



Clinical metagenomic analysis and Cancer

Burgos-Molina AM.1, Mercado-Sáenz S.2, Morales-Moreno F.3, González-Vidal A.4, Ruiz-Gómez MJ.4

1: Surgical Specialties, Biochemistry and Immunology. School of Medicine. Malaga University. Spain

2: Medical Biology and Histology PAI Ref: CTS429. Department of Human Physiology, Human Histology, Pathological Anatomy and Physical Sport Education. School of Medicine. Malaga University. Spain. smercad@uma.es. 952131587.

3. Xenogene Laboratories. NICA 46447. F.morales@xenogene.es

4. Radiology and Physical Medicine. Ophthalmology and Otorhinolaryngology. School of Medicine. Malaga University. Spain

Introduction

The implication of microorganisms in cancer has been known for more than a century. Parasites, bacteria and viruses have been associated with cancer. The following bacteria, among others, have been associated with cancer: *Helicobacter pylori*, the first to be recognized as an oncogenic organism, capable of causing gastric cancer and could be related to extragastric cancers. *Helicobacter hepaticus* linked to liver cancers, *Chlamydia psittaci*, *Borrelia burgdorferi*, and *Streptococcus bovis*, have been linked to eye, skin, and colorectal cancers, respectively. *Bacteroides fragilis*, a commensal bacterium of the human intestine, has been associated with colorectal cancer in case of overgrowth. Among the viruses associated with cancer, the following have been studied, among others: *Human papillomavirus*, associated with breast and ovarian cancer, *Hepatitis B and C virus* associated with liver cancer, *Epstein-Barr virus* associated with Burkitt's lymphoma, nasopharyngeal cancer, and B-virus T-cell lymphomas, Human herpes 8 causes Kaposi's sarcoma, and Human T-cell lymphotropic virus is associated with leukemia and T-cell lymphoma.

The following parasites have also been associated with cancer: *Opisthorchis viverrini*, a trematode endemic to Southeast Asia, can cause cholangiocarcinoma. *Schistosoma hematobium*, another parasitic flatworm, lives in freshwater snails in Africa and the Middle East and causes bladder cancer.

In the mid-1980s, microbiologists accepted that 99.8% of microorganisms are nonculturable.

Among the methods designed, metagenomics has become a powerful study tool, mainly environmental, however, its clinical application is extremely useful.

Metagenomics is the functional analysis that, through genomic and bioinformatic technologies, allows studying the entire collection of genomes of a sample to obtain sequences of the different microorganisms present in it, extracting and analyzing their DNA and RNA globally, directly, without cultures, which represents a change of course in Microbiology.

Currently, Xenogene's clinical metagenomic analysis identifies over 77,000 pathogens and their antimicrobial resistances in the same analysis (archaea, bacteria, fungi, viruses, protists, and parasites). It does not require a prior hypothesis about the origin of the infection or infestation, it uses metagenomic techniques without the need for cell cultures or PCR, so no artifacts are introduced into the results.

Objetives

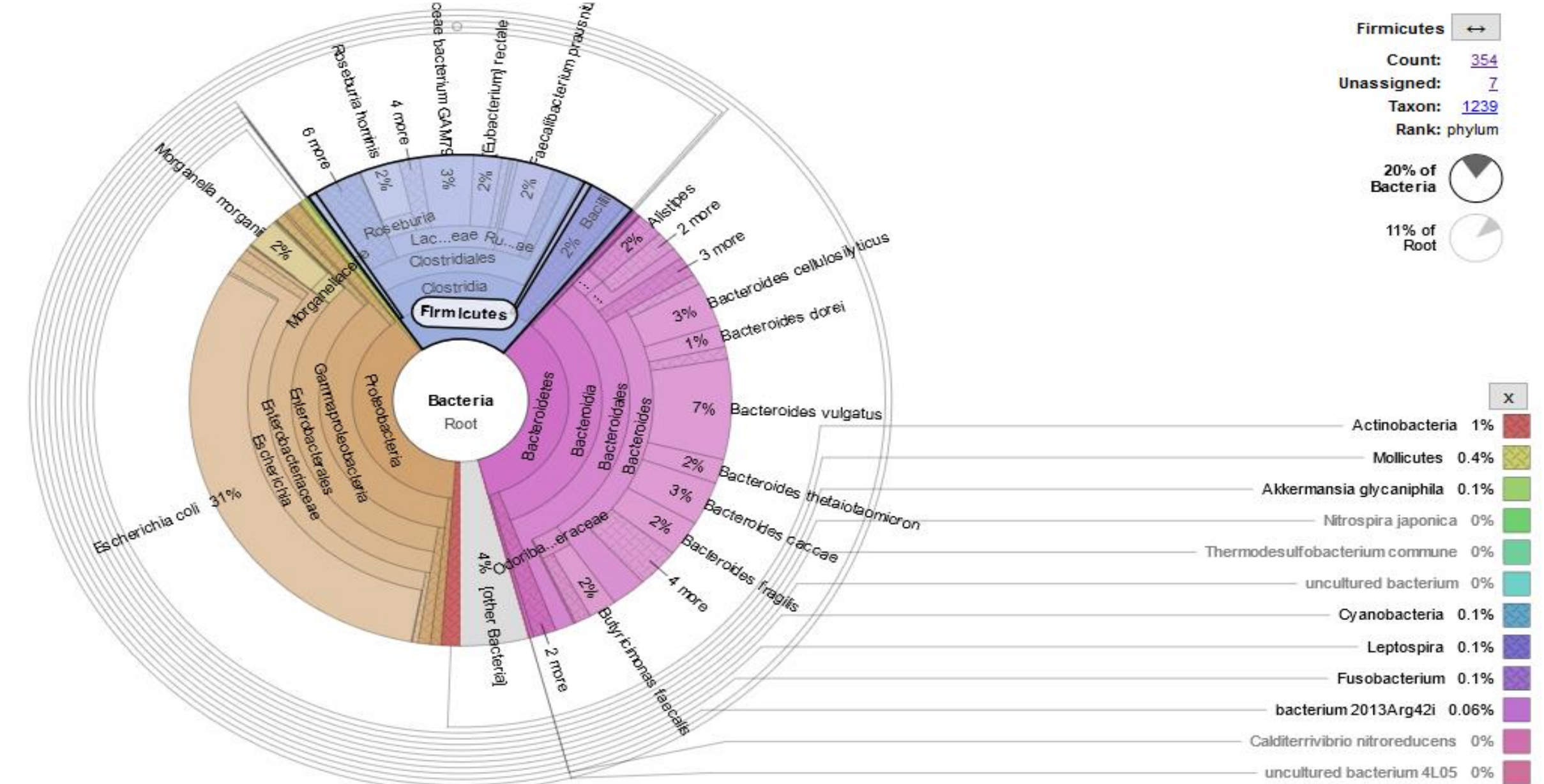
The objectives of the present study are to demonstrate that the AMC (Clinical Metagenomic Analysis) is capable of identifying the various microorganisms, associating the microorganisms with the diseases they cause and relating the metagenome with the metabolome, which allows the application of personalized therapies for the patient, based on the combination of all the factors studied.

Material and methods:

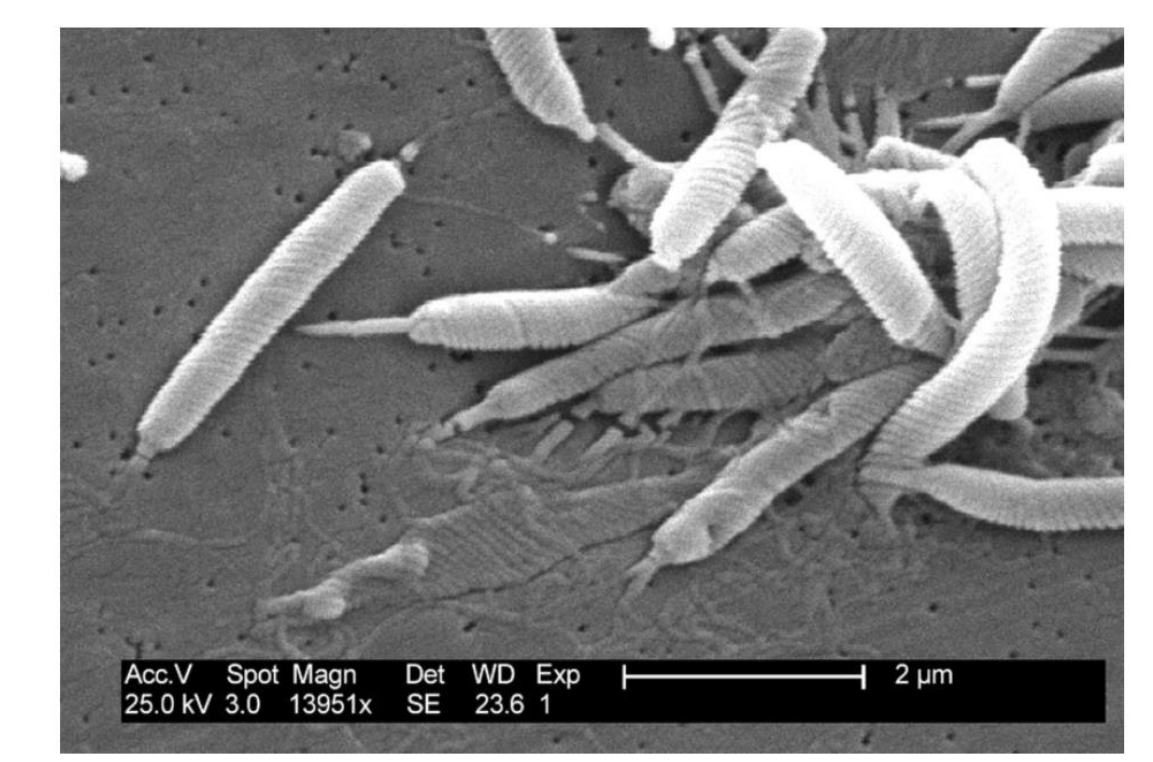
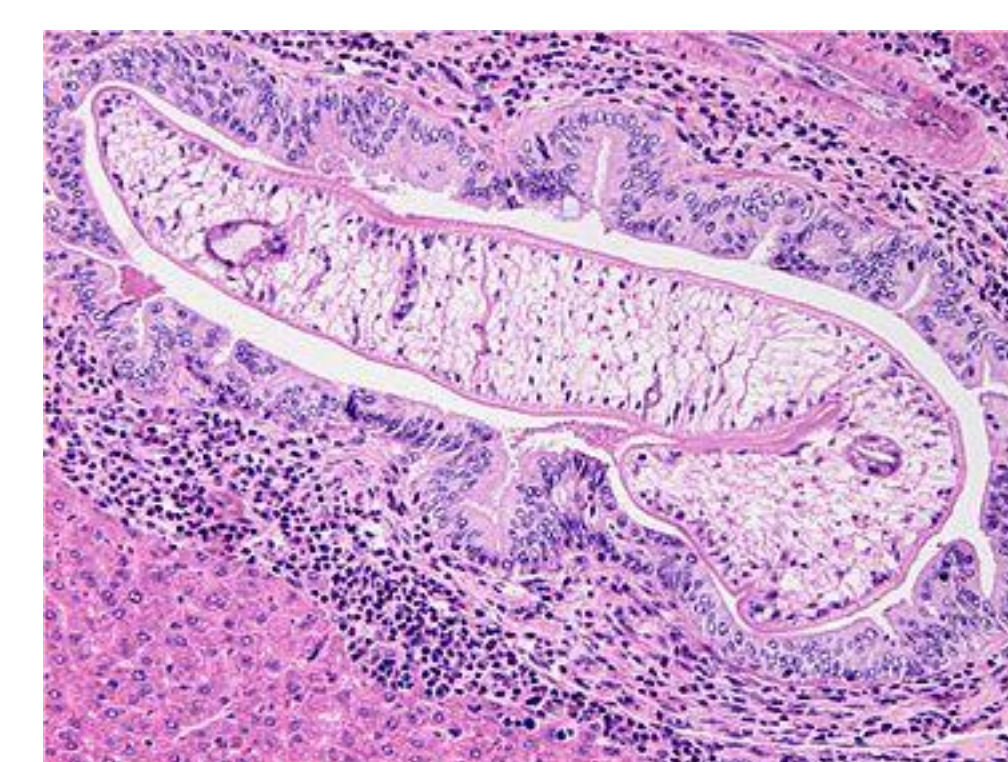
In Metagenomics, the nucleic acids of the different microorganisms that make up the sample are globally extracted and the genomes are directly sequenced. It is a change of course in microbiology. The Fasta and FastQ files obtained from the sequencing are compared with various databases (NCBI, ASSEMBLE...) using bioinformatics, for their correct identification. Subsequently, bioinformatics allows, through mathematical algorithms and statistical application to the management and analysis of biological data, to obtain refined results and more precise data, which are treated with an artificial intelligence system, capable of interpreting data, learning from them and using those data. knowledge to accomplish specific tasks and goals through flexible adaptation, as Kaplan and Haenlein put it.

Microorganism	Associated cancer
Bacteria	
<i>Helicobacter pylori</i>	Gastric cancer and extragastric cancer
<i>Helicobacter hepaticus</i>	Liver cancer
<i>Chlamydia psittaci</i>	Eye cancer
<i>Borrelia burgdorferi</i>	Skin cancer
<i>Streptococcus bovis</i>	Colorectal cancer
<i>Bacteroides fragilis</i>	Colorectal cancer
Viruses	
<i>Human papillomavirus</i>	Breast and ovarian cancer
<i>Hepatitis B and C virus</i>	Liver cancer
<i>Epstein-Barr virus</i>	Burkitt's lymphoma, nasopharyngeal cancer
<i>B-virus</i>	T-cell lymphomas
<i>Human herpes 8</i>	Kaposi's sarcoma
<i>Human T-cell lymphotropic virus</i>	Leukemia and T-cell lymphoma
Parasites	
<i>Opisthorchis viverrini</i>	Cholangiocarcinoma
<i>Schistosoma hematobium</i>	Bladder cancer

Some microorganisms associated with cancer



Ratio and percentages of bacteria in a patient's urine sample. Clinical metagenomic analysis



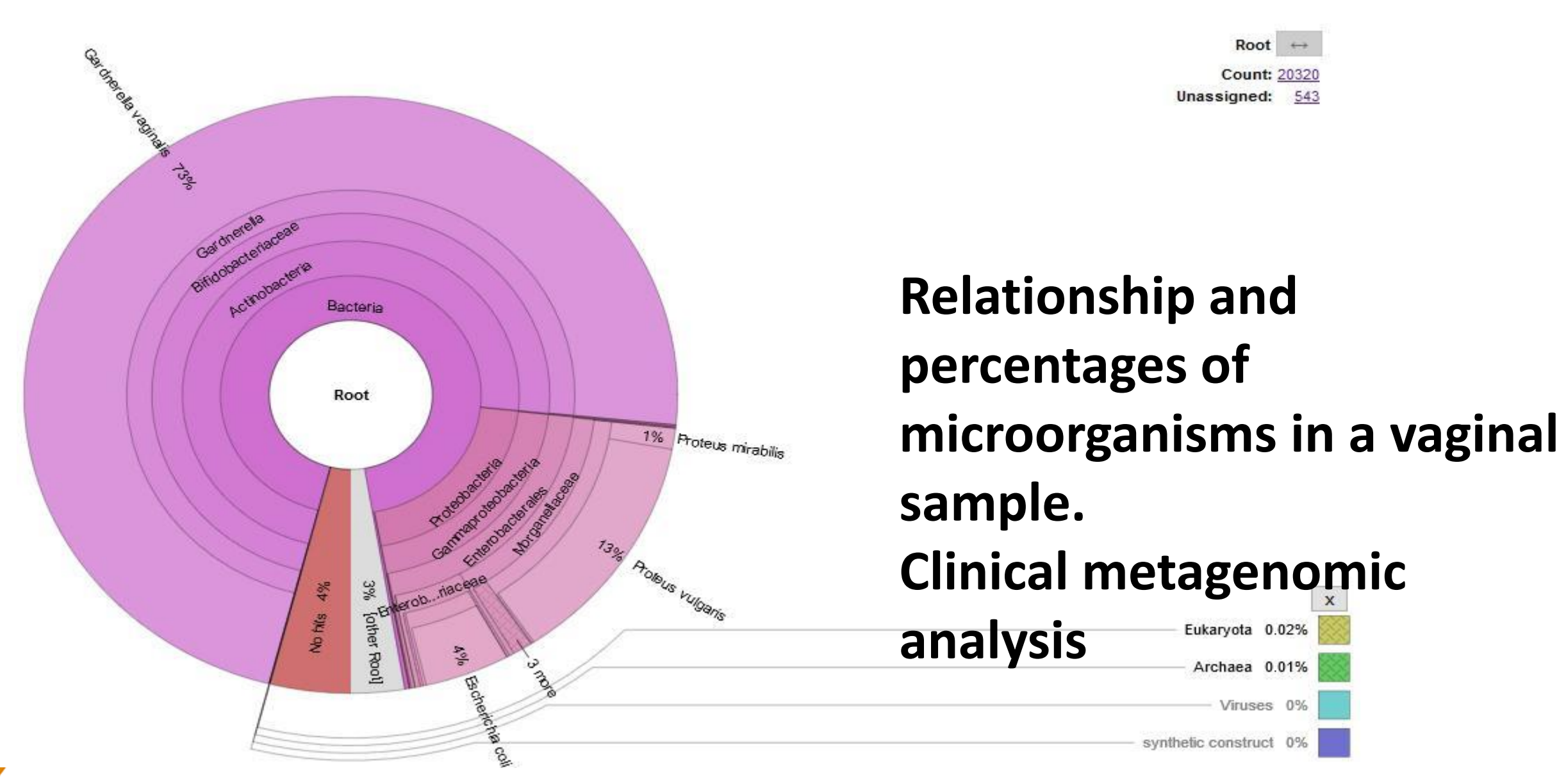
Opisthorchis viverrini

Dr. Patricia Fields, Dr. Collette Fitzgerald, USDCDP

Results & Conclusions

After seven years of periodic controls by the SEIMC (Spanish Society of Infectious Diseases and Clinical Microbiology), it can be affirmed that the analysis is capable of detecting microorganisms in any type of sample (Blood, CSF, Saliva, BAL, Urine, Sputum, Faeces, Tissues, Prosthetic Material, Exudates, Swabs, Etc...), it requires a small amount of sample, it identifies more than 77,000 pathogens in a single test, simultaneously detects Archaea, G+ and G- Bacteria, Fungi, Viruses, Protists and parasites, it detects nonculturable pathogens and those that revert to false negatives, it is not affected by inhibition by antibiotics or other causes, resistance to antibiotics and antimycotics are detected, results are obtained in 24 hours, it is the most sensitive and reliable direct microbial identification technique and specific today.

The analysis is 87% more sensitive than a culture, 99% reliable in gender determination, 91% reliable in sensitivity, increases the rate of accurate diagnosis of infections by more than 50%, as it is NGS sequencing it is more sensitive, specific and reliable than 16s and 18s sequencing. The test is highly useful for detecting microorganisms associated with cancer as well as their resistance plasmids.



Relationship and percentages of microorganisms in a vaginal sample. Clinical metagenomic analysis