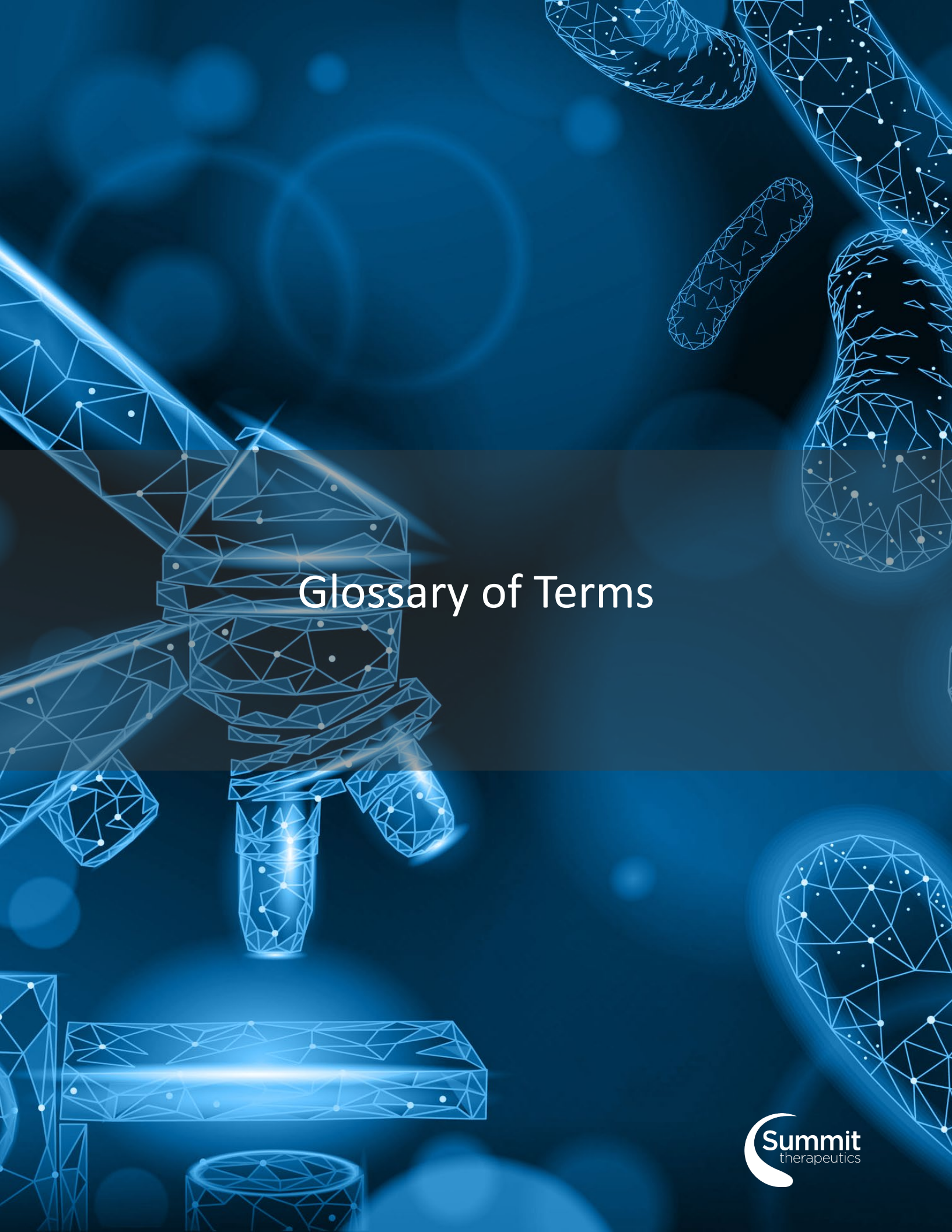

Glossary of Terms

Summit therapeutics

Glossary of Terms

Term	Definition
Antibiotic resistance genes	Genes known to be involved in bacterial resistance; such genes may include for example beta-lactamases which can inactivate various beta-lactam antibiotics.
Bile Acids	A collection of steroid-based gut metabolites, the balance of the amount of and types of bile acids in the gut microbiome are believed to play an important role in the development of or prevention of an initial and potential recurrent instance of C. difficile Infection.[i]
Bloodstream infections	An infectious disease defined by the presence of viable bacterial or fungal microorganisms in the bloodstream that elicit or have elicited an inflammatory response.[ii]
Carbapenem-Resistant Enterobacteriaceae (CRE)	Enterobacteriaceae that are resistant to carbapenems, a type of antibiotic used to treat some of the most resistant forms of gram-negative bacteria. This resistance means that there are fewer options available to treat infections caused by these bacteria, as CRE do not respond to commonly used antibiotics. In many cases, including infections such as urinary tract infections caused by CRE germs, more complex treatments are required. Instead of taking oral antibiotics at home, patients with these infections might require hospitalization and intravenous (IV) antibiotics. Occasionally CRE are resistant to all available antibiotics. CRE are a threat to public health.[iii]
Clostridia	A class of bacteria that exist within a healthy gut microbiome that likely plays a largely crucial role in microbiome homeostasis by interacting with the other resident microbe populations and providing specific and essential functions to the overall microbiome. While most groups of Clostridia have a commensal, or co-existing, relationship with the rest of the gut microbiome, some Clostridia can be pathogenic, when larger concentrations of the bacteria exist, such as Clostridioides difficile bacteria.[iv]
Clostridioides difficile (C. difficile or C. diff.)	A germ (bacterium) that can cause severe diarrhea and colitis (an inflammation of the colon). C. difficile can live naturally in the intestines (gut) of humans and not cause any problem. Sometimes changes in the gut microbiome lead the bacteria to grow and produce toxins from which illness can develop.[v]
C. diff. Infection (CDI)	A bacterial infection of the colon that produces toxins causing inflammation of the colon and severe watery diarrhea, very painful and persistent abdominal cramping, nausea, fever, and dehydration. CDI can also result in more serious disease complications, including bowel perforation (a tear in the gastrointestinal tract), sepsis, and death. Most cases of C. diff. infection occur while a person is taking antibiotics or not long after a person has finished taking antibiotics. CDI is an insidious and debilitating disease that necessitates patient isolation because of its contagious nature, making it able to be passed from one person to another either in a hospital or long-term care facility setting or in the community.[vi]
DDS-04	A series of new mechanism antibiotics targeting Enterobacteriaceae. DDS-04 acts via LolCDE, an essential bacterial complex responsible for the transport of lipoproteins from the inner to outer membrane in gramnegative bacteria. Because this complex has not been a previous target of existing antimicrobials, bacterial resistance does not yet exist to this targeted approach, potentially allowing for the treatment of highly-resistant Enterobacteriaceae-caused infections. Some of these infections, particularly in a subset of CRE-caused infections, do not have effective treatments through currently available antibiotics.[vii]
Discuva Platform	Summit Therapeutics' proprietary platform that enables the identification of novel antimicrobials to expand Summit's pipeline of investigational drugs. The Discuva Platform focuses on identifying new antibiotics against bacteria where increasing resistance has limited treatment via existing antibiotics currently on the market.[viii]

Term	Definition
Enterobacteriaceae	A large family of different types of bacteria (germs) that commonly cause infections both in healthcare settings, such as hospitals and long-term care facilities, and in communities. Examples of germs in the Enterobacteriaceae family include Escherichia coli (commonly known as E. coli) and Klebsiella pneumoniae. Enterobacteriaceae are frequent carriers of resistance genes to many of the currently available antibiotics used to treat bacterial infections. Because they are bacteria, Enterobacteriaceae can be passed from person to person.[ix]
Escherichia coli (E. coli)	A type of Enterobacteriaceae found in the environment, foods, and intestines of people and animals. E. coli are a large and diverse group of bacteria. Although most strains of E. coli are harmless, others can make a person sick. Some kinds of E. coli can cause diarrhea, while others cause urinary tract infections, bloodstream infections, respiratory illness and pneumonia, and other illnesses.[x]
Gastrointestinal tract	A series of hollow organs joined in a long, twisting tube from the mouth to the anus. These organs also include the esophagus, stomach, small intestine, and large intestine.[xi]
Gut microbiome	Within the human gastrointestinal tract, the gut microbiome is a collection of microbiota, consisting of trillions of microorganisms that inhabit the gut. The gut microbiota is considered an important partner to human cell systems, interacting extensively with other organs in the body to influence a wide range of functions from digestion to immunity. The balance of the different types of cells and microorganisms within the microbiome is considered to be important in the microbiome's ability to properly play its role within the human body. Disruption in the balance of microorganisms within the gut microbiome (known as dysbiosis) is believed to impact the gut microbiome's role in keeping a person healthy and free of certain conditions or diseases.[xii xiii]
Gut microbiota	The trillions of microorganisms, including symbiotic and pathogenic microorganisms, that inhabit the gut. Examples of these microorganisms include bacteria, fungi, viruses, protists, and archaea.
Gut resistome	Within the human gastrointestinal tract, the diversity and dynamics of the antibiotic resistance genes that are harbored by the gut microbiota. Examples of the gut resistome include genes associated with resistance to carbapenem antibiotics.[xiv]
Hospital-acquired pneumonia (HAP)	Pneumonia that occurs 48 hours or more after a patient has been admitted to a hospital and was not present and incubating at the time of admission. Ventilator-associated pneumonia (VAP) is a significant sub-set of HAP, often occurring in intensive care units (ICUs) with a patient on a ventilator. Common pathogens of HAP and VAP include Enterobacteriaceae and Pseudomonas species. Due to the presence of the bacteria in a hospital, these bacteria may be resistant to different antibiotics, potentially causing the resulting infection to be more difficult to treat.[xv]
Klebsiella pneumoniae	A type of Enterobacteriaceae that can cause different types of healthcare-associated infections, including pneumonia, bloodstream infections, wound or surgical site infections, and meningitis. Increasingly, Klebsiella bacteria have developed resistance to antibiotics, most recently to the class of antibiotics known as carbapenems. Klebsiella bacteria are normally found in the human intestines (where they do not cause disease). In healthcare settings, Klebsiella infections commonly occur among sick patients who are receiving treatment for other conditions. Patients whose care requires devices like ventilators (breathing machines) or intravenous (vein) catheters, and patients who are receiving long courses of certain antibiotics are most at risk for Klebsiella infections. Healthy people typically do not develop Klebsiella infections.[xvi]

Term	Definition
Sepsis	The body's extreme response to an infection and a life-threatening medical emergency. Sepsis occurs when an existing infection triggers a chain reaction throughout a person's body via the bloodstream. Without timely treatment, sepsis can rapidly lead to tissue damage, multi-organ failure, and death. Almost any type of infection can lead to sepsis. Infections that lead to sepsis most often start in the lung, urinary tract, skin, or gastrointestinal tract. Sepsis is a condition and is not contagious; however, the underlying cause of the infection (e.g., bacteria) can be spread from person to person. Bacterial infections cause most cases of sepsis.[xvii]
Shotgun metagenomic analysis	Shotgun metagenomic sequencing sequences all genomic DNA present in a sample. This allows a more accurate taxonomic annotation of the microbiota compared to other techniques such as 16S rRNA amplicon sequencing as well as antibiotic resistance gene profiling and metabolic function profiling.
Urinary tract infections (UTI)	Common infections that happen when bacteria, often from the skin or rectum, enter the urethra, and infect the urinary tract. The infections can affect several parts of the urinary tract, but the most common type is a bladder infection. Kidney infections are another type of UTI and can be more serious than bladder infections. UTIs are usually caused by bacteria and are treated with antibiotics. People who have had multiple UTIs requiring multiple courses of antibiotics are at increased risk of developing antibiotic-resistant infections that can become increasing complex to treat.[xviii]
Vancomycin	An antibiotic that is used to treat CDI

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