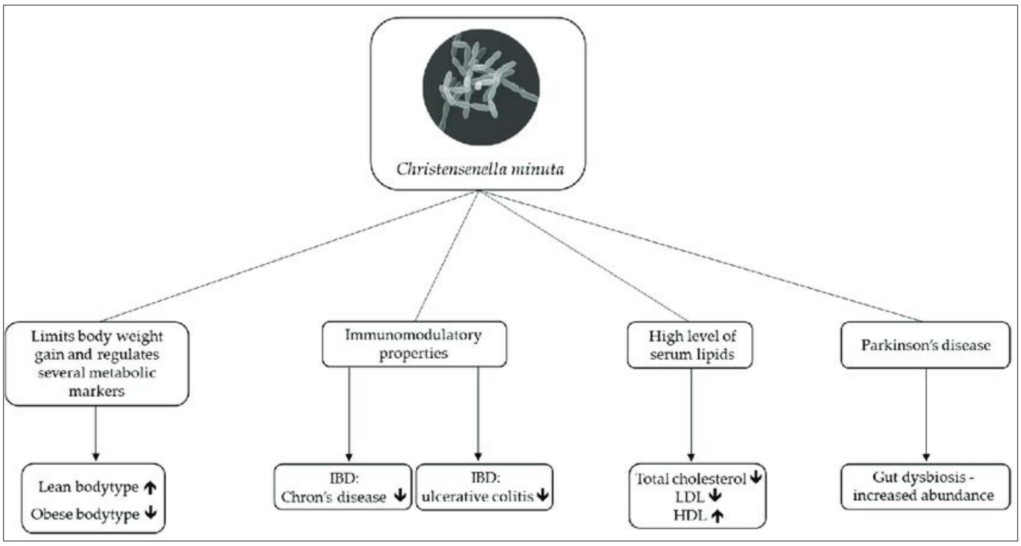

Figure 6: Relation of *Christensenella minuta* Morotomi *et al.*, 2012 (Christensenella: Christensenellaceae) levels with different diseases and health conditions

Source: https://www.researchgate.net/figure/Relation-of-Christensenella-minuta-levels-with-different-diseases-and-health-conditions_fig1_373212194

3.4. Bacterium in the Maintenance of Intestinal Homeostasis

This bacterium participates in maintaining intestinal homeostasis thanks to a strong interaction with host cells and the intestinal microbiome. It is essential to ensure adequate mucus production and thickness, which is critical in maintaining the gastrointestinal tract's health and its functional integrity, as it represents an efficient barrier that protects the epithelial surface. Deficiency in mucus formation characterizes the impaired metabolic state present in overweight individuals since the amount of *K. muciniphila* is reduced in these people (Figure 7) (Backhed *et al.*, 2004; Ley *et al.*, 2005; Spezia *et al.*, 2009b; De *et al.*, 2010; Tilg and Kaser, 2011).

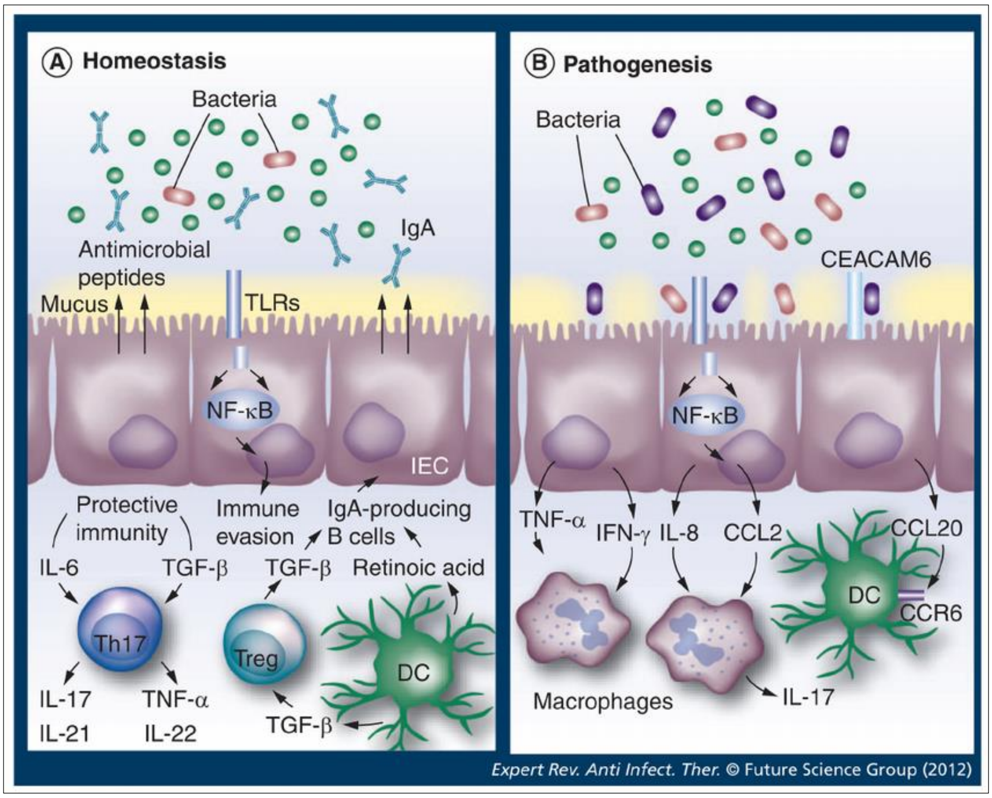

Figure 7: Intestinal homeostasis and its breakdown during pathogenic processes

Source: https://www.researchgate.net/figure/ntestinal-homeostasis-and-its-breakdown-during-pathogenic-processes_fig1_221684235

It stimulates the increase in Akkermansia (AKK), and some foods can help, such as apples, beans, grapes, berries, flaxseed, green tea, nuts, olives, asparagus, onions, and oats. These foods contain polyphenols considered prebiotics, which feed beneficial bacteria in the intestine, including Akk. Patients with eradicated *Helicobacter pylori* (Marshall *et al.*, 1985) Goodwin *et al*., 1989, had a higher proportion of pre-obesity compared to the other groups evaluated, highlighting that the *H pylori* negative group had the highest proportion of people with obesity (Backhed *et al.*, 2004; Ley *et al.*, 2005; Spezia *et al.*, 2009b; De *et al.*, 2010; Tilg and Kaser, 2011).

Bacteria influences obesity, says An American study showed that bacteria that live in our digestive system can contribute to weight loss. The bacteria studied are part of a group of thousands of types of microbes that affect our health. A laboratory experiment revealed that mice gained weight when they received bacteria from the digestive tracts of obese people. The opposite was also proven when receiving bacteria from thin people, the guinea pigs gained less weight. The discovery made in the United States was published in the prestigious specialized magazine Science (Figure 8) (Gallagher, 2013).

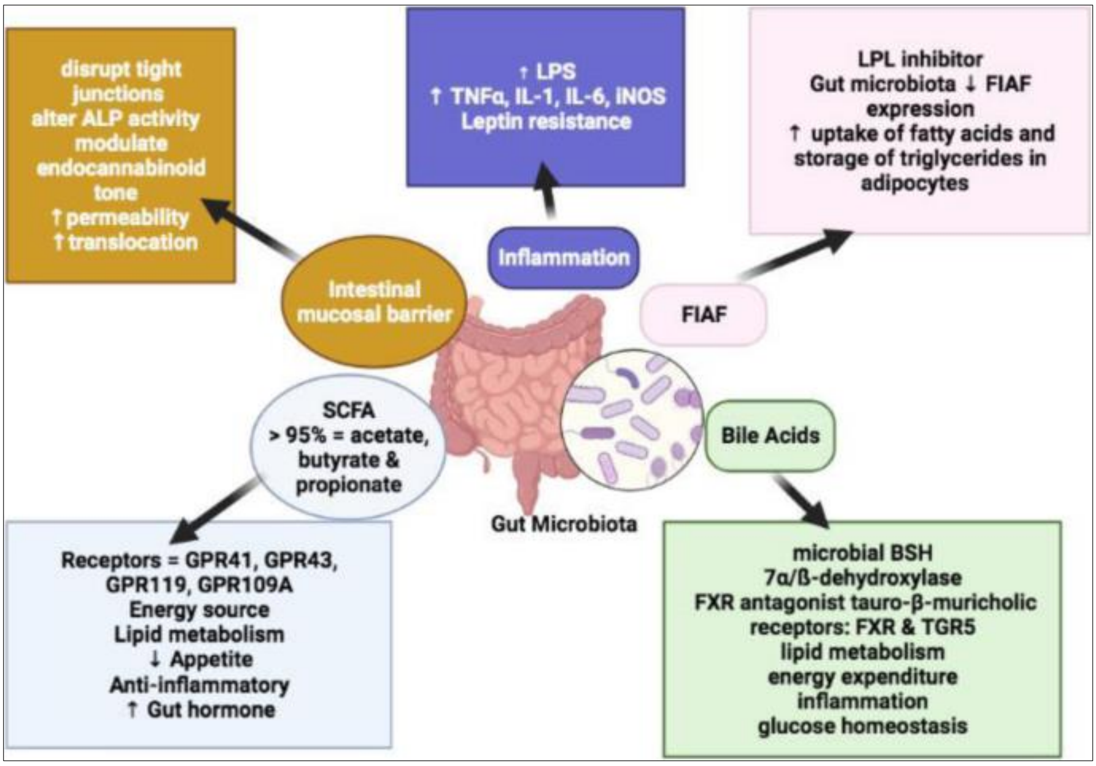

Figure 8: Host metabolic pathways influenced by gut microbiota and metabolites including SCFAs, Fiaf
Source: https://doi.org/10.1186/s12944-021-01491-z

3.5. Human Therapy

One of the scientists responsible for the research, Jeffrey Gordon, highlighted the influence of bacteria in the digestive system on people's diets. "We don't eat dinner alone, we eat with trillions of friends we have to consider the microbes that live in our intestines," [Jeffrey Gordon] said. Despite this, experts do not believe that transplanting thousands of bacteria from thin people will be a viable weight loss therapy, due to the risk of carrying diseases in the process. It would be more likely to transplant an exact group of bacteria that promote weight control, and to use foods that promote their proliferation in the intestine [Jeffrey Gordon] (Gallagher, 2013).

Gordon states that the next step would be to "try to determine how widespread the effects of these bacteria are and which foods can promote their activities in the body". He also emphasizes that we should "take a step forward and start considering foods in light of the microbes that live inside our intestines" [Jeffrey Gordon]. "There is a lot of work to be done, but this [the US study] is proof that bacteria can control obesity in adults," he says. He adds: "This is a very promising area, but we need to be cautious about promoting this as a cure-all." [Jeffrey Gordon] (Gallagher, 2013).

3.6. Dysbiosis (Intestinal Dysbiosis Is an Imbalance in the Growth of Microorganisms)

Intestinal dysbiosis is an imbalance in the growth of microorganisms that are naturally found in the intestine and can cause symptoms such as nausea, excess gas, abdominal discomfort, diarrhea, or constipation in some cases. Imbalances in the intestinal flora, also called intestinal microbiota, are mainly caused by a diet rich in protein and fat and low in fiber but can also be a consequence of the use of certain medications or stress, for example. The main symptoms of intestinal dysbiosis are Nausea or vomiting; Excessive gas and burping; Discomfort or bloating in the abdomen; Diarrhea or constipation; Fatigue; and Irritability. In most cases, intestinal dysbiosis is temporary and symptoms tend to improve as the intestinal flora recovers naturally. However, the person may develop persistent symptoms in some cases (Figure 9) (Backhed *et al.,* 2004; Ley *et al.*, 2005; Spezia *et al.*, 2009b; De *et al.*, 2010; Tilg and Kaser, 2011).

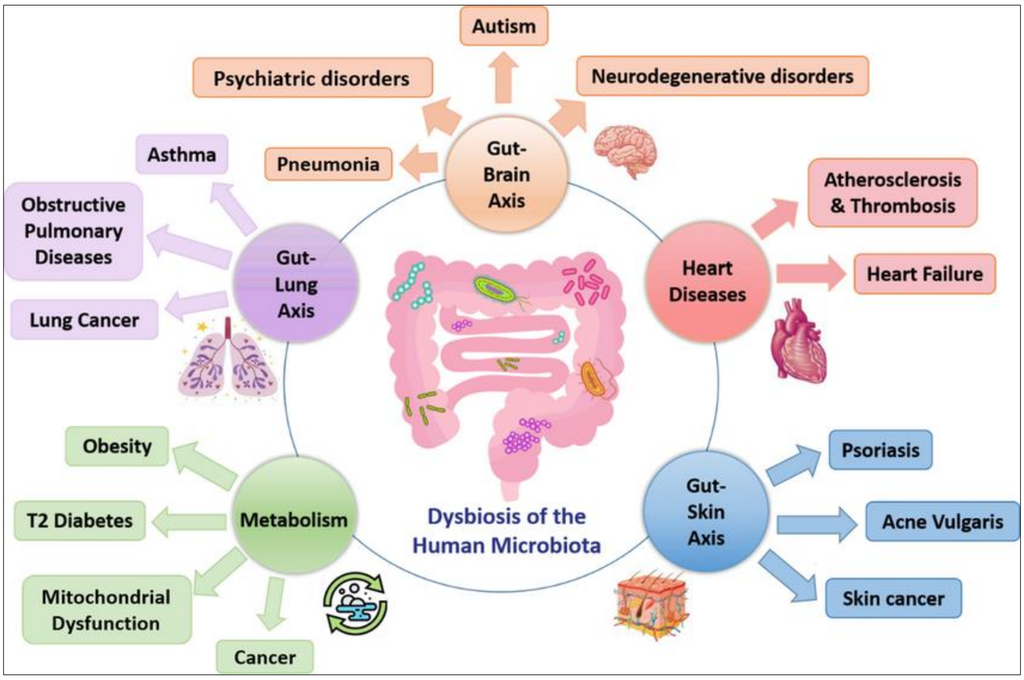

Figure 9: The human microbial dysbiosis in human diseases. Gut microbiota is implicated in the right functioning of many organs, such as the lungs, kidneys, liver, heart, and brain. However, any disruption to the microbiota homeostasis results in the malfunctioning of these affected organs, and the progression of many related diseases
Source: https://www.researchgate.net/figure/The-human-microbial-dysbiosis-in-human-diseases-Gut-microbiota-is-implicated-in-the_fig1_359066312

3.7. Relationship between Bacteria/Obesity/Diabetes

3.7.1. But why, after all, can a Higher Concentration of Harmful Bacteria Increase an Individual's Risk of Developing Obesity and DM2?

Obesity is a chronic, progressive disease defined by the excessive accumulation of body fat, which can have several health implications in the medium or long term. According to the World Health Organization, obesity is considered when the BMI is above 30 kg/m², and a BMI equal to or greater than 40 kg/m² is classified as morbid or severe. This emergence is associated with multifactorial causes related to lifestyle, and genetic, hereditary, psychological, cultural, and ethnic factors (World Health Organization, 2013).

Due to its complexity and because it develops several diseases in humans, obesity must be recognized and treated as a disease, according to the World Health Organization (Spezia *et al.,* 2009a; Abeso, 2012). In 2012 obesity was associated with the deaths of 2.8 million people, and 12% of the world population is considered obese. Today, in the United States (USA), one in three adults is obese. In Brazil, the prevalence of obesity reached approximately 10% of the population between 2008 and 2009. This rate is estimated to be 20% by 2025 Its development may be related to the imbalance of the intestinal microbiota, which may have a different composition in eutrophic and obese humans (World Health Organization, 2013; Andrade *et al.,* 2015; Santos *et al.,* 2016).

First, there is a mechanism that concerns the impact that the intestinal microbiota can have on the regulation of appetite and satiety in the Central Nervous System (CNS), studies suggest that a healthy microflora results in a greater production of short-chain fatty acids (SCFA), which would be associated with increased satiety and decreased food intake. These effects would be related to the increased production of some types of peptides (GLP-1, GLP-2, and PYY), which can act on the hypothalamus, activating mechanisms responsible for increased satiety and decreased food intake, improving the glycemic and insulinemic response and reducing systemic inflammation, commonly present in obese individuals and those with DM2 [Moraes] (Figure 10) (Moraes *et al.*, 2014; Vivian, 2015; Das and Nair, 2019; Yang *et al.*, 2021).

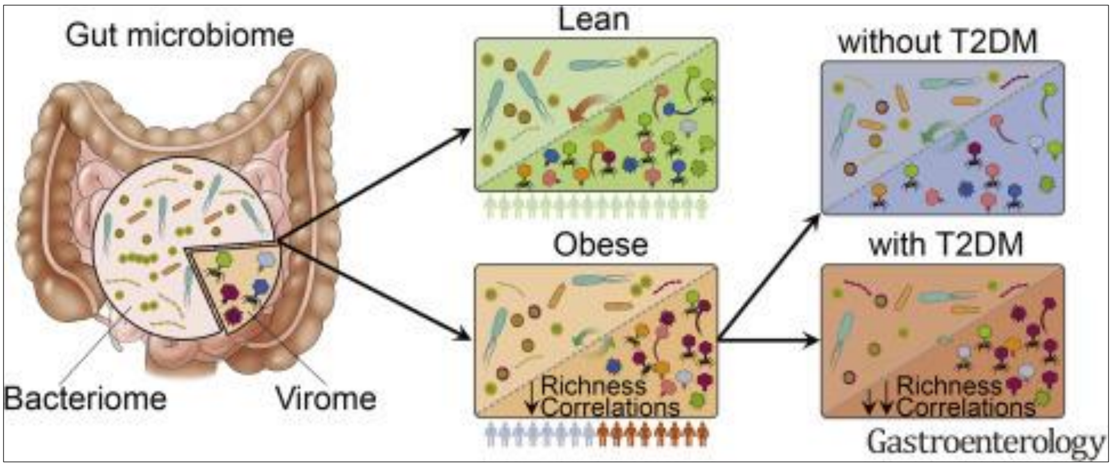

Figure 10: Obesity and type 2 diabetes mellitus (T2DM) are associated with changes in the gut bacterial composition, but little is known about the role of the viral community in disease development
Source: https://www.gastrojournal.org/action/showPdf?pii=S0016-5085%2821%2903170-X

This happens because lipopolysaccharides (LPS) present on the surface of gram-negative bacteria (the most harmful) can cross the host's intestinal barrier (in this case, us!), triggering an inflammatory response and insulin resistance. According to Moraes and collaborators, studies suggest that individuals who have a diet with a higher amount of fat have greater intestinal permeability, facilitating the entry of LPS into the circulation, that is, the increase in blood concentrations of LPS, associated with diets rich in fat, can lead to chronic inflammation, which is present in obesity and favors the development of DM2 (Moraes *et al.*, 2014; Vivian, 2015).

Prebiotics are characterized by non-digestible food components that, when fermented by intestinal bacteria, produce substances capable of beneficially altering intestinal flora's composition and/or activity. Some of these products are peptides, satiety, and decreased food intake. Probiotics are live microorganisms that, when administered in sufficient quantities, positively affect the balance of intestinal flora. People have different bacterial compositions in the GI tract, with the most common bacteria belonging to the Firmicutes or Bacteroidetes kingdoms. In humans, it was found that obese individuals have a higher concentration of Firmicutes and a lower concentration of Bacteroidetes than individuals with a healthy weight [Study carried out by Ley *et al.*,] (Moraes *et al.*, 2014; Vivian, 2015).

4.0. COLLAGEN BACTERIA

Collagen is one of these ingredients with functional characteristics. It is a protein of animal origin, whose function in the body is to contribute to the structural integrity of the tissues in which it is present. However, with the onset of adulthood, collagen deficiency begins to be noticed, as the body reduces its production, making its supplementation necessary. Given this, there has been an increase in interest in the industrial application of collagen in food supplements and food products, such as yogurts, sausages sausage and ham, teas, juices, and easy-to-prepare desserts, such as gelatin, puddings, and maria-mole. These foods with added collagen can be used in treatments to improve the elasticity and firmness of the skin and prevent diseases such as osteoarthritis, osteoporosis, hypertension, and gastric ulcers (Figure 11) (Chen *et al.*, 2021; Watanabe *et al.*, 2021).

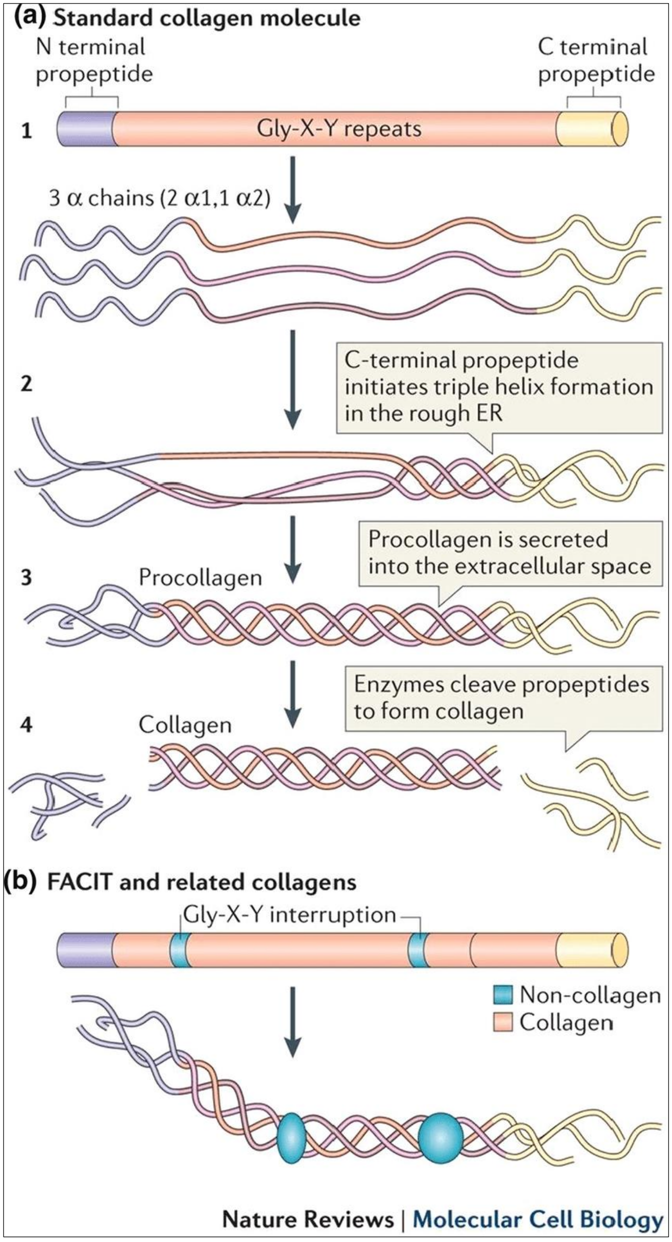

Figure 11: Collagen structure and formation. The standard collagen molecule has amino-(N) and carboxy-(C) terminal propeptide sequences, which flank a central domain of Gly-X–Y repeats where X and Y are frequently proline and hydroxyproline (1). Three α-chains (the figure shows an example of heterotrimer, which is representative of type I collagen) are intracellularly assembled into a triple helix after initiating this process by the C-terminal domain (2). Procollagen is secreted into the extracellular space (3) and converted into collagen by cleavage of the N- and C-propeptides via metalloproteinases (4)
Source: Nature Reviews Molecular Cell Biology

Collagen, a protein discovered in the 1930s, is present in large quantities in the human body, especially in the skin, ligaments, tendons, hair, and nails. Its main function is to ensure structure, stability, and strength for tissues. This protein behaves like a viscous and elastic material, is resistant to traction, and has low immunogenicity, ensuring its use in supplements and foods (Carstens *et al.,* 2019; Axarlis *et al.,* 2021).

Collagen has long been used to minimize chronological aging and photoaging exposure to sun and blue light; improve skin quality, elasticity, and hydration, minimizing wrinkles and expression lines; as an adjuvant in the healing process; and in the prevention of bone and joint diseases due to its high antioxidant and antimicrobial capacity. However, recent studies have demonstrated a positive effect of collagen peptide supplementation in improving microbiota health. Collagen can help recover and maintain the intestinal barrier (Figure 12) (Chen *et al.,* 2021; Watanabe *et al.,* 2021).

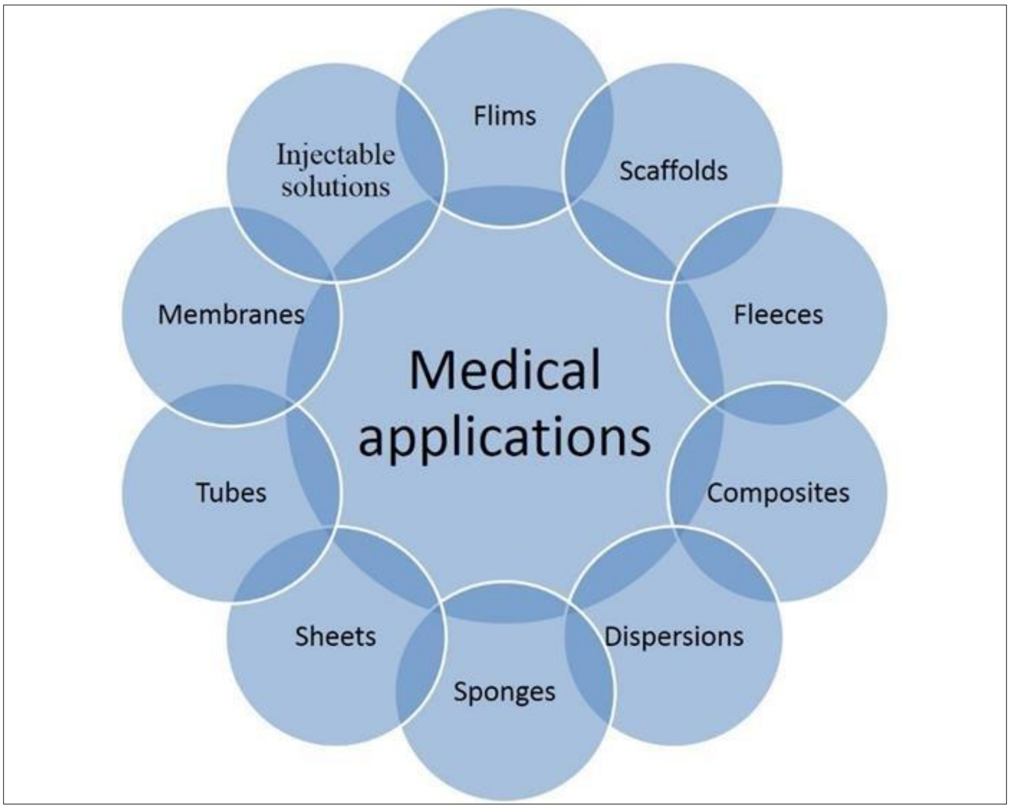

Figure 12: Medical applications of collagen

Source: https://www.researchgate.net/figure/Medical-applications-of-collagen_fig3_341089281

Collagen has a wide range of biomedical applications, as it is widely used as a carrier for drugs, proteins, and genes. It has also been successfully used as a substitute for human skin, blood vessels, and ligaments. Collagen-based biomaterials are expected to become useful matrix substances for a variety of medical applications. The intestine is a crucial organ for health (Silva and Penna, 2012; Carstens *et al.*, 2019; Axarlis *et al.*, 2021).

It metabolizes, absorbs, and distributes nutrients and other substances. Within the intestine, it is determined what enters the bloodstream to be directed to other tissues. This happens through the intestinal barrier, composed of enterocytes intestinal cells connected by tight junctions. This junction forms a highly selective barrier, preventing toxins from leaking and reaching other organs, causing harm to health (Chen *et al.*, 2021; Watanabe *et al.*, 2021).

Another means of regulating the human organism is through the microbiota, a community of microorganisms viruses, fungi, bacteria, mites, and archaea that make up the gastrointestinal tract. Microbiota exists in other tissues, such as skin, hair, and vagina, however, they differ according to the type of colony of microorganisms predominant in that region. The microbiota is of great importance to the health of individuals because it is involved in the fermentation of carbohydrates and fibers; synthesis of amino acids and vitamins; modulation of xenobiotic toxicity and promotion of the immune system, through the production of mucus and antimicrobial peptides (Carstens *et al.*, 2019; Axarlis *et al.*, 2021; Chen *et al.*, 2021; Watanabe *et al.*, 2021).

Collagen peptides and collagen precursor amino acids alanine, proline, hydroxyproline, lysine, glycine, and hydroxylysine have been associated with improved gastrointestinal health. Some collagen peptides are resistant to digestion and can maintain their beneficial properties within the gastrointestinal system. Thus, supplementation can maintain, reinforce, or repair the intestinal barrier through mechanisms of action, including modulation of intestinal immune reactions, reduction of oxidative stress or modification of intracellular binding proteins tight junctions, reducing the space between enterocytes, and ensuring a protected intestinal barrier (Figure 13) (Carstens *et al.*, 2019; Axarlis *et al.*, 2021; Chen *et al.*, 2021; Watanabe *et al.*, 2021).

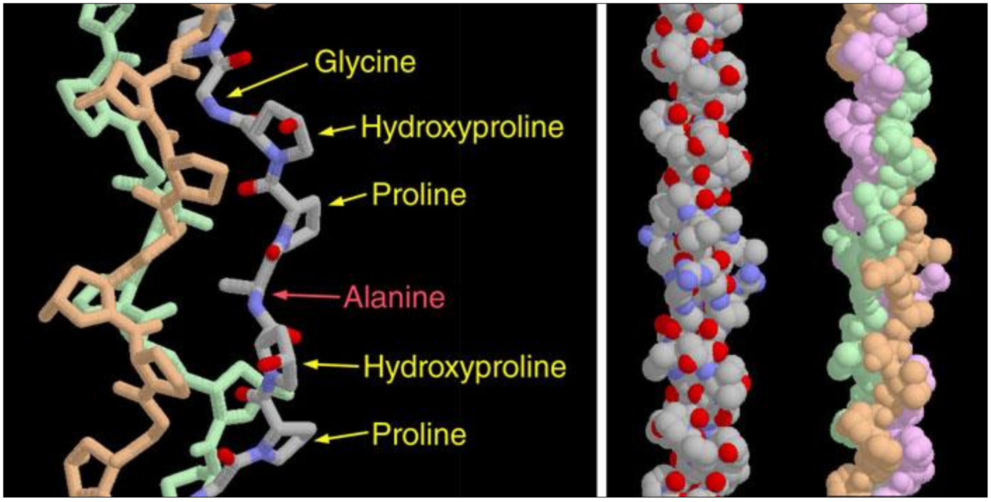

Figure 13: The collagen helix shown on the right contains a segment of human collagen, and may be viewed in the PDB file 1bkv. Notice that the top half is very uniform, where the sequence is the ideal mixture of glycine and prolines. At the bottom, the helix is less regular, because many different amino acids are placed between the equally-spaced glycines

Source: https://pdb101.rcsb.org/motm/4

Collagenase is an enzyme produced by a bacterium called *Clostridium histolyticum* (Weinberg and Séguin, 1916) Lawson and Rainey, 2016, which needs to break down collagen, present in components of animal origin, to feed on it (Chen *et al.*, 2021; Watanabe *et al.*, 2021). In this way, intestinal permeability and, consequently, the leakage of toxins and pathogens into the circulation are minimized. The best-known and most-used bacterial strains are *Lactobacillus*, *Bifidobacterium*, *Enterococcus*, and *Streptococcus*, but there are many others (Moura, 2014; Das and Nair, 2019; Vijayan *et al.*, 2021; Schwarz *et al.*, 2022).

The skin aging bacteria, three species of bacteria are the most prominent: *Cutibacterium acnes* (Gilchrist, 1900), Scholz and Kilian 2016, *Staphylococcus epidermidis* (Evans 1916), and *Corynebacterium* sp. The first is more abundant in women in the younger group and the other two in women in the older group (Figure 14) (Moura, 2014; Das and Nair, 2019).

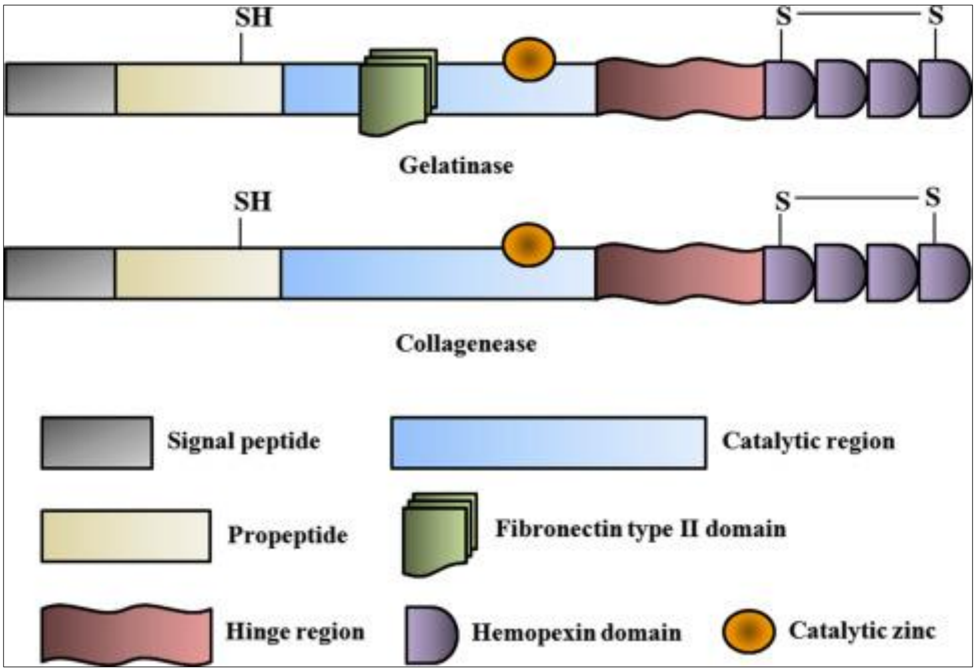

Figure 14: The domain structures of collagenase and gelatinase

Source: https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/collagenase

Staphylococcus epidermidis is a species of firmicute bacteria, characterized by being coagulase-negative. It belongs to the genus *Staphylococcus* Rosenbach (1884). It is a gram-positive bacterium arranged in clusters and tetrads. For a long time, it was considered a commensal species. Still, today it is known that it is an opportunistic pathogen mainly responsible for hospital infections, through catheters, probes plastic material as well as prostheses due to its ability to form biofilms. Biofilms make it difficult for antimicrobial drugs and even phagocytic cells to reach the source of infection (Trabulsi and Alterthum, 2008).

Cutibacterium acnes Scholz and Kilian, 2016 (Verrucomicrobiales: Akkermansiaceae) is a species of gram-positive anaerobic bacteria of the genus *Corynebacterium*, typically aerotolerant, relatively slow-growing, which feeds on the secretion produced by the sebaceous glands and which, when in contact with the epithelial pores, promotes inflammation of the hair follicles, causing lesions commonly known as "pimples" or acne. The genome of the bacteria was sequenced and a study showed several genes that can generate skin-degrading enzymes and proteins that can be immunogenic and activate the immune system (Costa, 2008).

4.1. *Borrelia burgdorferi* Johnson *et al.*, 1984 amendment. Baranton *et al.*, 1992 (Spirochaetales: Spirochaetaceae) Binds, Invade, and Colonize Native Type I Collagen Networks

The etiological agent of Lyme disease is transmitted to animals and humans primarily by the nymphs of the tick *Ixodes scapularis* Say, 1821 (Ixodida: Ixodidae), which during a blood meal deposit a small number of microorganisms on the skin. Inoculation of the bacteria by the tick bite results after a few days in a characteristic rash, erythema migrans, which may be accompanied by systemic symptoms including malaise, fatigue, fever, headache, stiff neck, arthralgias, or myalgias. Adhesion, colonization, and proliferation within the skin and other organs and tissues of the host by *B. burgdorferi* require interaction between the spirochete and connective tissue cells, including macrophages, dendritic cells, fibroblasts, and the associated extracellular matrix (Figure 15) (Zambrano *et al.*, 2004, Lopes, 2017; Radolf and Samuel, 2021).

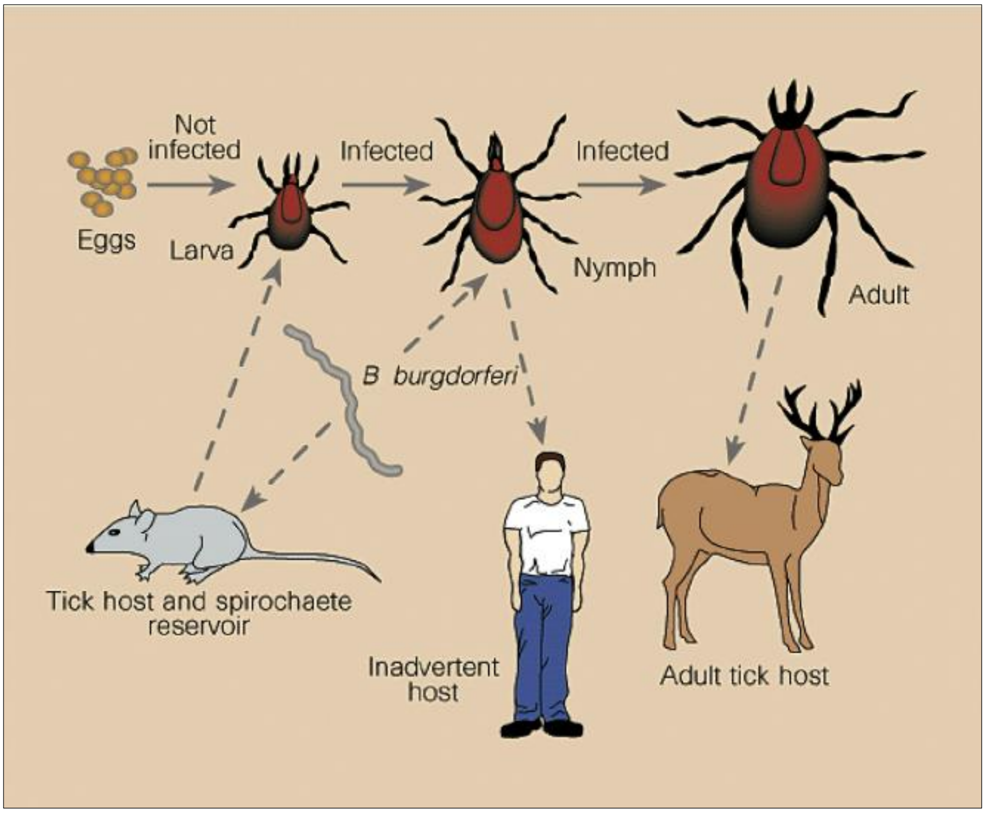

Figure 15: The life cycle of the Ixodes tick vectors of *Borrelia burgdorferi* Johnson *et al.*, 1984 amendment. Baranton *et al.*, 1992 (Spirochaetales: Spirochaetaceae). Reservoir hosts, such as mice, transmit to the larva or nymph stages of the tick when they take a blood meal. Infected nymphs or adult ticks then transmit the spirochetes to other reservoir hosts and humans, who are inadvertent. Deers are important hosts for adult ticks, but they are ineffective reservoirs for *B. burgdorferi*

Source: From Barbour, A. G., & Zuckert, W. R. (1997). Genome sequencing: new tricks of the tick-borne pathogen. *Nature, 390,* 553; with permission

4.2. Technological Initiation Work Studies the Identification of Peptides Capable of Inhibiting the Action of Hyaluronidase; the Study is Initial but Has Aesthetic and Medical Potential

A research project conducted at the Laboratory of Structure and Function of Biomolecules at the Butantan Institute identified peptides capable of inhibiting and activating the action of hyaluronidase, an enzyme responsible for degrading hyaluronic acid in the body, a substance that gives skin its firm appearance (Figure 16) *(*Jiang, *et al.*, 2024; Neumam, 2024).

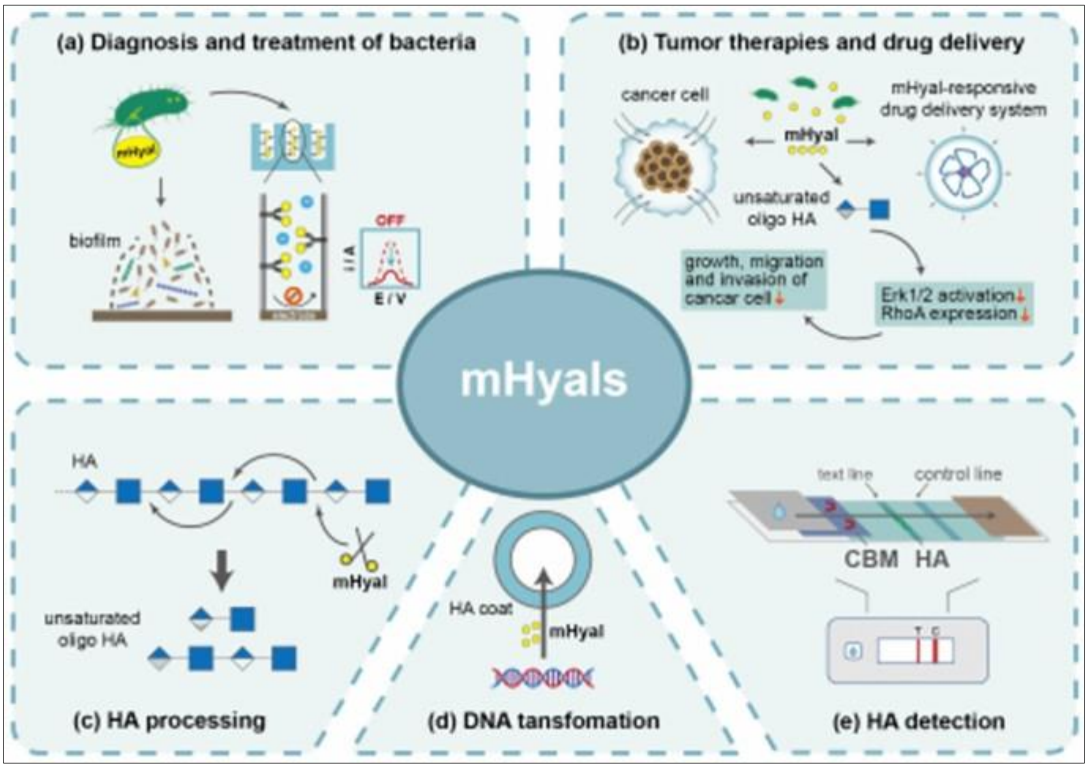

Figure 16: Hyaluronan (HA), a natural high molecular weight polysaccharide, has extensive applications in cosmetology and medical treatment. Hyaluronan-degrading enzymes (Hyals) act as molecular scissors that cleave HA by breaking the glucosidic linkage. Hyals are present in diverse organisms, including vertebrates, invertebrates, and microorganisms, and play momentous roles in biological processes. In recent years, microbial Hyals (mHyals) have gained considerable attention for their exceptional performance in the production and processing of HA

Source: https://doi.org/10.1186/s40643-024-00832-x

In initial tests, enzyme-inhibiting peptides were identified with the potential for treating skin wrinkles and cartilage lesions. Activating peptides have the potential to treat bruises. The technological initiation project still has a long way to go, but it already shows promise for possible aesthetic and medical use based on the primary results. "If our hypothesis is confirmed, we could think about an anti-aging cream and even medications with the potential to treat some chondropathies, which are cartilage lesions treated with recurrent intra-articular applications of hyaluronic acid [Julho Bruno Duzzi] (Neumam, 2024).

The other possible application would be in bruises, as it would treat blood extravasation more quickly, helping to avoid possible characteristic spots on the skin", says the medical student [Caio Mendes, through the professor of Medicine at Universidade Nove de Julho Bruno Duzzi] (Neumam, 2024). "The use of a peptide molecule as a therapeutic agent is potentially safe for possible treatments because it is natural, coming from human collagen itself, which we believe does not confer toxicity to human cells", highlights the researcher [Dr. Fernanda Portaro] (Neumam, 2024).

4.3. Brazilian Biodiversity: The Wealth of Nature

Brazil is home to the greatest biodiversity on the planet. The country has several climates, each with different fauna, flora, soil, and biomes. And it is to this wealth, which can bring cures or prevention of diseases, that the eyes of the scientists at Cristália are focused (Cristália, 2025).

Instead of looking abroad for new health solutions, Cristália decided to focus its research on Brazilian biodiversity. And that was precisely how the Active Pharmaceutical Ingredient (API) Collagenase Biological was born. The product generated by this API is the Kollagenase ointment, indicated for treating skin lesions, promoting gentle and fast cleaning, without bleeding and pain (Cristália, 2025). From carnivorous to vegetarian: Collagenase is traditionally an enzyme produced when a bacterium called *C. histolyticum* needs to break down collagen, present in components of animal origin, to feed on it (Figure 17) (Cristália, 2025).

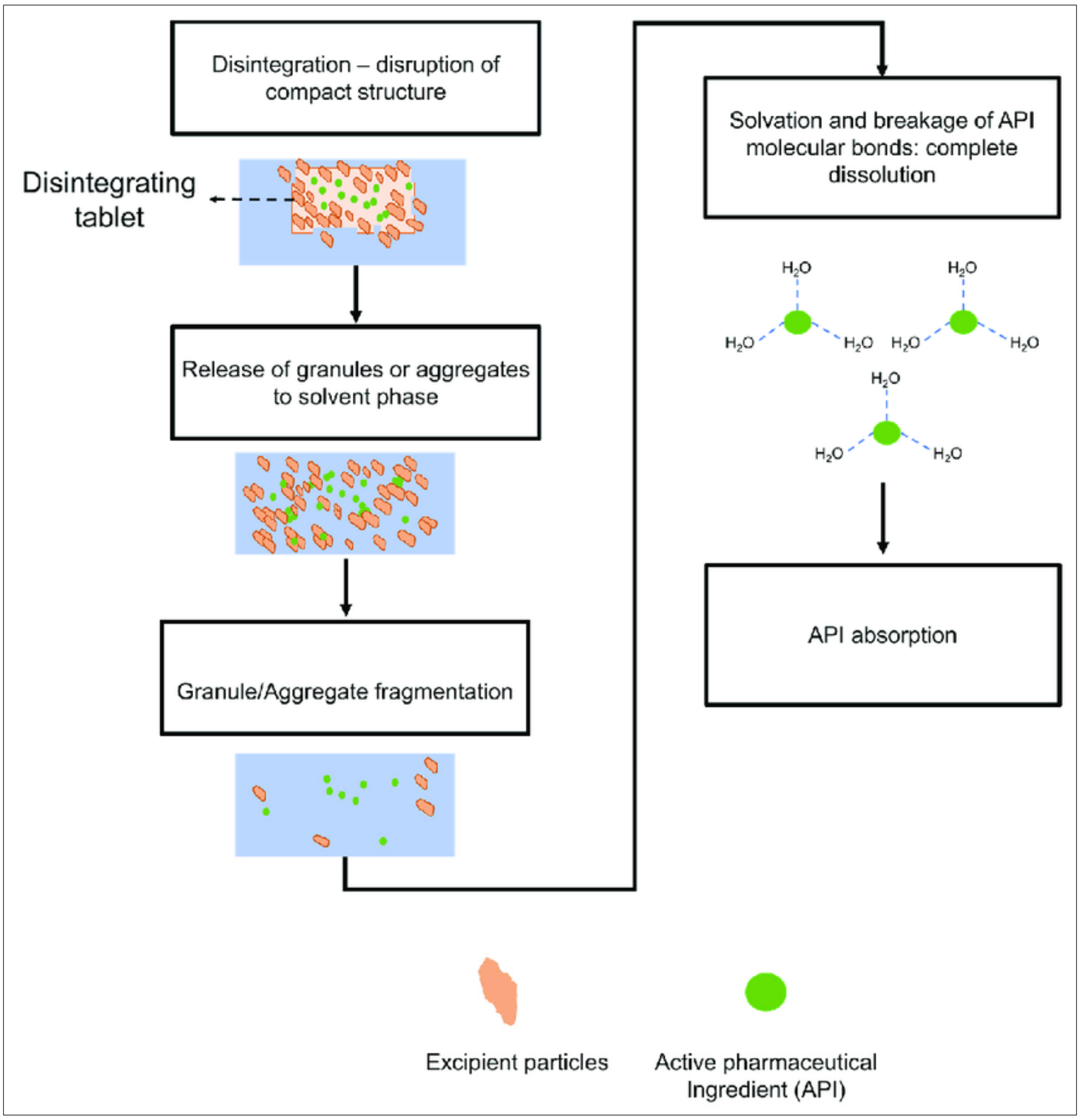

Figure 17: Schematic of active pharmaceutical ingredient (API) release in immediate-release tablets
Source: https://www.researchgate.net/figure/Schematic-of-active-pharmaceutical-ingredient-API-release-in-immediate-release-tablets_fig1_368632780

While researching a strain of the bacterium *C. histolyticum* in Brazilian soil, Cristália scientists discovered and collected a slightly different strain in Espírito Santo do Pinhal, in the interior of São Paulo. They mimicked the presence of collagen in a plant culture medium as if it were present. And they "tricked" the bacteria, inducing it to produce collagenase without collagen. Thus, Cristália's animal-free collagenase was born (Cristália, 2025).

National technology and purity: The idea of producing something free of animal components comes from several issues. The main one is the achievement of a purer, more active input free of animal components, which means that animal-free collagenase can be used in stem cell isolation and cell therapy, which require maximum purity since these are external enzymes that come into contact with organic cells. Additionally, as a result of this achievement, Brazil can export biotechnology for the first time in history, eliminating the need to import collagenase (Cristália, 2025).

4.4. The Appearance of Wrinkles May Be Linked to Skin Bacteria

Wrinkles are lines and depressions on the face due to the loss of elasticity and tone and a reduction in collagen and hyaluronic acid. Drinking water and sleeping at least 8 hours a night are habits that are very good for the skin, however, some practices seem healthy, but in fact, accelerate skin degradation (Zambrano *et al.*, 2004; Lopes, 2017; Radolf and Samuels, 2021; Editora Globo, 2024).

Researchers from the Center for Microbiome Innovation at the University of California in San Diego and L'Oréal Research and Innovation have discovered that wrinkles and crow's feet, often seen as one of the main signs of skin aging, are aggravated in women by bacteria that live on the skin. The research analyzed 13 studies on the skin condition of 650 female participants between the ages of 18 and 70 and found that people with a more diverse microbiome in other words, with many different species of bacteria on their skin had more wrinkles and crow's feet (Figure 18) (Zambrano *et al.*, 2004; Lopes, 2017; Radolf and Samuels, 2021; Editora Globo, 2024; Jiang *et al.*, 2024).

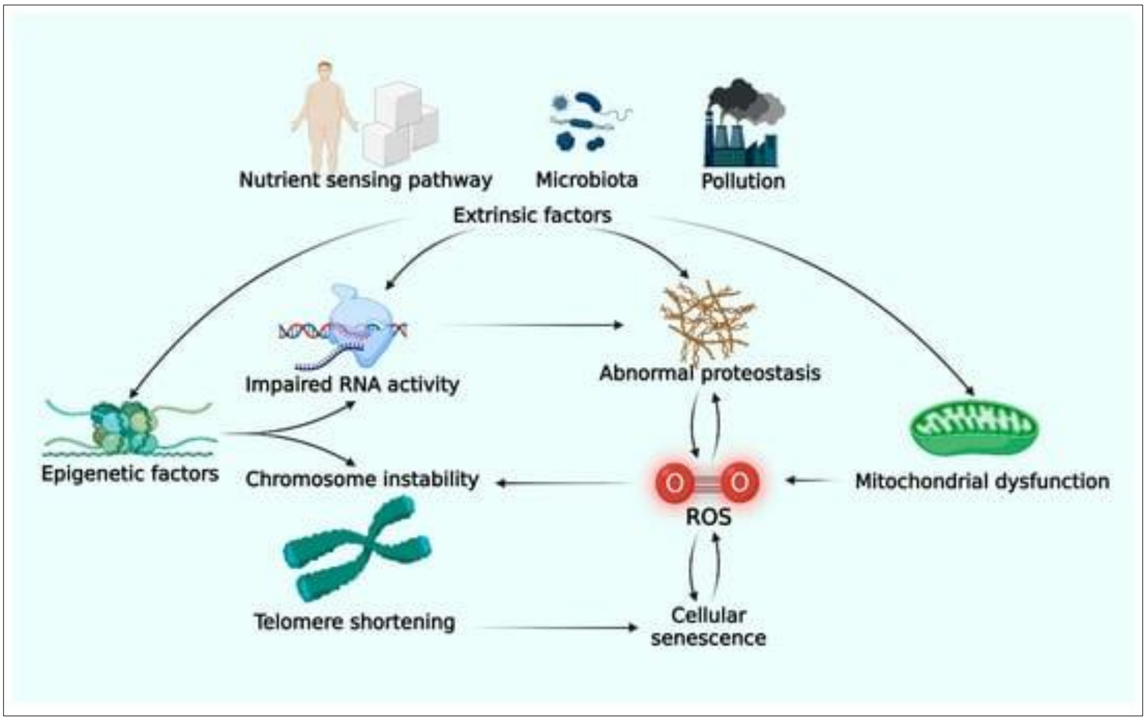

Figure 18: Molecular mechanism of aging. Intrinsic pathways believed to play a major role in aging are genetic and epigenetic alterations, accumulation of abnormal proteins, oxidative stress and mitochondrial dysfunction, and cellular senescence. Extrinsic factors such as pollutants, microbiota, and dietary nutrients also interact with intrinsic mechanisms and may accelerate or decelerate aging. Abbreviation: RNA; ribonucleic acid, ROS; reactive oxygen species

Source: Created with BioRender.com

In addition, these women were also more likely to suffer from water loss under the skin, which makes it appear saggy. Based on their research, the authors say it’s still too early to say whether there’s a way to stop crow’s feet or keep skin looking youthful. “This research is groundbreaking in identifying new microbial biomarkers linked to visible signs of aging, such as crow’s feet. This marks a significant step forward in developing technologies for healthier, more youthful skin,” says Qian Zheng, Head of Advanced Research, North America, L’Oréal] (Zambrano *et al.,* 2004; Lopes, 2017; Radolf and Samuels, 2021; Editora Globo, 2024).

4.5. How Collagen Can Be Vegan

Instead of being sourced from animals, collagen can now be produced using genetically modified yeast and bacteria. Researchers have found that the bacterium *Komagataella pastoris* (Guilliierm., 1919) Y. Yamada, M. Matsuda, K. Maeda & Mikata, 1995, is the most effective and commonly used for genetically engineering high-quality collagen. Four human genes that code for collagen are added to the genetic structure of the microbes to produce collagen. Once the genes are in place, the yeast or bacteria then begin producing human collagen building blocks. Pepsin, a digestive enzyme, is added to help structure the building blocks into collagen molecules with the exact structure of human collagen (Figure 19) (Marengo, 2019).

Figure 19: Organic vegan collagen-boosting powder (aloe gorgeous)
Source: https://www.naturelova.com/organic-vegan-collagen-boosting-powder-aloe-gorgeous-vanilla-240g/

4.5.1. Benefits of Vegan Collagen:

1. Potential lower cost for consumers.
2. Lower risk of allergies.
3. Higher safety profile for products.
4. Wider and cheaper availability for medical procedures. 5. Beauty benefits for vegans (Marengo, 2019).

4.6. Biofilm of Bacterial Cellulose of Plant Origin and Hydrolyzed Collagen

Bacterial cellulose (BC) is a polysaccharide excreted by bacterial cells, such as those of the genera Gluconacetobacter, Agrobacter, and Sarcina, which forms as a film at the air/culture medium interface. It has a chemical structure similar to that of plant cellulose, differing in the degree of polymerization and high purity, that is, BC is free of hemicellulose, lignin, and pectin. In addition, it has a high water absorption capacity, peculiar mechanical properties, high crystallinity, good permeability, biocompatibility, and biodegradability, among others (Figure 20) (Arruda, 2019).

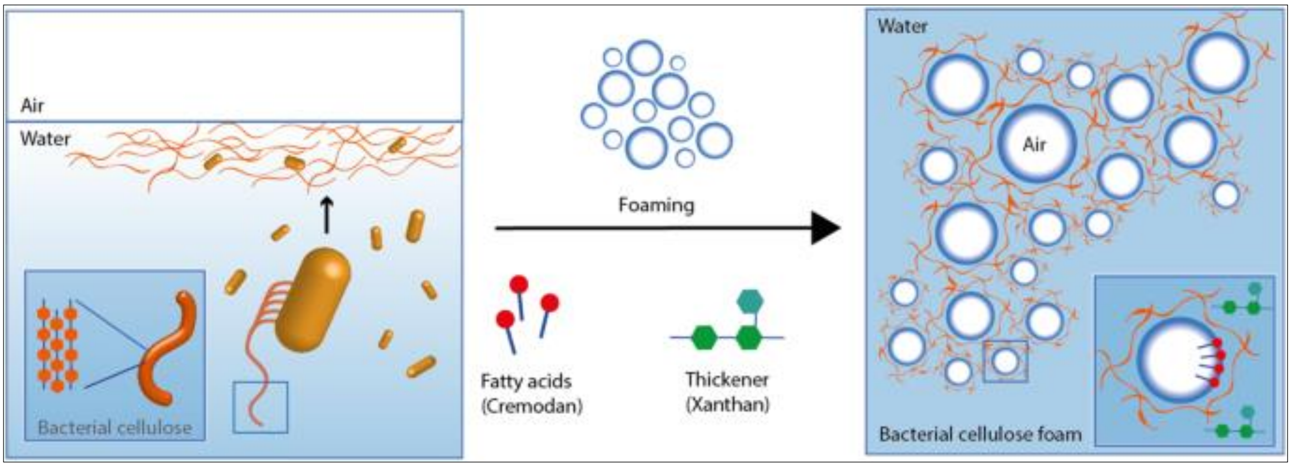

Figure 20: Subdivision of the genus *Gluconacetobacter* Yamada, Hoshino, and Ishikawa 1998:extrudes bacterial cellulose as a function of oxygen and migrates toward the air-water interface. To construct a bacterial cellulose foam, a suspension of *Gluconacetobacter* sp. in growth media is foamed. The air bubbles are stabilized through interfacial stabilization by Cremodan. To avoid water drainage and to enhance the stability of the foam Xanthan is added as a thickener. After bacterial growth, the foam was increasingly stabilized by BC formation leading to stable cellulose foam structures after 4 days
Source: Doi: org/10.1038/s41522-018-0064-3

Due to these aspects, it is commonly used in wound dressings, burn treatments, tissue regeneration, and medical devices. Despite its broad positive aspects, bacterial cellulose has limitations in some applications due to its absence of bioactive compounds, consequently presenting an absence of antioxidant properties. Bioactive compounds are secondary metabolites of plants and animals known for their beneficial biological activity, mainly in preventing neural diseases, cardiovascular diseases, diabetes, cancer, and inflammation, among other diseases (Arruda, 2019).

4.7. Nanocellulose from Bacterial Cellulose with Hydrolyzed Collagen

Fermenter models, different nutrient formulations, and modification of partial O2 and CO2 pressures. Among the strains used is Gluconacetobacter xylinus, the model microorganism in the study of CB production. It is the only known species capable of producing cellulose in commercial quantities, presenting it free of undesirable components (Figure 21) (Gil, 2016; Popa *et al.*, 2022).

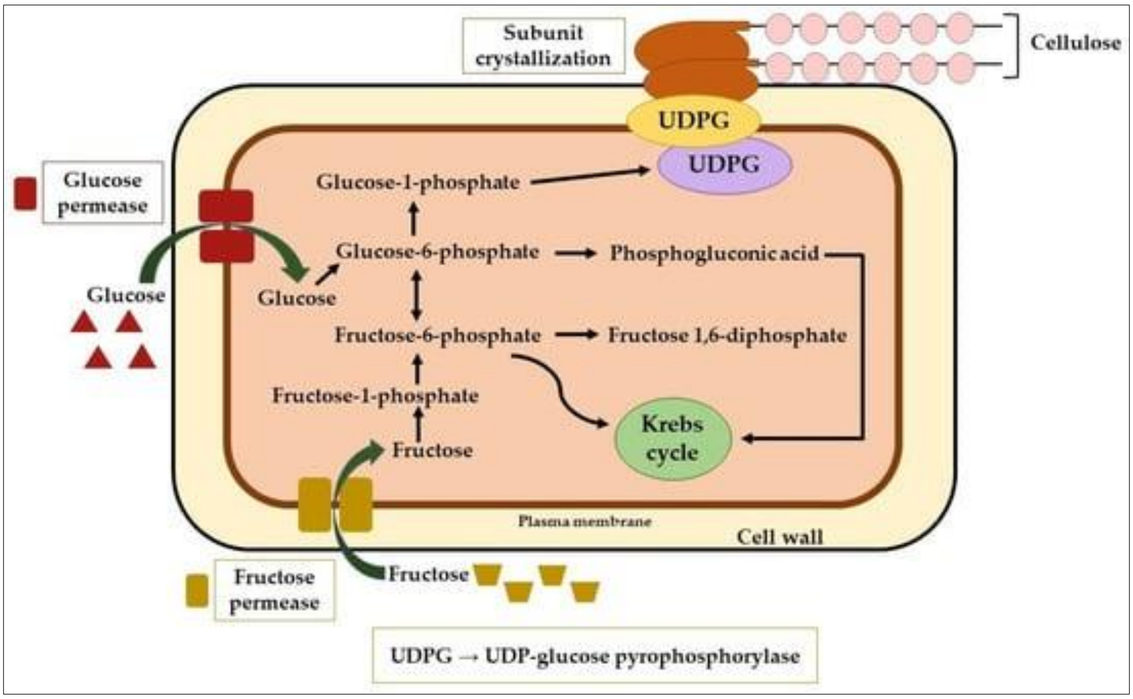

Figure 21: The microscopic cytoplasm synthesis of bacterial cellulose
Source: Doi.org/10.3390/ma15031054

The production of nanocellulose and its application as reinforcement of biodegradable composites and nanocomposites have attracted great attention in recent years, due to its excellent mechanical properties, better than CB itself, combined with low weight, biodegradability and the environmental benefits caused by its use. This nanocellulose is formed from the acid hydrolysis of cellulose. In this process, mainly the amorphous region ruptures with the release of the crystalline portion, resulting in rods of cellulose polymers of the nanometric order. These are highly rigid and crystalline, properties of great interest to the industry (Gil, 2016).

5.0. CONCLUSION

Recent evidence has suggested that the intestinal microbiota is involved in energy regulation and the inflammatory process, an environmental factor related to the pathophysiology of obesity. The microbiota contains a variety of living microorganisms that colonize the intestine, and its development occurs throughout the life cycle from birth to adulthood. Collagen is one of these ingredients with functional characteristics. It is a protein of animal origin, whose function in the body is to contribute to the structural integrity of the tissues in which it is present. However, with the onset of adulthood, collagen deficiency begins to be noticed, as the body reduces its production, making its supplementation necessary.

REFERENCES

- Almeida, L. B., Marinho, C. B., Souza, C. S., & Cheib, V. B. P. (2009). Intestinal dysbiosis. *Brazilian Journal of Clinical Nutrition, 24*(1), 58-65.
- Andrade, V. L. A. (2015). Obesity and intestinal microbiota. *Revista Medica de Minas Gerais, 25*(4), 583-589.
- Arruda, F. I. A. (2019). Development of bacterial cellulose biofilm enriched with bioactive compounds of plant origin and hydrolyzed collagen. Rerieved Jan, 01, 2025, from file:///c:/users/usuario/downloads/r%20-%20d%20-

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- Axarlis, K. L. (2021). Diet supplementation with fish-derived extracts suppresses diabetes and modulates the intestinal microbiome in a murine model of diet-induced obesity. *Marine Drugs, 19*(5), 268.
- Backhed, F. (2004). The gut microbiota is an environmental factor that regulates fat storage. *Proceedings of the National Academy of Sciences, 101*(44), 15718-15723.
- Bervoets, L. (2013). Differences in gut microbiota composition between obese and lean children: a cross-sectional study. *Gut Pathogens, 5*(10), 01-10.
- Carstens, A. (2019). The gut microbiota in collagenous colitis shares characteristics with inflammatory bowel disease-associated dysbiosis. *Clinical and translational gastroenterology, 10*(7), e00065.
- Chen, J., Yang, Y., Yang, Y., Dai, Z., Kim, I. H., Wu, G., & Wu, Z. (2021). Dietary supplementation with glycine enhances intestinal mucosal integrity and ameliorates inflammation in c57bl/6j mice with high-fat diet-induced obesity. *Journal Nutrition, 151*(7), 1769-1778.
- Conde, W. L., & Borges, C. (2011). The risk of incidence and persistence of obesity among Brazilian adults according to their nutritional status at the end of adolescence. *Brazilian Journal of Epidemiology*, *14*(1), 71-79.
- Costa, A., Alchorne, M. M. D. A., & Goldschmidt, M. C. B. (2008). Etiopathogenic factors of acne vulgaris. *Brazilian annals of Dermatology, 83*(5), 451-459.
- Cristália. (2025). Brazilian biodiversity. The wealth of nature. Retrieved Jan, 01, 2024, from https://www.cristalia.com.br/biodiversidade-brasileira
- Das, B., & Nair, G. B. (2019). Homeostasis and dysbiosis of the gut microbiome in health and disease. *Journal Bioscience, 44*(5), 117.
- De, L. A., Serre, C. B., Ellis, C. L., Lee, J., Hartman, A. L., Rutledge, J. C., & Raybould, H. E. (2010). The propensity to high-fat diet-induced obesity in rats is associated with gut microbiota changes and inflammation. *American Physiological Society Journal, 299*(2), 440-448.
- Delzenne, N. M., & Cani, D. C. (2007). Gut microflora as a target for energy and metabolic homeostasis. *Current Opinion in Clinical Nutrition & Metabolic Care*, *10,* 729-734.
- Dibaise, J. K. (2008). Gut microbiota and its possible relationship with obesity. *Mayo Clinic Proceedings, 83*(4), 460-469.
- Editora Globo (2024). The appearance of wrinkles may be linked to skin bacteria. Retrieved Jan, 01, 2025, from https://oglobo.globo.com/saude/noticia/2024/01/12/surgimento-de-rugas-pode-ter-ligacao-com-bacterias-da-pele-entenda.ghtml
- Fleissner, C. K., Huebel, N. A. B. D., El-Bary, M. M., Loh, G., Klaus, S, & Blaut, M. (2010). The absence of intestinal microbiota does not protect mice from diet-induced obesity. *British Journal of Nutrition, 104*(6), 919-929.
- Flório, C. F. L., & Silva, M. C. (2024). Intestinal microbiota and its relationship with obesity: A literature review. *Research, Society and Development, 13*(6), e9213646120.
- Gallagher, J. (2013). Bacteria can be a weapon in the fight against obesity. Retrieved Dec 01, 2025, from https://www.bbc.com/portuguese/noticias/2013/09/130906_bacteria_intestino_obesidade_gm
- Gil, G. G. A. (2016). Functionalization of bacterial cellulose nanocellulose with hydrolyzed collagen. Retrieved Jan, 01, 2024, from https://repositorio.uel.br/srv-c0003-s01/api/core/bitstreams/093bf0b6-ab67-499a-a829-e697d0088f9b/content
- Jiang, J. Y. (2024). A comprehensive review on microbial hyaluronan-degrading enzymes: from virulence factors to biotechnological tools. *Bioresource Bioprocess, 11*, 114.
- Lenharo, M. (2011). Researchers link the presence of intestinal bacteria with obesity. Jornal da Tarde. Retrieved Dec 29, 2024, from Researchers link the presence of intestinal bacteria with obesity.
- Ley, R. E., Bäckhed., F., Turnbaugh, P., Lozupone, C. A., Knight, R. D., & Gordon, J. I. (2005). Obesity alters gut microbial ecology. *Proceedings of the National Academy of Sciences, 102*(31), 11070-11075.
- Lopes, F. A. (2017). Molecular evidence of *Borrelia burgdorferi* sensu lato in patients in the Brazilian Midwest. *Brazilian Journal of Rheumatology, 7*(6), 641–645.
- Marengo, K. (2019). Here's what you need to know about vegan collagen. Retrieved Jan, 01, 2025, from https://www-healthline-com.translate.goog/health/food-nutrition/vegan-collagen?
- Moraes, A. C. F. (2014). Gut microbiota and cardiometabolic risk: mechanisms and dietary modulation. *Brazilian Archives of Endocrinology & Metabolism, 58*(4), 317-327.
- Moura, L. I. (2014). Neurotensin-loaded collagen dressings reduce inflammation and improve wound healing in diabetic mice. *Biochemical et Biophysical Act, 1842*(1), 32-43.
- Neumam, C. (2024). Research at Butantan identifies collagen molecules capable of inhibiting an enzyme that accelerates aging. Retrieved Jan, 01, 2025, from https://butantan.gov.br/noticias/pesquisa-feita-no-butantan-identifica-moleculas-de-colageno-capazes-de-inibir-enzima-que-acelera-envelhecimento-

- Nieuwdorp, M., P., Gilijamse, P. W., Nikhil P. M., Lee, M., & Kaplan, L. M. (2013). Role of the microbiome in energy regulation and metabolism. *Gastroenterology, 146*, 1525–1533.
- Nonino-Borges, C. B., Borges, R.M., & Santos, J. E. (2006). Clinical treatment of obesity. *Medicine, 39*(2), 246-52.
- Park, J. S., Seo, J. H., & Youn, H. S. (2013). Gut microbiota and clinical disease: obesity and nonalcoholic fatty liver disease. *Pediatric Gastroenterology, Hepatology & Nutrition, 6*(1), 22- 27.
- Popa, L., Ghica, M. V., Tudoroiu, E. E., Ionescu, D. G., & Dinu-Pîrvu, C. E. (2022). Bacterial cellulose-a remarkable polymer as a source for biomaterials tailoring. *Materials*, *15*(3), 1054.
- Radolf, J. D., & Samuels, D. S. (2021). Lyme disease and relapsing fever spirochetes: genomics, molecular biology, host interactions, and disease pathogenesis. Caister: Academic Press.
- Rodrigues, A. (2011). Intestinal microbiota and its possible relationship with obesity. *ABESO, 53(*5), 5-7.
- Santos, V. S. (2008). Bacteria Brasil Escola. Retrieved Jan, 02, 2025, from https://brasilescola.uol.com.br/biologia/bacterias.htm
- Schwarz, D., Lipoldová, M., Reinecke, H., & Sohrabi, Y. (2022). Targeting inflammation with collagen. *Clinical and Translational Medicine, 12*(5), e831.
- Shen, J., Obin, M. S., & Zhao, L. (2013). The gut microbiota, obesity, and insulin resistance. *Molecular Aspects of Medicine*, *34*, 39-58.
- Silva, S. T., Santos, C. A., & Bressan, J. (2013). Intestinal microbiota; relevance to obesity and modulation by prebiotics and probiotics. *Hospital Nutrition, 28*(4), 1039-1048.
- Silva, T. F., & Penna, A. L. B. (2012). Chemical characteristics and functional properties of collagen. *Revista do Instituto Adolfo Lutz, 71*(3), 530-539.
- Spezia, G. (2009b). Gut microbiota and its relationship with obesity. *Brazilian Journal of Obesity, Nutrition and Aging, 3*(15), 260-267.
- Spezia, G., Silva, L. T., Santos, S. P., Liberati, R., & Navarro, F. (2009a). Intestinal microbiota and its relationship with obesity. *Brazilian Journal of Obesity, Nutrition and Weight Loss*, *3*(15), 260-267.
- Tilg, H., & Kaser, A. (2011). Gut microbiome, obesity, and metabolic dysfunction. *Journal of Clinical Investigation, 121*(6), 2126-2132.
- Trabulsi, L. R., & Alterthum, F. (2008). Microbiology. Goiânia: Atheneu.
- Varella, D. (2011). Some gut bacteria can make you fat. Retrieved Dec, 29, 2024, from https://drauziovarella.uol.com.br/obesidade/bacterias-que-engordam-artigo/
- Vieira, N., & Zaramel, L. (2022). Some gut bacteria can make you gain weight. Retrieved Dec, 29, 2024, from https://canaltech.com.br/saude/algumas-bacterias-do-intestino-podem-fazer-voce-engordar-234348/
- Vijayan, D. K., Sreerekha, P. R., Dara, P. K., Ganesan, B., Mathew, S., Anandan, R., & Ravisankar, C. N. (2021). Antioxidant defense of fish collagen peptides attenuates oxidative stress in gastric mucosa of experimentally ulcer-induced rats. *Cell Stress and Chaperones, 27*(1), 45-54.
- Vivian, T. A. B. (2015). Gut microbiota, obesity, and type 2 diabetes mellitus: what is the relationship? Retrieved Jan, 02, 2025, from https://www.fsp.usp.br/crnutri/index.php/2015/10/16/microbiota-intestinal-obesidade-e-diabetes-melito-tipo-2-qual-a-relacao/
- Watanabe, R., Yamaguchi, M., Watanabe, K., Shimizu, M., Azusa, T., Sone, H., & Kamiyama, S. (2021). Effects of collagen peptide administration on visceral fat content in high-fat diet-induced obese mice. *Journal of Nutritional Science and Vitaminology, 67*(1), 57-62.
- World Health Organization (WHO). (2013). World Health Statistics 2012. Retrieved Dec, 31, 2024, from http://www.abeso.org.br/noticia/oms-obesidade-mata-28-milhoes-por-ano
- World Health Organization (WHO). (2024). Updates list of bacteria that pose the greatest threat to human health. Retrieved Dec 02, 2024, from https://news.un.org/pt/story/2024/05/1831781V
- Yang, K. (2021). Alterations in the gut virome in obesity and type 2 diabetes mellitus. *Gastroenterology, 161,* 1257–1269.
- Zambrano, M. C., Beklemisheva, A. A., Bryksin, A. V., Newman, S. A., & Cabello, F. C. (2004). *Borrelia burgdorferi* binds to, invades, and colonizes native type I collagen lattices. *Infection and Immunity Journal*, *272*(6), 3138-3146.
- Zhang, H, Q. L., Shen, Q., Wang, R., Guo, Y., Zhang, C., & Richel, A. (2022). Comparative analysis of the bioactive compounds in chicken cartilage: protective effects of chondroitin sulfate and type ii collagen peptides against osteoarthritis involve gut microbiota. *Frontiers Nutrition, 30*(9), 843360.