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AACR 2022: A Plethora of New Products and Product Previews

The American Association for Cancer Research (AACR) held its annual meeting April 8–13 2022, in New Orleans, Louisiana. While this marked the return of in-person conferences for the organization, the meeting was offered in a hybrid format to accommodate participants who could not yet attend in-person, with presentations streamed through the online conference portal and some panelists presenting remotely. According to AACR, there were 15,179 attendees in person and 4,311 virtual attendees. These figures easily topped 2021, when attendance reached around 13,500. Next year's AACR meeting will be held in Orlando, Florida April 14–19.

This year marked the 115th anniversary of AACR, which was celebrated with an extensive lobby display highlighting the history of cancer research and the enormous progress that has been made, while also reminding attendees that the future of cancer research is in their hands.

Exhibition Hall Highlights

In total, 450 exhibitors were represented in the exhibition hall. After two years of virtual trade shows, this year's exhibition hall showcased not only new instruments that were being unveiled at the show, but also systems that had entered the market in the past two years but were being displayed for the first time. There were also many newer vendors that were premiering their inaugural entries into the analytical instrumentation space, introducing many new and exciting concepts.

490 BioTech showcased its auto-bioluminescent technology, which it introduced in late 2021. Traditional luciferase assays require external activation by the addition of luciferin. However, luciferin does not readily penetrate cell walls, and requires destructive treatments in order for the luciferin to permeate the cells resulting in cell death and only point-in-time data. 490 BioTech offers a solution through its kits that encode the enzymes needed to enable the cells to assemble luciferin from cytosolic components, without harming the cells. 490 BioTech's plasmids are simply transfected into the cells or organism being studied via the end-user's preferred transfection method. This creates a continuous reporter for further assays. Several kits are currently available for both in vitro and in vivo applications.

10x Genomics showcased two upcoming spatial transcriptomics systems. The Visium CytAssist, which will launch in the late second quarter or third quarter, is a compact platform that will analyze the whole transcriptome from fresh or frozen tissue samples, or up to 20,000 targets from FFPE samples. The system is aimed towards histology labs, with a simplified workflow that can be initiated on standard histology slides before being transferred to Visium slides that capture and barcode transcripts for analysis.

Also exhibited by 10x Genomics was the Xenium In Situ platform, which the company will release in the fourth quarter. The system will initially be able to analyze a panel of 400 pre-selected transcript targets at subcellular levels. Also in development is a proteomics component, which will enable spatial protein analysis. Custom panels may also be available following the platform launch.

Agilent Technologies displayed several recently released systems that highlighted the company's Cell Analysis Division. Introduced at the show was the Agilent Seahorse XF Pro. Designed for high-throughput T-cell profiling and mitochondrial toxicity profiling assays, the system is aimed towards the pharma and biotech sector but also aims to simplify working with large datasets by automatically detecting questionable data. The platform accommodates 8-, 24- and 96-well plates as well as microsphere plates. Mitotox assays for the system will launch later this month.

Also showcased by Agilent was the Magnus NGS Prep System, which was launched last year. This low-to-medium throughput, fully automated benchtop system features on-deck thermal cycling enabling a complete library prep workflow. Proprietary reagents leverage Agilent's expertise in oligo printing.

The xCELLigence RTCA eSight was launched by Agilent two years ago. The live-cell analysis platform is built on biosensor technology that Agilent gained through its acquisition of ACEA Biosciences (see ***IBO*** 9/30/18). It is the first instrument on the market that incorporates cell impedance with imaging, so that multimodal fluorescent and label-free assays can be performed together and are noninvasive to cells. The system has spaces for five plates; three of the spaces have both impedance and imaging functions, while the remaining two have imaging only and are suitable for imaging nonadherent cells.

Akoya Biosciences exhibited the PhenoImager system, which was released earlier this year. The spatial phenotyping platform can quantitate 100 RNA and protein biomarkers in a run at single-cell resolution. The system accepts standard histology slides prepared using standard histology workflows, a major convenience for end-users. Furthermore, the system's large field of view enables imaging of entire slides.

While the current version of FACSDuet is validated for clinical lab use, BD plans to introduce an RUO version in the coming year.

Becton, Dickinson (BD) displayed its FACSDuet, an automated sample preparation system for the clinical market that works in tandem with the company's FACSLyric flow cytometer platform. FACSDuet handles up to three carriers and features automated transfer of samples to the FACSLyric. While the current version of FACSDuet is validated for clinical lab use, BD plans to introduce an RUO version in the coming year.

Bio-Rad Laboratories showcased the QX600 Droplet Digital PCR System for advanced multiplexing, which the company expects to launch soon though a specific date has not been determined. The company has long been the been the leader in droplet-based dPCR, and its new system builds on the technology with six-color multiplexing capabilities to provide more data per sample and multiple targets per well to ultimately lower the cost per target. QX600 is compatible with Bio-Rad's Flex automated droplet generator, which generates up to 100K droplets. The QX600 is backwards

compatible, accommodating the use of reagents and consumables designed for the previous QX200 platform. In the cancer research space, the system is especially suited for cfDNA analysis.

Bio-Rad also displayed the QX1 dPCR platform, which has been on the market for a year. The relatively compact system features a fully integrated droplet generator and four color reader, saving bench space.

Bruker launched the Canopy CellScape, its latest ChipCytometry platform for spatial biology. The system accommodates up to five antibody staining per cycle; subsequent cycles using interative sets of antibodies allow analysis of a virtually unlimited number of targets. Reagents are open source, meaning that end-users may use antibodies from any source or vendor. The large field of vision and HDR camera allow fast imaging and capture of data at subcellular resolution. The system can analyze four samples in a run. Reagent inputs for each sample are separate, allowing each sample to be run as an independent assay.

Covaris displayed its R230 Focused ultrasonicator. The instrument, which was released in 2020, represents the company's shift towards integrating its systems into automated sample prep workflows. Sonication is an important step in most genomic workflows. The system can be fully integrated with many liquid handling platforms from major automation vendors, including Tecan and Hamilton, occupying four deck spaces. Control and programming of the R230 system can be inputted either through the liquid handler interface or separately using a laptop. In mid-2022, Covaris plans to release a workflow bundle for the system.

LevitasBio displayed its LeviCell EOS cell separation system, which will launch in the third quarter. The EOS expands the capabilities of the company's inaugural system, the LeviCell, which launched in 2020. Levitas' cell separation technology is label free and bead free, instead relying on density gradients to differentiate cells by type or viability. The result is gentler and faster sorting of cells with fewer hands-on steps, according to the firm. The LeviCell EOS system will process four samples per run.

Luminex showcased its xMAP INTELLIFLEX platform with a newly upgraded DR-SE RUO system. It features dual-reporter channels to analyze two colors simultaneously and is compatible with robotic decks. Luminex noted that there has been strong interest in the system among veterinary and agricultural labs.

MilliporeSigma highlighted the Auto2D 2-D Electrophoresis Device. The system had previously been available only in Japan and is newly available to the North American market. The Auto2D is an automated 2D Western blotting and isoelectric focusing system which reduces the Western and IEF workflows down to 1–2 hours versus the usual two days for a manual workflow.

NanoString Technologies introduced the nCounter Pro Analysis System, which emphasizes simplicity, reliability and security. The gene expression analyzer uses NanoString's molecular barcode chemistry to count individual RNA transcripts from 100 ng of extracted RNA, FFPE samples or from fresh lysate, with the capability to interrogate over 800 targets in a run with no enzymes needed. Requiring only 15 minutes to set up, the system goes from sample to data in 24 hours and features advanced cybersecurity. The platform consists of two modules: a prep station liquid handler and a digital analyzer. Up to six cartridges, with 12 samples per cartridge, can be processed in a run.

NanoString offers off-the-shelf panels that can be partially customized with the addition of up to 55 more targets; users can also design fully customized panels. The system is co-marketed with ROSALIND Bioinformatics, which provides web-based analysis services for data generated by the nCounter.

The first-of-its-kind system facilitates point-of-use production of cell culture media to reduce the environmental impact associated with cell culture consumables.

Nucleus Biologics, a supplier of custom and classical cell culture media, introduced its first entry into the instrumentation space, the Krakatoa Media Manufacturing System. The first-of-its-kind system facilitates point-of-use production of cell culture media to reduce the environmental impact associated with cell culture consumables. The system produces 500 mL batches of fresh, sterile media using either standard or customized formulations. Reusable, autoclavable glass bottles are inserted into the system, which has sterilizing UV-C lights and a bottle uncapping and capping mechanism. Krakatoa connects to existing laboratory water systems. Pod cartridges are pre-filled with powdered media and have integrated 0.2-micron sterile filters.

Nucleus Biologics claims that Krakatoa reduces greenhouse gas emissions by 88% by reducing energy used in shipping and refrigeration and eliminating the use of PET bottles. The pod consumables are reusable and recyclable. Furthermore, by adopting the point-of-use model, the company estimates that end-users will see a cost benefit after producing 21 L of media on the system, which is the point where the higher cost of buying and shipping liquid media exceeds the cost of the Krakatoa system, which is priced at about $50,000. Nucleus Biologics also provides software and mobile apps to aid users with media-formulation tracking and creation. Users can scan a QR code on the media pod to view the complete formulation of the media. The company's cloud-based software also enables users to design custom formulations or to view media formulations from published papers.

PerkinElmer showcased its many synergistic product offerings, displaying instruments from its various product lines, collaborations and recent acquisitions. On display was the JANUS G3 Blood iQ Workstation, which launched late last year. The automated platform facilitates the separation of fractionated blood samples, allowing the isolated collection of cfDNA and RNA, and genomic DNA. Cameras are used to discriminate fractions within individual tubes, allowing multiple samples of various volumes or contents to be processed simultaneously. The platform can be integrated into the rest of PerkinElmer's JANUS cfDNA and cfRNA workflow solutions.

The HIVE scRNAseq Solution, a single-cell transcriptional profiling platform introduced last October, was also displayed by PerkinElmer. The platform was developed by PerkinElmer and Honeycomb Biotechnologies. From a 1–3 mL sample, the handheld system captures and prepares cells for RNA-Seq. A range of cell types can be processed, including granulocytes, nephrons, hepatocytes and neurons. The non-fixative preservation employed by the system retains delicate cells such as granulocytes. In total, 65,000 picowells each contain a single bead, capturing transcripts from a single cell in each well. These beads are then used in downstream library prep workflows for sequencing.

Also shown at PerkinElmer's booth was OMNI International's Bead Mill homogenizer. OMNI was acquired by PerkinElmer in December 2021. The Bead Mill physically disrupts tissues and cells to release cellular contents, such as DNA. Beads of various sizes and materials are available to optimize sample preparation for various applications or sample types. The system uses a figure 8 motion which generates no heat. Between 2 and 48 tubes of up to 15 mL can be processed at once.

PerkinElmer's' most recent high-content screening system, the Opera Phenix Plus, was also featured at the booth. The confocal system, which was launched a year ago, applies advanced machine learning (ML) to create easier to manage data clusters to analyze over 3,000 features in a run.

In the in vivo imaging space, PerkinElmer introduced its first ultrasound system, Vega. The system is the first hands-free, high-throughput preclinical ultrasound system on the market. It does not require a trained sonographer to operate, making it more accessible to the research laboratory. The system can image three mice at once.

Also at the PerkinElmer booth was antibody and reagent supplier BioLegend, which was acquired by PerkinElmer last September (see ***IBO*** 8/2/21). Since the merger, BioLegend has optimized many of its offerings to PerkinElmer's validated assays, including reagents for flow cytometry. The company's proteogenomics products conjugate antibodies with oligonucleotides for RNAseq workflows, enabling simultaneous proteomics and transcriptomics analysis of the same single cell. BioLegend also introduced several new fluorescent dyes.

QIAGEN displayed the QIAcuity Eight digital PCR platform, which was introduced a year ago. The system is currently the highest-capacity system in the QIAcuity product line, with the ability to process eight plates at up to five plex. According to QIAGEN, the microfluidics-based digital PCR platform provides several benefits compared to droplet-based dPCR platforms: operating the system is as simple as using traditional PCR, throughput is higher, the benchtop footprint is smaller and the $170,000 cost of the system is more affordable.

Standard BioTools (formerly Fluidigm) unveiled the Hyperion+ Imaging System for high-plex spatial imaging, which provides improved performance from the previous Hyperion system. Hyperion+ is able to scan over 40 markers in a run at subcellular resolution. Unlike other spatial imaging platforms on the market, Hyperion+ detects metal-tagged antibodies rather than fluorescent tags. The system combines imaging with Fluidigm's Helios CyTOF mass cytometry platform; this combination allows the system to feature dual modes: an imaging mode and a separation mode for cells in suspension.

Also on display was Standard BioTools' CyTOF XT system, which was launched in mid-2021. This mass cytometry system, which also utilizes metal-tagged antibodies, is capable of scanning over 50 markers in a run and features an automated sample carousel.

Stilla Technologies launched the naica system, the first six-color digital PCR system on the market. The entire workflow is done within the Ruby Chip consumable, which is pre-filled with oil. Approximately 30,000 droplets are generated per sample, with chips available for 4–16 samples per chip. The system has spaces for up to three chips per run. The six fluorescent channels provide high multiplexing capability, while digital imaging allow visualization of individual droplets.

The platform enables spatial whole proteomic analysis at a subcellular level by exploiting complexes formed by the interactions between T cells and B cells

SYNCELL previewed the Microscoop Platform for spatial biomarker discovery. The system, which does not yet have a planned launch date, will be Syncell's inaugural product. The platform enables spatial whole proteomic analysis at a subcellular level by exploiting complexes formed by the interactions between T cells and B cells. These immune synapse complex regions express many biomarker proteins. The Microscoop uses glass slides coated with photoreactive reagents and biotin. Where immune synapse complexes are photolabeled and detected by on-board imaging and AI, a laser is directed, creating a cross-linked complex with a biotin tag. The complexes are isolated, and all proteins are identified by MS. The resulting contextual proteomics will have applications in biomarker and cellular interaction discovery. Currently being validated, the platform will be available through an early access program once validation is completed.

Thermo Fisher Scientific launched the Applied Biosystems QuantStudio Absolute Q, a four-color microfluidics-based digital PCR system that uses Applied Biosystems' microfluidic array plate (MAP) technology. The system boasts a 99.99% successful fill rate, enabling over 95% of the input sample to be analyzed. Sixteen reactions can be run per plate, with sample input requirements of 9 µL. The platform takes five minutes to load and has a run time of 90 minutes.

Vizgen displayed the MERSCOPE platform, which it introduced in January. The FISH-based system, which uses the company's MERFISH (Multiplexed Error Robust Fluorescence In Situ Hybridization) technology, provides high-resolution spatial genomics analysis at subcellular resolution, detecting transcripts from up to 500 genes in a square centimeter. The system accepts mounted slides and is currently compatible with fresh or fixed tissues samples. FFPE sample compatibility will launch this summer. Users may select gene panels of 140, 300 or 500 genes per panel.

Zymo Research launched the Zymo-Seq Cell Free DNA WGBS (whole genome bisulfite sequencing) Library kit for preparation of whole genome cfDNA. The company's Lightning Chemistry is gentle, resulting in little to no additional fragmentation of fragile short cfDNA while also being very fast. The kit uses bisulfite conversion to prepare methyl-seq libraries in as little as three steps.

Presentations

Deep Learning for Cancer Imaging

In a session entitled "Deep Learning for Cancer Imaging," models of ML were presented in observing and quantifying the cellular state transitions that occur in cancer and diagnostics. Of particular focus was the interplay between the transcriptome and cellular morphologies. Four models of ML to quantify imaging data were discussed: "Label-Free," "ML Segmenter," "Transfer Function," and "Statistical Cell." The first three models augment microscopy images, while Statistical Cell builds a computational model of the cell.

The Label-Free method involves predicting fluorescence from brightfield microscopy. Label-free brightfield observes only what is seen as visible light passes through the cells, with no fluorescent labels. To train the model, images are fed into the program where both the brightfield and fluorescence channel images are used to create a unit architecture that is able to identify patterns at large scale and small scale. The resulting ML can then predict organelle location and shape from the brightfield channel. Combining outputs from multiple models enables prediction for multiple organelles in a brightfield stack. But some organelles can be better predicted than others.

ML Segmenter brings in quantification, describing the cell and organelle segmentation. From a typical workflow, an initial 3D binary image stack is generated. But if the segmentation is not good enough, experts can correct and annotate the segmentation to create a new "ground truth," which becomes the new basis to train the ML model. Training requires images with fluorescence channel and ground truth segmentation. The result allows prediction of cell and organelle segmentations from fluorescence with improved accuracy and robustness. Several ML-based tools are currently coming on-line, made available from several institutions.

Transfer Function is a deep learning model that computationally transforms a lower-resolution image to a higher resolution

A third technique is Transfer Function, which addresses challenges in resolution and field of view. Larger field of view imaging allows easier cell tracking but makes it difficult to segment organelles. However, higher-resolution imaging provides only a small field of view, which cells may migrate out of over time, while also increasing phototoxicity. Transfer Function is a deep learning model that computationally transforms a lower-resolution image to a higher resolution. To train this model, fixed cell images at both lower (20x) and higher (100x) resolution are needed. An architecture based on U-Net-, a convolutional neural network, transforms the low-resolution live-cell images to high resolution, enabling quantitative analysis.

Finally, the Statistical Cell model encodes the biological image contents to build and interrogate a computation model of the cell. Starting from high-dimensional input data as a reference model, such as 3D images of the cells, the data are encoded into low-dimensional, interpretable latent space from which images can be reconstructed to interpret target structures in the cell. This allows visualization of predicted and generated organelles, with potential applications to drug-treated cells.

Breaking Down Silos

In a session entitled, "Breaking Down Silos: If We Did It During the COVID Pandemic, Why Not for Cancer?" lessons learned in administering clinical trials during the two years of the pandemic were discussed, as were positive changes that will result from the flexibilities developed during this time.

Dr. James Doroshow of the NCI discussed the impact of the pandemic on the NCI's 2030 Strategic Vision for Clinical Trials. In April 2020, at the onset of the pandemic, the NCI experienced a 47% drop in accrual, or enrollment in trials, at NCI cancer centers. The limitation of in-person study activities during the pandemic presented challenges in gaining informed consent, the collection of too much

test data of limited importance, collection of low-grade adverse event data, and limited access to cancer care personnel and facilities, which further diminished the availability of trials for underserved populations.

Rapid responses implemented by the NCI within a few weeks of the pandemic onset included increased use of electronic consenting, electronic study audits, telemedicine study visits, and decentralized testing for lab and imaging studies. These experiences have informed the NCI's 2030 Strategic Vision for Clinical Trials, which calls for flexible, faster, simpler, less expensive, high-impact clinical trials that seamlessly integrate with clinical practice. This includes streamlining processes for trial design and execution, increasing the efficiency of data collection, focusing on only essential endpoints, decreasing regulatory hurdles and broadening trial access.

Recommendations to achieve these goals include limiting clinical trial data collection to essential data elements, particularly in late-phase trials, and better use and integration of electronic health records (EHRs). To this end, the NCI is funding grants to facilitate EHR systems and documentation, while also funding consortia to advance automated data extraction from EHRs into cancer trial data management systems.

Based on feedback from clinical trial sites, the NCI is developing best practices for the use of telehealth in cancer clinical trials.

Decentralizing trial activities will be necessary to reduce the cost of trials. Trial procedure modifications during the pandemic revealed activities that can be performed locally or remotely can be adopted as standard clinical trial practice. Decentralized procedures that the NCI recommends continuing post-pandemic include shipping of Cancer Therapy Evaluation Program (CTEP) oral agents, remote consent, remote auditing, and local laboratory and imaging testing. Based on feedback from clinical trial sites, the NCI is developing best practices for the use of telehealth in cancer clinical trials.

The pandemic also highlighted new and existing challenges in patient access to trials. To this end, the NCI recommends broadening eligibility criteria to address clear and distinctive medical problems experienced by minority and underserved patients that make accrual difficult. This includes examining co-morbidities that often limit eligibility to NCI clinical trials.

Finally, Dr. Doroshow brought up the workforce issues that are affecting skilled clinical staff and will need to addressed going forward. Like so many other sectors, workforce recruitment and retention challenges have resulted in severe personnel shortages, curtailing accrual and delaying data reporting in a majority of NCI-supported Cancer Centers.