

# TECHNOLOGY INNOVATION PROGRAM <sup>2019</sup>

# The Technology Innovation Program



Delivering new technologies and solutions to industry to help increase the nation's economic competitiveness is an important part of Oak Ridge National Laboratory's (ORNL) mission. The Technology Innovation Program (TIP) was created to accelerate the commercial adoption of promising ORNL technologies by making targeted investments to increase the technologies' commercial readiness and raise their visibility to prospective partners. TIP is funded by royalties from previously licensed ORNL technologies.

Each year, ORNL scientists and engineers compete to participate in TIP. A panel of laboratory managers and commercial experts selects 4–5 of the most compelling technologies for a year of research and development investment and increased outreach to prospective partners. Toward the end of the year, prospective industry partners are invited to submit applications to commercialize the TIP technologies, and the companies with the most compelling commercialization plans are offered licenses. A portion of TIP teams whose technologies are successfully licensed are competitively awarded additional funding for further research and development to be performed at ORNL in partnership with the licensing companies.

The 2019 cohort of TIP technologies includes:

- CellSight - Rapid, Native Single Cell Mass Spectrometry
- Nanocapsular Radiation Track Etch Indicator
- Rapid Regeneration of Recalcitrant Plant Species
- BEST: Biomacromolecule Engineering by Soft Chain Coupling
- Genetic Improvement of Salt and Drought Tolerance in Crop Plants

Each of these technologies is believed to be an important breakthrough with significant commercial potential.

Since 2013, ORNL has invested more than \$7M in 34 TIP projects, resulting in 26 commercial licenses and options with partners ranging from Fortune 100 companies to early-stage startups. This brochure provides brief descriptions of the 2019 TIP technologies, introductions to the inventors behind the innovations, and contact information for the technology transfer managers responsible for licensing. ORNL will accept license applications for each technology beginning in the third quarter of calendar year 2019, with a goal of entering license agreements by the end of the year.

## About Oak Ridge National Laboratory



ORNL is the largest US Department of Energy science and energy laboratory, conducting basic and applied research to deliver transformative solutions to compelling problems in energy and security. With an annual budget of \$1.4 billion, ORNL is home to 4,750 research and mission support staff, including 1,100 staff scientists and engineers.

ORNL's diverse capabilities span a broad range of scientific and engineering disciplines, enabling the laboratory to explore fundamental science challenges and to carry out the research needed to accelerate the delivery of solutions to the marketplace. ORNL supports DOE's national missions of scientific discovery, clean energy, and national security through leadership in four major areas of science and technology: neutrons, computing, materials, and nuclear technologies.

Over the past decade, ORNL researchers have produced a portfolio of nearly 700 US patents, and the laboratory currently has more than 150 active technology licenses.

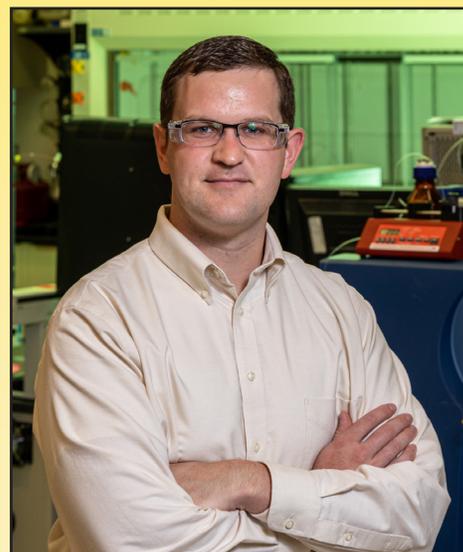
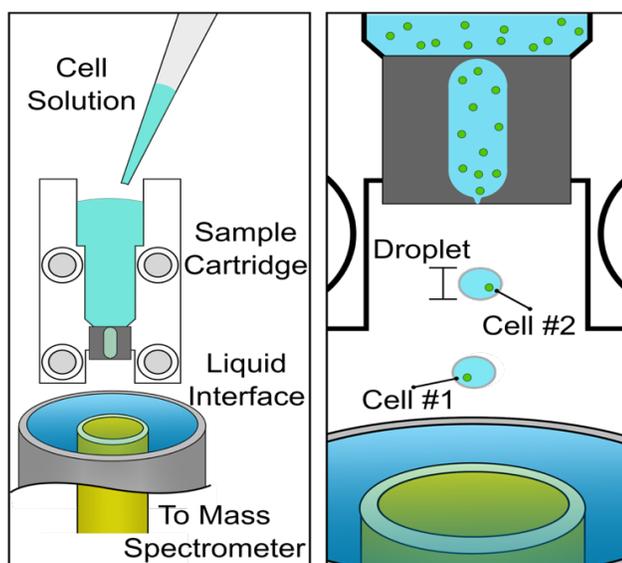
For more information, please visit our webpage at [www.ornl.gov](http://www.ornl.gov).

# CellSight — Rapid, Native Single Cell Mass Spectrometry

**Problem:** Cells are naturally heterogeneous, exhibiting differences in chemistry due to their history, age, and microenvironment, among other factors. Tumors, for example, are heterogeneous mixtures that include epithelial, mesenchymal, stromal, and immune cells. Even when they start from a single genetic precursor, natural stochastic cellular processes create variation in cell chemistries over time. Conventional measurements of cell chemistry fail to identify cellular variations by providing only an average picture of the cell. New technologies that offer single cell resolution are needed to understand cellular heterogeneity.

**Solution:** CellSight enables untargeted chemical analysis of cell suspensions with single-cell resolution. The system utilizes single-cell droplet ejection and liquid extraction mass spectrometry to measure cellular chemistry quantitatively, with high throughput, in an untargeted manner and without any sample preparation or molecular staining required. Droplet ejection isolates individual cells that are captured in a continuously flowing liquid solvent via an extraction–mass spectrometry technology pioneered and patented at ORNL. Upon being exposed to the solvent, the cell ruptures due to the change in osmotic pressure. The analyte molecules are then measured using mass spectrometry in an untargeted or targeted manner. The CellSight system measures cellular chemistry quickly (1 s/cell) and can process thousands of molecules simultaneously. These unprecedented capabilities will provide critical insights into cell chemistry.

**Impact:** Knowledge of the chemical constituents in single cells, including lipids, metabolites, and proteins, is valuable for applications such as determining cellular function, understanding molecular mechanisms inside cells, and designing targeted therapies. Most studies measure cellular chemistry in aggregate, and, thus, information on cellular variations is lost and understanding of cellular function impeded. Research related to disease treatment, pharmaceutical drug development, cell signaling, and cell function will be aided by rapid characterization and quantitation of a cell's molecular components, with detail provided by resolving single cells.



## John "Jack" F. Cahill, PhD Chemical Sciences Directorate

Dr. Cahill is an associate research scientist in the Chemical Sciences Directorate at ORNL. His research focuses on the development and application of novel surface sampling and high-throughput mass spectrometry techniques to chemically characterize tissues, plant systems, bacterial colonies, and materials at small spatial scales. Dr. Cahill's work on elucidating metabolic chemistry with cellular resolution led to the CellSight system.

## Intellectual Property

CellSight—Rapid, Native Single Cell Mass Spectrometry, ID-201804255

## Publications

- J. F. Cahill, J. Riba, and V. Kertesz, "Rapid, Untargeted Chemical Profiling of Single Cells in Their Native Environment," *Anal. Chem.* 2019; 91 (9): 6118–5126. DOI: 10.1021/acs.analchem.9b00680.

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### Timothy McKnight Energy and Environmental Sciences Directorate

Timothy McKnight is a research staff member in the Electrical and Electronics Systems Research Division's Sensors and Embedded Systems Group. He holds engineering science degrees from the University of Michigan and University of Tennessee. His research interests include chemical, biological, and radiological nano- and microstructured systems. His work has resulted in over 65 publications and 18 patents. In 2014, he was recognized as a Battelle Distinguished Inventor.

### Intellectual Property

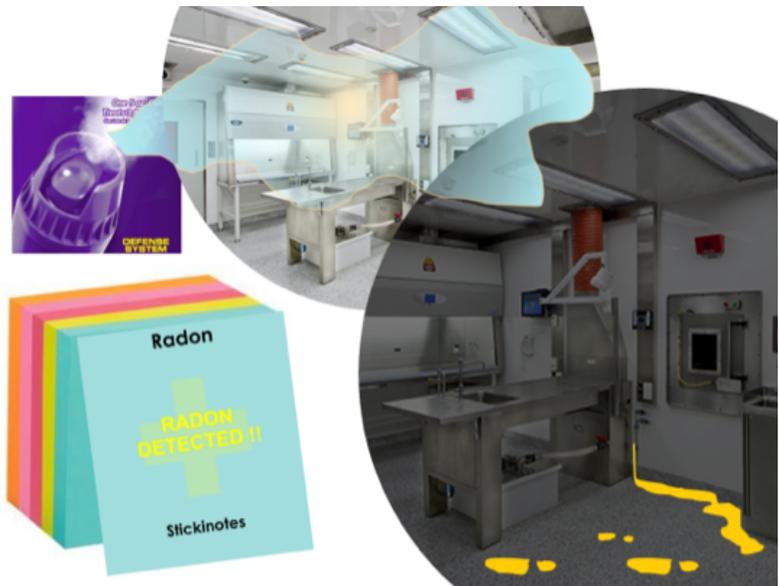
Radiation Contamination Visualizer;  
ID-201804293, DOE S-138,964

## Nanocapsular Radiation Track Etch Indicator

**Problem:** Radioactive contamination from phenomena such as spills of radioactive materials and accumulation of radon gas within homes can be colorless, odorless, and essentially invisible without proper detection equipment. These characteristics result in a significant risk of harmful interaction with radioactive contamination and the uncontrolled spread of these materials. Conventional track etch materials, used for detection of radioactive materials, must be processed under laboratory conditions using caustic chemical etching, increasing risk and reducing flexibility.

**Solution:** ORNL is developing a nanocapsular track etch material that delivers a visible indication following exposure to alpha-particle radiation. Unlike conventional track etch materials, the new capsules feature a biodegradable etch mechanism that provides feedback to users without laboratory processing. The technology may be implemented on small, fixed surfaces such as wipes and sticky notes to provide low-cost single-point test strips or may be aerosol dispersed to larger surfaces, including entire laboratories, to facilitate safe and effective cleanup following radiological spill events.

**Impact:** Low-cost, passive indication of local areas of alpha-emitting radioactive contamination will significantly improve the health and safety of radiological technicians, contamination remediation personnel, and the public by reducing the time workers are exposed to potentially harmful materials and the uncontrolled spread of these materials during remediation operations. The technology, formulated as low-cost test strips, will also significantly impact in-home testing of radon, a hard-to-detect radioactive substance that causes approximately 21,000 lung cancer deaths each year in the United States.



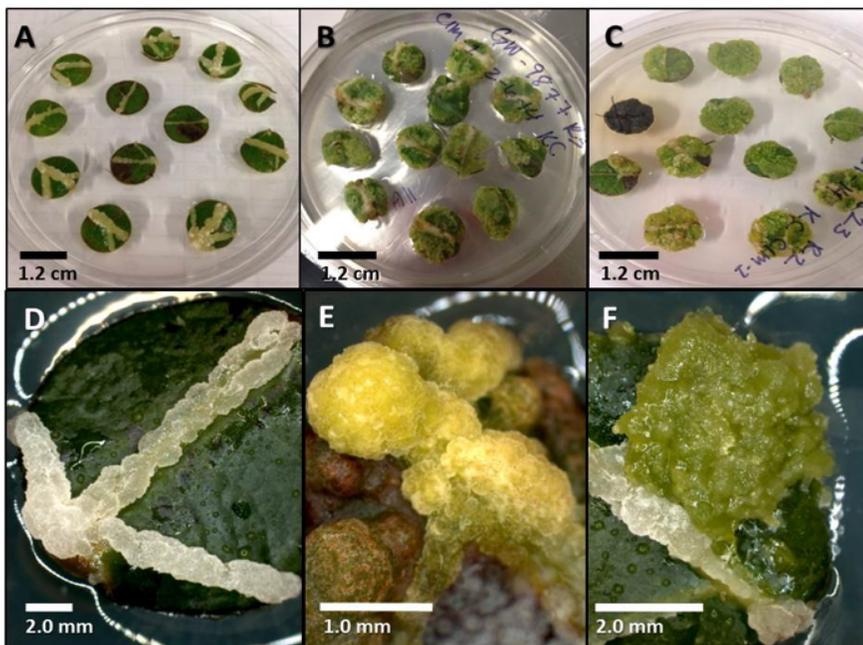
*ORNL's nanocapsular radiation track etch indicators can visualize the spatial extent of contamination within a facility via aerosol dispersal or may be immobilized onto paper and fabric substrates to provide low-cost single-point test strips.*

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# Rapid Regeneration of Recalcitrant Plant Species

**Problem:** Despite rapid advances in development of genome-editing tools such as CRISPR-Cas9, regenerating viable plants during transgenesis remains a major barrier to cost-effective deployment of these tools in the biotechnology field to enhance plant performance.

**Solution:** Enhancing regeneration of inherently recalcitrant plant species can be achieved by utilizing four major regulators of DNA replication and cell division that are highly conserved across eukaryotes. Developments in this area would broaden the portfolio of genome-editable plant species. A four-gene construct carrying 2-RNAi-mediated gene-silencing cassettes as well as 2-overexpression cassettes will simultaneously inhibit cell division suppressors (i.e., SOK1 kinase and Histone Deacetylase RPD) and enhance the activity of cell division inducers (i.e., mitogen-activated protein kinase and targeting protein for XKLP2).



**Impact:** This genetic technology leverages materials and methods to improve the transformation efficiency of plant cells, particularly for those commercially important species that have been difficult to genetically engineer or where transformation efficiencies are low. The simple, easy-to-use approach enhances the efficiency of callus regeneration to enable the creation of intact fertile plants bearing desired genetic improvements.



## Wellington Muchero, PhD Energy and Environmental Sciences Directorate

Dr. Wellington Muchero is a quantitative geneticist in the Biosciences Division at ORNL. He holds joint appointments in the Plant Sciences Department and the Bredesen Center for Interdisciplinary Research and Graduate Education at the University of Tennessee–Knoxville. Dr. Muchero received a PhD in plant pathology from the University of California, Riverside, and an undergraduate degree in crop science from California State Polytechnic University, Pomona. He is a 2016 recipient of the US Department of Energy's Early Career Research award. He holds three issued patents, three technology licensing agreements, and numerous invention disclosures related to plant biotechnology.

## Intellectual Property

Genes regulating plant regeneration; ID-201804190

Genes regulating plant regeneration; 16/525,724  
and PCT/US2019/044048

## Publications

- G. A. Tuskan, et al. Defining the Genetic Components of Callus Formation: A GWAS Approach." *PLOS ONE*, 2018; 13.8: e0202519.

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## Soydan Ozcan, PhD Energy and Environmental Sciences Directorate

Dr. Soydan Ozcan is a senior scientist in ORNL's Energy and Environmental Sciences Directorate and joint associate professor in the Mechanical, Aerospace and Biomedical Engineering Department at the University of Tennessee–Knoxville. He also serves as the thrust lead for development of bioderived polymer composites for additive manufacturing at ORNL. His research addresses the broad and vital issue of identifying novel, high-value biomaterials from biomass, along with viable processes for preparing biomaterials for composite and additive manufacturing applications. Dr. Ozcan is developing manufacturing techniques and exploring new materials to improve energy efficiency during composite manufacturing, decrease material waste, and improve material performance. He has actively initiated new programs and has been the principal investigator for over 30 R&D projects including research in the areas of fiber and composite manufacturing, composite recycling, and bioderived-materials additive manufacturing. Dr. Ozcan's team engages over 30 industrial partners and delivers research with direct applications to society. He has published nearly 80 papers; holds 18 issued and pending patents; has published 7 book chapters; and is an active speaker, having delivered more than 100 presentations and short courses on manufacturing of fibers and composites topics and research.

## Intellectual Property

Silane-Modified Polyester Blends and Methods of Preparation; 16/110,138

Biomacromolecule Engineering by Soft Chain Coupling Technology, ID-201904306

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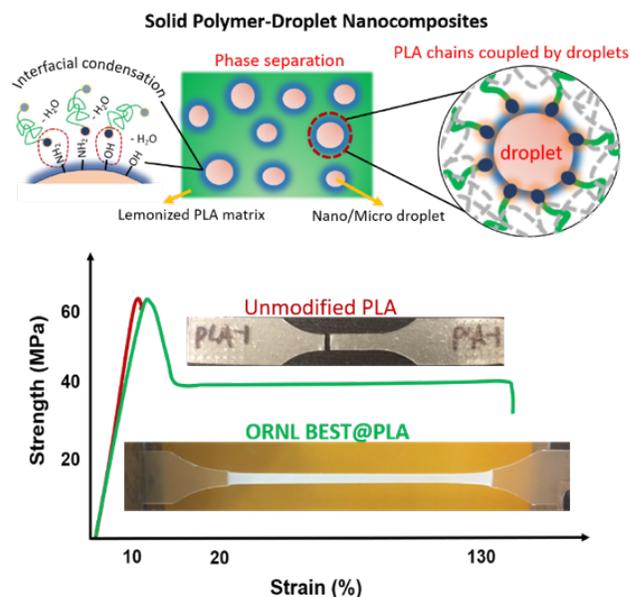
# BEST: Biomacromolecule Engineering by Soft Chain Coupling Technology

**Problem:** Poly(lactic acid) (PLA) is the most widely used bioplastic today. Its biodegradability, biocompatibility, high strength, and stiffness as a commodity polymer make PLA one of the most promising bioplastics under development. Its many application areas include but are not limited to biomedical devices, biodegradable films and packages, and 3D printing. However, PLA's brittle nature is a major barrier to its adoption in much wider application areas.

**Solution:** The BEST approach dramatically improves the ductility and toughness of PLA via a novel industry-friendly soft-coupling technology based on small droplets and chain end/tail modification. This technology is realized by a scalable, environmentally friendly process that uses only nontoxic additives and a melt-phase process to achieve the desired droplet-in-polymer microstructures, referred to as polymer–droplet composite. The droplets work as a unique topological modifier to manage the topological defects of chain entanglement networks. As a result, with minimal loading of modifiers (<1.5 wt%), the modified PLA offers significant improvements in toughness as well as processability without sacrificing the material's mechanical strength.

**Impact:** The production capacity of the biobased-polymer industry is projected to triple, from 3.5 million tons in 2011 to nearly 12 million tons in 2020. As the fastest-growing segment of this market, PLA is expected to account for over \$6.5 billion because of its use in packaging, biomedical devices, composites, additive manufacturing, and other areas. Overcoming the issue of brittleness without sacrificing other valuable mechanical properties would revolutionize the already rapidly growing PLA industry. Improvements in mechanical performance would not only extend existing markets, but also enable

new applications such as films and packages and penetration into new polymer markets. The new materials derived using the BEST approach exhibit outstanding mechanical toughness and processability, which are of great value for its broad applications.



## Publications

- X. T. Meng, N. A. Nguyen, H. Tekinalp, E. Lara-Curzio, and S. Ozcan, "Supertough PLA-Silane Nanohybrids by In Situ Condensation and Grafting," *ACS Sustain. Chem. Eng.*, 2018; 6 (1): 1289–1298.

# Genetic Improvement of Salt and Drought Tolerance in Crop Plants

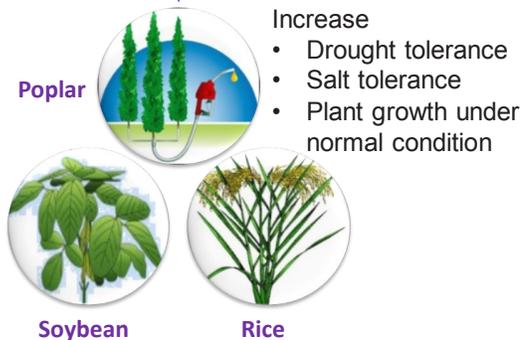
**Problem:** Drought and salt stresses impose big challenges on crop production. To keep American farmers competitive, developments that increase crop tolerance to seasonal drought and salt stresses—and enhance growth under normal conditions—are urgently needed. However, it has been very challenging to simultaneously improve growth, drought tolerance, and salt tolerance in plants, and it is very difficult to find a single solution that achieves improvements in all three areas.

**Solution:** Crassulacean acid metabolism (CAM), a natural water-use efficiency mechanism that facilitates plant adaptation to water-limited and salinized environments, employs a key CAM gene from the desert-dwelling plant *Agave* to



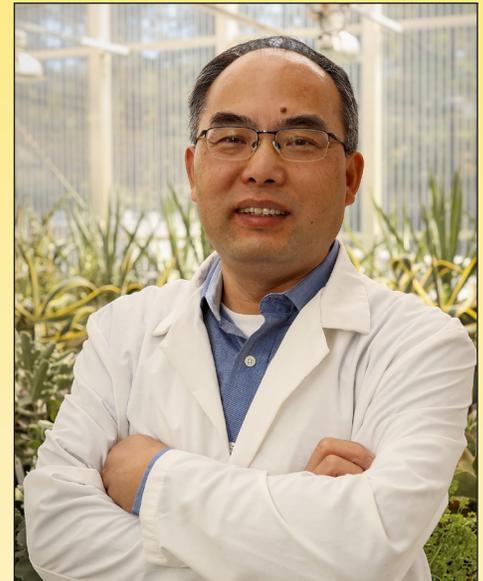
Desert-living plant  
*Agave*  
(*Agave americana*)

Transferring a key gene  
in CAM pathway



simultaneously increase biomass yield under normal conditions and resistance to both drought and salt stresses. This technology has been successfully established in model plant tobacco, and it is currently being extended to food crops (e.g., rice, soybean) and bioenergy feedstocks (e.g., poplar). Overexpression of this key gene enhances the expression of multiple genes relevant to CO<sub>2</sub> fixation, consequently improving photosynthetic efficiency and biomass yield, and increases the accumulation of proline, a key player in plant tolerance to drought and salt stresses.

**Impact:** This technology facilitates the sustainable production of food and bioenergy on marginal lands or under seasonal drought conditions, with potential to generate significant positive impact on the food, bioenergy, landscape, and timber industries, which together represent a combined market opportunity of hundreds of billions of dollars each year. Such markets are essential for our national food, energy, and economic security. In an average year, the world experiences a 50–80% yield loss of crops due primarily to drought and high soil salinity. Application of this technology will help meet the increasing demand for food, biofuel, and animal feed while increasing the competitiveness of the US agricultural industry in an environmentally friendly way.



## Xiaohan Yang, PhD Energy and Environmental Sciences Directorate

Dr. Xiaohan Yang is a senior research staff member in the Biosciences Division at ORNL. He obtained his PhD in horticulture, plant molecular biology, and plant breeding from Cornell University. He has expertise in plant genomics, bioinformatics, and plant synthetic biology. Dr. Yang's research focuses on molecular signaling, plant-gene editing, and plant biosystem design in relation to bioenergy research and plant-microbe interactions. He has published more than 80 journal articles. His research garnered a 2018 R&D 100 award, which is considered the "Oscars" of research and innovation toward commercialization.

## Intellectual Property

Gene for enhancing salt and drought tolerance in plants; ID -201804140

BESC-Gene for Enhancing Salt and Drought Tolerance in Plants; 62/797,452

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