Imagine you take your car to the shop because there's something funny with it. Only the mechanics can't figure out what - they only do clutches and brakes. With modern vehicles becoming ever more complex, tracking down malfunctions requires a team effort by specialists with different skills and knowledge. BIO5, in a way, is a state-of-the-art garage for bioresearch. Unraveling the complex workings of living systems is only possible by combining different technologies and disciplines that have traditionally been separated. In BIO5's research labs, biologists work side by side with physicists, chemists, medical experts and engineers, to name but a few. Deciphering the human genome has provided researchers with huge amounts of data: a DNA sequence encompassing three billion letters. Life science research has now moved to a functional approach, seeking to understand how the genes and their products, the proteins, interact and what their roles are in the molecular workings of life. Analogous to genomics, this has brought about disciplines such as proteomics and metabolomics, to investigate an organism's full inventory of proteins and metabolites, respectively. Due to their comprehensive scope, the new "-omics" approaches require new methods to gather, store and analyze these data. Using high-throughput technologies, bioscientists now can analyze thousands of genes and proteins in a single experiment and within a few hours. They can obtain snapshots of the state of activity of all genes or proteins interacting in biochemical pathways under different circumstances. For example, it is now possible to precisely pin down what makes a cancer cell different from a normal cell.

BIO5 combines disciplines and technologies to develop new treatments for cancer, heart and respiratory diseases, to improve crops, use plants to produce pharmaceuticals, and to explore the potential of compounds that could become new drugs.

Turning spices into drugs: The potential of combining genomics, proteomics and metabolomics

Spices get David Gang all excited. In two greenhouses, the assistant professor in plant sciences cultivates several varieties of basil, turmeric and ginger plants. Cherished mostly for their culinary value, they hold medicinal secrets as well. Gingerols, oily substances from ginger, have anti-inflammatory properties and act as anti-oxidants, i.e. they fight cell-damaging processes in the body. Eugenol, extracted from basil, is a widely used antiseptic. Together with his co-workers, Gang studies the molecular pathways by which plants make their beneficial ingredients. "Once we figure out which genes are involved in the production process and which job each gene performs, we can reproduce these pathways and develop new crops or functional foods," Gang explains. His work exemplifies how new products and applications can arise from bringing together new technologies and traditionally separated disciplines. His research takes advantage of genomics, proteomics and metabolomics and unites plant science, biochemistry, pharmacology and agriculture. Currently, Gang's research focuses on curcumin, the colorful ingredient of turmeric. The substance inhibits inflammation and has cancer-preventive activity. Turmeric requires hot, humid conditions, which limits its range as a
crop to Hawaii and Florida. Gang's research goal is to modify tomato or potato plants so they produce curcumin. According to Gang, potatoes are ideal candidates. "They have all the necessary precursor molecules. All it would take is a few extra genes and they'll make curcumin."

(Image caption: Using a mass spectrometer, David Gang and graduate student Zhengzhi Xie analyze plant metabolites with potential medicinal properties.)

Gaining a molecular understanding of disease using human genomics: BIO5's route to a "personalized medicine"

Complex lung diseases such as asthma and chronic obstructive pulmonary disease (COPD) take a major toll on the health and life of people in the United States. Asthma affects 12 million to 15 million Americans and is reaching epidemic levels in children. COPD, which is strongly linked to smoking, affects more than 15 million adults and is the fifth-leading cause of death in the country. The complexity of asthma and COPD stems from an intricate interplay between genetic factors and environmental triggers, which interact to disturb immunologic pathways, leading to chronic inflammation in the lungs and breathing problems. Since the genetic mechanisms and environmental influences that predispose to complex lung diseases differ among individuals, it is necessary to develop "personalized" therapies. These therapies will integrate genetics, immunology, respiratory biology and medicine. Donata Vercelli's group uses functional genomics to elucidate the mechanisms that govern the activity of genes playing important roles in immune responses and how subtle genetic variations between individuals influence these processes. The goal of her work is to identify the genes and regulatory processes that are crucial in the development of complex lung diseases.

(Headshot Donata Vercelli)

If one were to label traditional genetics work as "one gene at a time", Walt Klimecki's lab door would read "Sorry, bulk only". In his high-throughput facility, everything goes by the hundreds and thousands, except staff. Place a DNA sample into a test tube, dilute it to the right concentration, transfer the solution to another test tube, seal it and pass it on for analysis - what would take hours of technician work is a matter of seconds for Klimecki's high-throughput robots. Only that each one processes 384 samples in one go. Klimecki and his group compare gene sequences from different persons and look for individual variations known as polymorphisms. Subtle as they are, polymorphisms determine a person's susceptibility to diseases or the response to certain drugs. "With high-throughput technology we can analyze DNA samples from thousands of individuals," Klimecki explains. "This makes it possible for us to detect associations between a certain polymorphism and how it affects disease susceptibility or drug effectiveness." According to the researcher, understanding polymorphisms is likely to move healthcare from the current "one-drug-for-all" to a personalized "my medicine" approach. "We'll be able to
determine an individual's risk to develop a disease like asthma and to identify the environmental factors that a particular person should avoid. If people know their individual risks, they can adjust their lifestyle."

Image: Walt Klimecki loads a high-throughput robot with DNA samples for processing.

From the Lab to the Greenhouse: The Art of Improving Crops Through Basic Research

Chieri Kubota and Gene Giacomelli come from different scientific backgrounds but share a love for veggies. Kubota is a plant physiologist whose research focuses on improving the nutritional value and storage life of produce. Giacomelli is an agricultural engineer and heads The University of Arizona's Controlled Environment Agriculture Center (CEAC), which is dedicated to developing cost-effective ways of utilizing water, energy, labor and other resources in innovative crop production practices. The new partnership with the CEAC is part of BIO5's Translational Agriculture Initiative, which tackles the global challenges associated with the population increase, such as food production, sustainable natural resource use, and environmental conservation. The CEAC provides the link in transforming findings from basic research in plant genomics and physiology into commercial applications for agricultural crop production. Kubota and Giacomelli, for example, work together on new strategies for the development and cost-efficient production of improved crop plants. One of Kubota's projects involves increasing the natural level of lycopene in tomatoes, a substance with proven anti-oxidant activity. In the greenhouses at the Controlled Environment Agriculture Center, the researchers can figure out the optimal growth conditions. All factors critical to growth and yield can be tightly manipulated and controlled, for example temperature, humidity, sunlight intensity, water and nutrients - even pests. Another approach BIO5 is pursuing is to introduce recently discovered, functionally useful genes into agricultural and horticultural crop species to overcome food and fiber deficiencies and environmental problems worldwide.

(Image showing Gene and Chieri crouching in front of hydroponic tomato plant)
Caption: Homegrown results: Dr. Chieri Kubota and Dr. Gene Giacomelli seek ways to enhance the nutritious value of crops such as tomatoes.

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