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Over three decades of biotechnological research in health and agriculture: Interdisciplinary applications for a sustainable future

Más de tres décadas de investigación biotecnológica en salud y agricultura: aplicaciones interdisciplinarias para un futuro sostenible

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Resumen: Las interrupciones de los sistemas de salud y agricultura a nivel global resaltan la necesidad de soluciones biotecnológicas innovadoras que fortalezcan la resiliencia y sostenibilidad locales. En las últimas décadas, la Universidad del Valle de Guatemala (UVG) ha avanzado la investigación en biotecnología en la salud y agricultura. Avances en ingeniería genética, biotecnología molecular y celular se han aplicado para mejorar la vigilancia de enfermedades, el desarrollo de nuevas estrategias de control vectorial y aplicaciones en bioprospección para producir soluciones localmente relevantes, incluyendo potenciales terapias para cáncer. Se están desarrollando biosensores diseñados como instrumentos de punto de atención de bajo costo para diagnósticos, como una alternativa prometedora ante el incremento de costos de diagnóstico. En agricultura, el uso de microorganismos locales y el potencial de la edición génica para mejorar la salud del suelo y las plantas han recibido mayor reconocimiento como estrategias sostenibles. Presentamos el desarrollo en UVG de un portafolio diverso de aplicaciones biotecnológicas para mejorar el control, tratamiento y diagnóstico de enfermedades, promoviendo prácticas agrícolas sostenibles. El avance de estas líneas de investigación requerirá un abordaje interdisciplinario y colaboraciones intersectoriales e internacionales fortalecidas.

Palabras clave: biosensores, biología celular, cáncer, insecto, microbiología, microbioma de suelo, transgénico, vector.

Abstract: Global disruptions in health and agricultural systems highlight the need for innovative biotechnological solutions that strengthen local resilience and sustainability. Over the past decades, Universidad del Valle de Guatemala (UVG) has advanced biotechnological research in both health and agriculture. Advances in genetic engineering, molecular, and cellular biotechnology have been applied for improved disease surveillance, the development of novel vector control strategies, and bioprospecting applications aimed at producing locally relevant applications, including potential cancer therapies. Biosensors, designed as low-cost point-of-care tools, are being developed as promising alternatives in face of rising diagnostic costs. In agriculture, research on the use of local soil microorganisms and the potential of gene editing to improve soil and plant health are gaining increasing recognition as a sustainable strategy. Here, we present the development at UVG of a diverse portfolio of biotechnology applications aimed at improving disease control, treatment, and diagnostics, while promoting sustainable agricultural practices. Advancing these research lines will require interdisciplinary approaches and strengthened intersectoral and international collaborations.

Key words: biosensors, cancer, cell biology, insect, microbiology, soil microbiome, transgenic, vector.

INTRODUCCIÓN

Over the past three decades, biotechnological research at UVG has evolved from the adoption of polymerase chain reaction (PCR) in the 1990s at the Center for Health Studies (CES) for the control of parasitic disease vectors, to the introduction of genetic engineering in the 2000´s for the control of vector-borne disease through a collaboration with the Center for Biotechnology Studies (CEB), established in 2010. Since 2020, new cell biology capabilities and collaborations with the Biochemistry and Biomedical Engineering Departments at the UVG allowed new research lines in bioprospection for novel cancer treatments and low-cost biosensors for diagnostics. Concurrently, alliances between CEB and industry have advanced research on microorganisms and gene editing to improve soil health, while the Center for Agricultural and Food Studies (CEAA) has supported rural agriculture through microbial biofactories. Overall, this progression reflects the increasingly interdisciplinary nature of biotechnology at UVG (Fig. 1).

Biotechnology for vector and insect pest control

Biotechnological tools such as PCR and DNA sequencing were introduced in Guatemala in the 1990´s, enabling advances in molecular epidemiology and genetic engineering. Early studies at the Center for Health Studies (CES) focused on parasitic diseases, including malaria vector identification (De Merida *et al.* 1995) and monitoring the elimination of onchocerciasis (Oskam *et al.* 1996). Innovative vector control approaches later emerged, such as genetically modifying symbiotic bacteria in Chagas' disease vectors (Beard *et al.* 2001) to produce anti-parasitic molecules targeting the parasite *Trypanosoma cruzi.* The proof-of-principle was demonstrated using *Rhodococcus rhodnii* in the vector *Rhodnius prolixus* (Beard *et al.* 2001).

With the discovery of RNA interference (RNAi), the strategy evolved in 2010 to target the vector itself by engineering symbiotic bacteria to express dsRNA against egg development genes in *Rhodnius prolixus*, reducing oviposition when feeding the transgenic symbionts to adult females (Taracena *et al.* 2015). RNAi based gene silencing methods were also later extended to the sterile insect technique in malaria vectors and fruit flies of agricultural importance (García Cáffaro *et al.* 2017; González López *et al.* 2018). Larvae of *Anopheles albimanus* were fed transgenic *Escherichia coli,* expressing dsRNA targeting genes specific for (1) spermatogenesis as a strategy for male sterilization and (2) actin associated with female flight for female elimination (Flores Ayuso *et al.* 2016; González López *et al.* 2018). Similarly, *Anopheles gambiae* fed transformed *E. coli* producing dsRNA against sex determination genes exhibited gene silencing and reduced female development (Taracena *et al.* 2019). Additionally, feeding adult mosquitoes heat-killed recombinant *E. coli* expressing dsRNA targeting salivary gland genes inhibited gland development (Taracena *et al.* 2022).

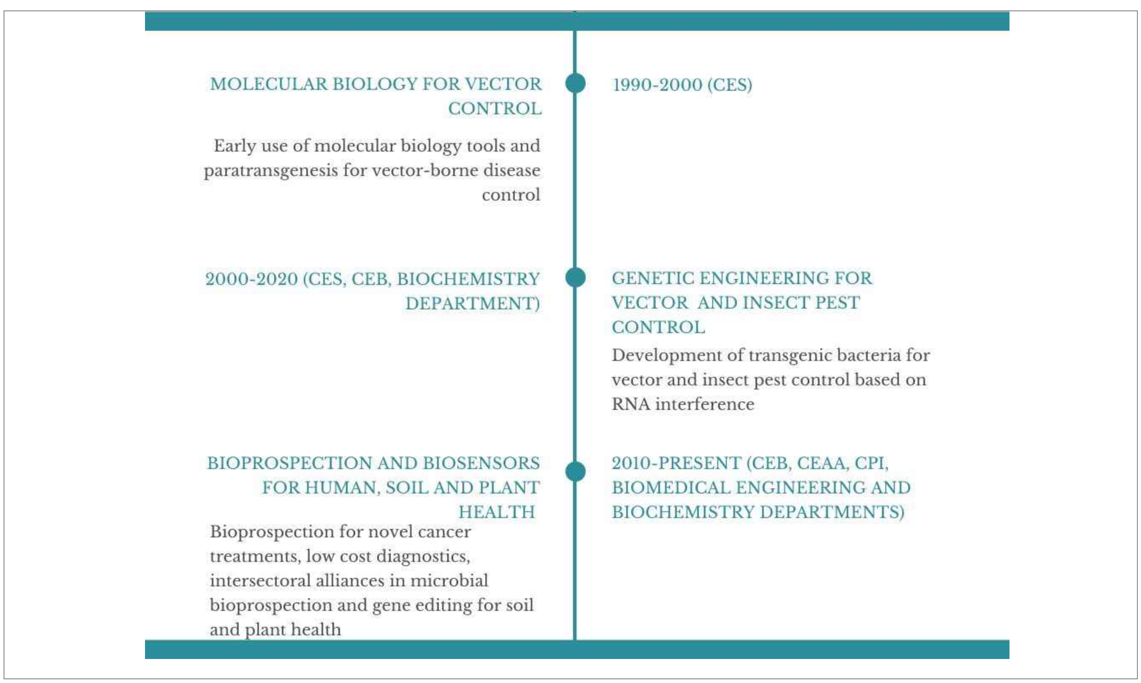

Figura 1. Development of research lines for biotechnological applications in health and agriculture at the Universidad del Valle de Guatemala. Research lines, the centers and departments involved are shown since the 1990´s. CES: Center for Health Studies; CEB: Center for Biotechnology Studies; CEAA: Center for Agricultural and Food Studies; CPI: Center for Industrial Processes.

Figure 1. *Desarrollo de líneas de investigación para aplicaciones biotecnológicas en salud y agricultura en la Universidad del Valle de Guatemala. Se presentan las líneas de investigación, así como los centros y departamentos involucrados desde la década de 1990. CES: Centro de Estudios en Salud; CEB: Centro de Estudios en Biotecnología; CEAA: Centro de Estudios Agrícolas y Alimentarios; CPI: Centro de Procesos Industriales.*

RNAi of genes involved in female fruit fly development were also evaluated to complement the sterile insect technique in collaboration with the national Mediterranean fly control program (García Cáffaro *et al.* 2017).

These studies demonstrated the potential of transgenic microorganisms as powerful tools for vector and insect control, particularly in the context of insecticide resistance. However, developing such biotechnological approaches requires robust ethical and regulatory frameworks. In Guatemala, a ministerial agreement approved in 2018 regulates research on transgenic organisms for agricultural applications (Ministerio de Agricultura 2018). With the rapid advancement of gene-editing technologies, these regulations will require to be updated to ensure continued compliance with ethical standards.

Natural resources for the development of novel pharmaceutical products

Cancer arises from uncontrolled cell growth that forms tumors capable of spreading throughout the body. It remains a leading cause of mortality worldwide, with nearly 10 million deaths annually and a growing global burden of disease (Bray *et al.* 2024). Health systems in developing countries often lack early diagnostic tools and adequate therapies (Knaul *et al.* 2015; Sung *et al.* 2021), highlighting the need for preventive and modulatory alternatives. In Guatemala, the most prevalent cancers include prostate, breast, liver, cervical and gastric cancer, although population-based data remain limited (Flood *et al.* 2018).

Among roughly 150 FDA-approved anticancer drugs - 61 cytotoxic and 89 targeted therapies - only a minority directly act on cell death pathways (Pushpakom *et al.* 2018). Most cytotoxic agents damage DNA or disrupt cell division, affecting both tumor and healthy cells and causing significant side effects. Targeted therapies improve selectivity by inhibiting proliferation and angiogenesis pathways, but likewise rarely modulate cell death pathways. Notable exceptions include Venetoclax, a BCL-2 inhibitor that induces mitochondrial apoptosis (Roberts *et al.* 2016), and histone deacetylase (HDAC) inhibitor, which can trigger cell cycle arrest and apoptosis (Marks & Breslow 2007).

In low- and middle-income countries such as Guatemala, where annual healthcare expenditure is approximately $341 USD per capita (Sung *et al.* 2021), the high cost and toxicity of current anticancer therapies severely limit access and long-term management. These constraints underscore the urgent need for cost-effective therapeutic alternatives that selectively target cancer cell survival pathways, such as those involved in programmed cell death, while minimizing systemic toxicity and improving patient outcomes.

Natural products from plants and fungi are promising anticancer alternatives due to their ability to modulate multiple cell pathways (Reshetnikov & Tan 2001). Bioactive compounds such as flavonoids, terpenoids, phenolics and polysaccharides can influence tumor progression by inducing apoptosis, arresting the cycle and modulating oxidative stress (Choudhari *et al.* 2020; Zhu *et al.* 2025).

Edible mushrooms such as *Pleurotus* spp. and *Cantharellus cibarius* are particularly promising due to their safety profiles, supported by long-standing dietary and medical use. This makes them especially relevant for low- and middle-income countries seeking cost-effective and accessible therapeutic strategies, positioning natural products as valuable complementary or alternative approaches in cancer prevention and therapy.

Polysaccharides from the mushroom *Pleurotus ostreatus*, such as POPS-1, show dose-dependent inhibition comparable to 5-FU in HeLA cells (Tong *et al.* 2009). Similarly, *P. ostreatus* extracts reduce proliferation in breast cancer cell lines in a concentration-dependent manner, supporting their antitumor potential (Jedinak & Sliva 2008). Although less studied, *C. cibarius* extracts have selective cytotoxicity against LS180 colorectal cancer cells with minimal effect on CCD841 CoN normal cells (Hao *et al.* 2022).

Recent studies at CEB, in collaboration with the Biochemistry Department, indicated that these edible fungi species, *P. ostreatus* and *C. cibarius*, may have relevant antitumor properties. Preliminary *in vitro* results show fractions-specific bioactivity in neuroblastoma models, with variable selectivity toward non-tumoral cell lines. Phytochemical analyses (Fourier Transform Infrared spectroscopy and chromatography) support the presence of polysaccharides, phenolic compounds, terpenoids and other metabolites consistent with previously described bioactive classes in medicinal fungi (Chugh *et al.* 2022). Early assays reveal dose-dependent cytotoxicity, and ongoing investigations are evaluating the underlying cell death pathways.

We also evaluated these fungal extracts on peripheral blood mononuclear cells from healthy donors. Preliminary data suggest that certain fractions exhibit immunomodulatory activity, depending on their composition. This dual functionality - direct antitumor effects alongside immune modulation - enhances their therapeutic potential. Nevertheless, further studies are needed to clarify the underlying mechanisms. Overall, these observations support the translational potential of *P. ostreatus* and *C. cibarius* as sources of antitumor and immunomodulatory agents, particularly in resource-limited settings as Guatemala, where accessible and selective therapies are urgently needed.

Our approach focuses on identifying bioactive molecules from Guatemalan species and advancing their development through biotechnology. By using recombinant systems and synthetic biology, we aim to enable scalable and controlled production while reducing dependance on natural extraction. We also seek to enhance efficacy through rational modification or combination with complementary agents. Overall, this integrating strategy

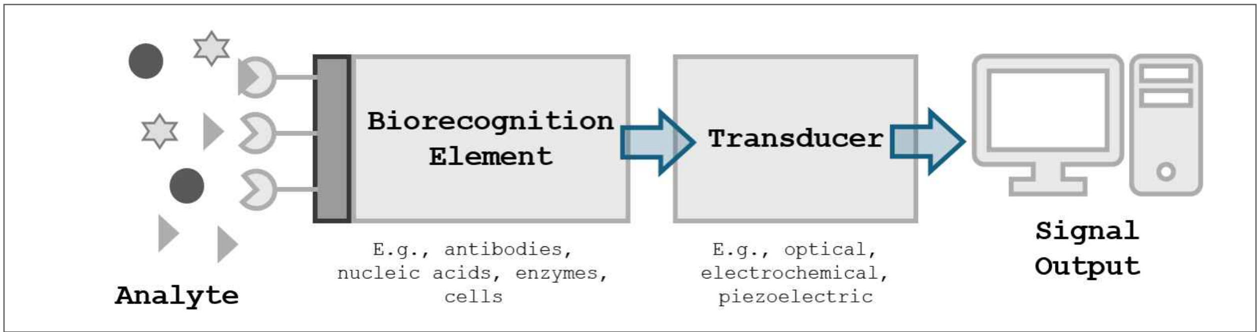

Figura 2. Schematic representation of a biosensor.
Figure 2. *Representación esquemática de un biosensor.*

aims to generate optimized bioactive compounds with strong translational potential to improve patient outcomes in our country.

Development of low-cost biosensors

Developing countries like Guatemala face significant economic and geographical barriers for health care, with over half of the population living in poverty and limited access to medical services (*Appeal - Guatemala*, n.d.). Improving diagnostic tools - particularly point-of-care (PoC) biosensors - could improve early detection of diseases and significantly enhance patient outcome in remote or resource-limited locations.

Biosensors are analytical devices that combine biological components with transducers to detect biomolecules (Fig. 2) (Nagel *et al.* 1992), with applications in diagnostics, environmental monitoring, or food safety.

Biosensors have evolved from specialized laboratory instruments into accessible tools capable of transforming disease surveillance into developing countries where centralized laboratory infrastructure remains scarce.

Electrochemical biosensors are the most popular low-cost platform, detecting changes in current or potential upon analyte interaction with a biorecognition element. Their simplicity, portability, affordability, and rapid response make them ideal for point-of-care diagnostics (Wang *et al.* 2021). Recent advances in graphene-based electrodes - particularly laser-induced graphene - offer improved electrochemical performance and ease (Peña-Bahamonde *et al.* 2018; Cui *et al.* 2025; Ramulu Torati & Slaughter 2025). As part of student project at the UVG, locally fabricated three-electrode systems based on this technology have successfully measured glucose concentrations and antigen-antibody interactions, demonstrating strong potential for low-cost diagnostics.

Paper-based biosensors are low-cost, portable, and disposable devices widely used for PoC testing. They rely on capillary action to move samples through patterned channels without external power and can be rapidly fabricated using simple methods such as wax printing (Singh *et al.* 2018). Typically employing colorimetric detection, they enable easy visual interpretation, making them crucial in resource-limited settings (Singh *et al.* 2018; Ko & Liao 2023). At UVG, protypes are developed using immersion and wax permeation techniques to generate hydrophobic barriers that define sample, reaction and waste zones (Fig. 3). A glucose colorimetric assay using glucose oxidase and a starch-iodine complex produces a response proportional to glucose concentration. The results confirm the feasibility of these prototypes for PoC diagnostics and recognize the impact of their simple, low-cost fabrication for healthcare system in developing countries.

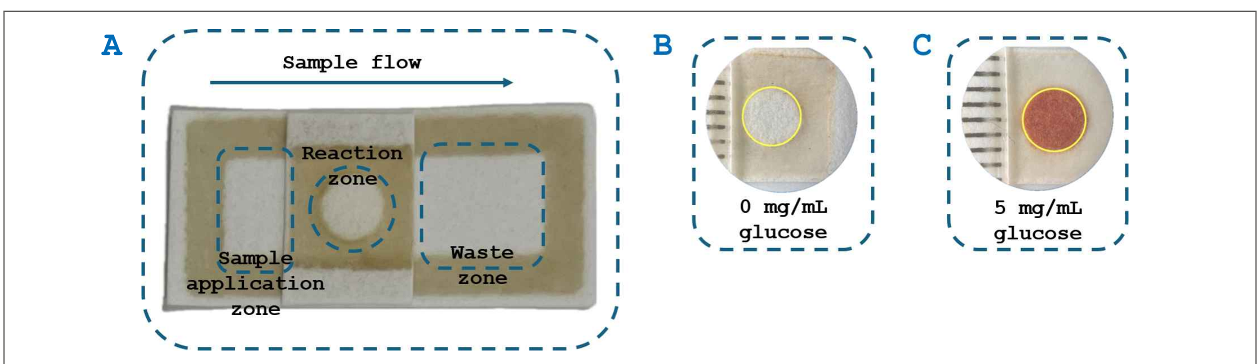

Figura 3. (A) Image of paper-based biosensor comprising a sample application zone, reaction zone, and waste zone. Colorimetric signal obtained in reaction zone upon application of (B) 0 mg/mL glucose and (C) 5 mg/mL glucose. Modified from Cabrera Porras (2025).
Figure 3. *(A) Imagen de un biosensor basado en papel que comprende una zona de aplicación de la muestra, una zona de reacción y una zona de desecho. Señal colorimétrica obtenida en la zona de reacción tras la aplicación de (B) 0 mg/mL de glucosa y (C) 5 mg/mL de glucosa. Modificado de Cabrera Porras (2025).*

Despite progress, biosensors must achieve large-scale commercialization as low-cost, on-site diagnostic tools. Key challenges include achieving sensitivity and selectivity comparable to laboratory, enabling multiplex detection of multiple analytes, and integrating data (e.g., through smartphones) into health information systems for effective surveillance and clinical decision-making. Addressing these limitations could unlock scalable, high-performance diagnostics that bridge the gap between laboratory capabilities and accessible, real-time applications in healthcare, agriculture, and environmental systems - particularly in developing countries.

Microorganisms for soil and plant health

Agriculture is a cornerstone of Guatemala's economy, contributing approximately 10 % of national GDP and 26 % of employment (Hernández *et al.* 2023; Banco de Guatemala 2025; MAGA 2025). Key crops - maize, beans, cacao, cardamom, and sugarcane - support both food security and exports (MAGA 2025). However, heavy reliance on inorganic fertilizers has led to soil degradation, water pollution, and reduced microbial diversity (Lu & Tian 2017), underscoring the need for more sustainable approaches.

Microbial biotechnology offers promising agricultural solutions based on biocontrol (Roche Recinos *et al.* 2009), such as biofertilizers and plant growth-promoting rhizobacteria (PGPR), which, although not full substitute for chemical inputs, can significantly mitigate environmental impacts and improve soil health (Mahanty *et al.* 2017; Schütz *et al.* 2018; Shahwar *et al.* 2023). Research at the Center for Agricultural and Food Studies (CEAA) and the Center for Biotechnology Studies (CEB) at UVG has focused on harnessing native soil microorganisms to enhance agricultural sustainability.

The CEAA has collaborated with farmers to systematize artisanal fermentation, isolate and evaluate native PGPR linked to key crops such as cacao, cardamom, maize and beans. In parallel, CEB has partnered with agro-industries to identify microorganisms with agricultural potential, including resistance to herbicides (Richter López 2011) and biofertilizers suited to tropical conditions and apply gene editing to enhance PGPR potential. Together, these efforts aim to reduce chemical fertilizer use while maintaining or improving productivity and soil health.

Extensive microbial screening of native soils (cacao, cardamom, maize, beans, milpa, and sugarcane) revealed strong plant growth-promoting traits, including nitrogen fixation, hormone production, and nutrient solubilization (Ochoa Elias 2022; Flores Solares 2025; Herrera-González *et al.* 2025). Similar capacities were found in fungi from sugar monoculture (Sánchez González 2023; Vela Torres 2023; Contreras Motta 2025). These findings demonstrate the rich microbial diversity and biotechnological potential of Guatemalan soils, underscoring the importance of their conservation and study for sustainable development (Ochoa Elias 2022; Sánchez González 2023; Herrera-González *et al.* 2025).

Soil microbiome analyses showed higher diversity complex systems like milpa and lower diversity in monocultures of cacao and cardamom (Herrera-González *et al.* 2025), though sugar monoculture did not present significant differences from native forest (Ochoa Elias 2022; Sánchez González 2023). This suggests that practices such as intercropping can enhance microbiome resilience and support long-term sustainability.

Strains from sugarcane mills were improved through UV-induced mutagenesis (Aguilar Rodriguez 2024) and CRISPR-Cas9 modifications (Say Agosto 2023, 2024) to enhance nitrogen fixation capacity. These strains were subsequently incorporated into biofertilizers (Castañon Castillo 2022) and tested in greenhouse trials, where they improved sugarcane growth.

Trials for maize biofertilizers, specially under nutrient-poor conditions show more moderate responses in beans; studies in cacao and cardamom are ongoing due to their longer growth cycles (Herrera-González *et al.* 2025). The Center of Industrial Processes (CPI) supported formulation, optimization, and scale-up. Work with community-run fermenters (biofactories or 'biofábricas') has identified valuable practices and challenges related to infrastructure, quality control, and standardization, revealing high variability among biofactories and the need to strengthen technical training and unified protocols to ensure consistent product quality.

These efforts demonstrate that Guatemalan soils harbor a rich reservoir of microorganisms with significant potential for sustainable agriculture. By integrating microbiology, genomics, and biotechnology with industry and community collaboration, UVG has advanced locally-adapted biofertilizers and soil management strategies, underscoring the role of academia-industry partnerships in bridging the gap between research and application, supporting more sustainable and resilient agricultural systems aligned with a One Health approach.

Conclusiones

Genetic engineering, bioprospection and biosensor technologies offer new tools to improve health and agriculture in the region (Fig. 4) but require multisectoral collaborations and strong ethical and regulatory frameworks. At UVG, research has evolved towards interdisciplinary and national collaborations, highlighting the need for open innovation and industrial partnerships to enable effective technology transfer.

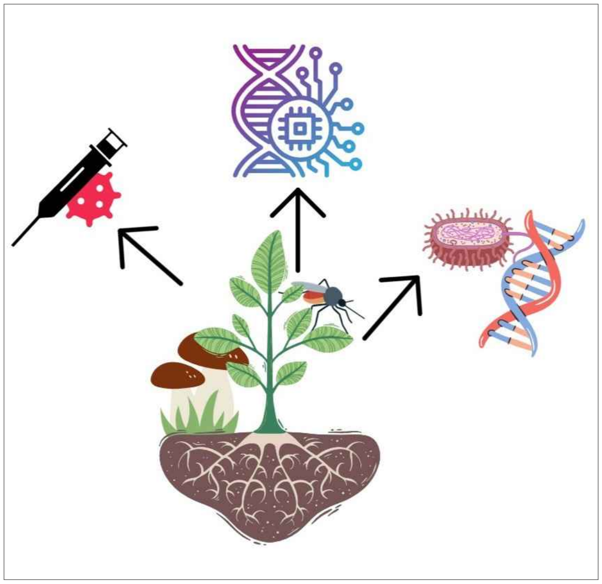

Figura 4. Biotechnological applications to enhance human, plant and soil health include biosensors, genetic engineering technologies, and the bioprospection of soil microorganisms and fungi.

Figure 4. *Aplicaciones biotecnológicas para promover la salud humana, vegetal y del suelo incluyen biosensores, tecnologías de ingeniería genética y bioprospección*

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