

18 May 2022 | **Analysis**

Seven Trending Technologies On The Cusp Of Mainstream Uptake

Progress In Pushing Back The Neo-Biological Frontiers Of Medicine

by **Ashley Yeo**

At HIMSS22, NEO.Life's Jane Metcalfe identified seven trending technologies that are set to move from the fringes of medicine to the center of attention.

HIMSS22 speaker Jane Metcalfe profiled seven technological advances that she believes are moving towards trends and will ultimately become mainstream in the not too distant future.

1. Protein Folding
2. 'Omics Technologies
3. Gero-Therapeutics
4. Aging Clocks
5. Aging Therapeutics
6. Noninvasive Neuromodulation
7. Expanding The Reach Of Ultrasound

With artificial intelligence (AI) deepening scientists' understanding of human biology and human health – protein folding has gone from fringe to foundational. “This is one of biology’s biggest mysteries going mainstream,” said Metcalfe, who is founder of NEO.Life, a self-funded

portal that “reports from the front lines of the Neobiological Revolution.”

Predicting a protein’s shape can help make sense of disease-causing gene variations that differ between people, and help scientists design novel proteins and create new drugs. It should also consign a lot of repetitive lab tasks to history, thereby freeing up a new generation of molecular biologists to spend more time on “the key questions to ask,” said Metcalfe.

Deep learning has been used in the past year to predict a protein’s 3D shape from its amino acid sequence. The AlphaFill procedure, for filling up missing information in AlphaFold models, “astonished the world” when one lab was able to predict a structure in just 30 minutes, when other labs had already spent 10 years on the task.

‘Omics technologies have practical applications and are able to generate enormous data sets on the structure of cells, tissues and organisms. But this in turn leads to an analysis bottleneck, which calls for the use of computational and bioinformatics tools to allow the integration of these complex “multi-omic” data sets. Those tools are in development.

At the same time, three ‘omics trends are emerging:

1) *The boundaries between AI companies and drug companies are becoming blurred*, given the energy now going into AI-powered drug discovery. ‘Omics maps and atlases, such as the cancer drugable gene atlas, are being seen as critical in charting the pathway and progress towards the “neo-biological frontier.”

2) *Genomic sequencing will become part of everyday medicine*. Sequencing children at birth and retesting them for epigenetic changes throughout their lifetime is one basis for transforming medicine from a reactive process to a proactive, precision and preventive discipline.

Yet various non-scientific or human factors persist in slowing down the progress of innovation, to the extent that it still can take up to 20 years for an innovation to become a standard operating practice.

"Genomic medicine is getting ready for primetime." – Jane Metcalfe

But genomics is set to move from the clinic and into the emergency room, as evidenced in a

project run by Stanford University in November 2021. The project on rapid nanopore genome sequencing was so fast that data could not be processed on existing software systems, so the researchers transferred the raw signal data to cloud storage in real time to distribute it to multiple cloud computing machines. This reduced the entire process from seven hours and 21 minutes to just 34 minutes.

To Metcalfe this indicates that a diagnosis could in future be made within a doctor's single work shift. "The reality is that genomic medicine is getting ready for primetime," she said. This means that cloud computing infrastructures must be put in place to handle the rapid mass sequencing of bioinformatics data. "That's how we get on the way to precision medicine."

3) *The microbiome, which had been fringe for 15 years, is now maturing.* In 2007, the US National Institutes of Health began a study on the human microbiome to systematically document the microbes likely to inhabit the gut microbiome. They looked at the implications for many conditions, such as inflammatory bowel disease (IBD) and colon cancer, etc.

In terms of treating disease, fecal transplants haven shown to be effective in treating *Clostridium difficile* infections, with more possibilities for fecal transplants opening up all the time.

Furthermore, three research papers since early 2022 have suggested microbiome links between: the gut microbiome and rheumatoid arthritis; the lung microbiome and multiple sclerosis-like autoimmune disease; and cognition and microbial diversity.

Another recent source suggested that a specific panel of gut microbes can be used to predict pancreatic cancer. In a study, machine learning was used to identify both high and low levels of certain microbes, producing information that can potentially aid diagnosis or even treat or prevent this high mortality form of cancer.

This whole area of research is trending, Metcalfe said, but fundamental questions remain: Are these microbes the cause or the result of disease? And how can we regulate the microbiome to give patients the balance of microbiomes they need?

Gero-therapeutics, the drugs given to extend health span and enable the prevention and cure of later life health conditions, are coming. Years of efforts have failed to eliminate any major age-related diseases, although lifespan has increased, morbidity has been reduced and the quality of life of sufferers has improved.

Scientists have made breakthroughs in gero-therapeutics in lab animals, and so this this year, it is likely that there will be a Phase III clinical trial of one these projects, Metcalfe predicted. An off-label use of metformin, a drug used by those with type 2 diabetes, is the most likely candidate.

The organ transplant drug, rapamycin, is another candidate for use as a gero-therapeutic. And another is nicotinamide adenine dinucleotide (NAD⁺), which is already on the market as a supplement, but not a prescription medicine. Clinical trials are underway testing tolerance and toxicity.

Drugs classed as senolytics, which selectively clear senescent cells, are another prospect, although the short- and long-term effects of use of this drug class as gero-therapeutics are not known. Other prospects are some cancer-fighting agents and flavonoid phytonutrients, which are not yet US-approved for therapeutic purposes.

Cellular senescence is one the nine hallmarks of aging. As published in 2013 by the NIH's National Laboratory of Medicine, the other hallmarks are: genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, deregulated nutrient-sensing, mitochondrial dysfunction, stem cell exhaustion and altered intercellular communication.

Questions about the effects of these drugs on people who are not sick are as yet unanswered, Metcalfe cautioned, but added: "Anti-aging drugs are going to have their moment very soon."

The fourth trend Metcalfe sees is aging clocks, an exciting development that measures the amount of DNA methylation. Foxo Technologies claims that biological clocks use epigenetic markers to accurately estimate a person's true internal age and rate of aging, which may tell a different story to the calendar. Metcalfe believes that the industry is set to hear much more about aging clocks, and not just for health, but also for insurance purposes too.

"Longevity medicine will become the new primary care"

Aging as field for research and investment is another trend predicted by the NEO.Life founder. Aging is not just for old people, said Metcalfe, it is a process that starts at the age of 30. This trend will gather pace as people see aging as a lifelong process that needs to be managed. "Longevity medicine will become the new primary care," she claimed.

In the coming year or two, therapies involving light, sound and electrical impulses, as noninvasive neuromodulation techniques, will increasingly make the headlines. One project leading the way is the EU-funded 48-month Neurotwin project, which borrows the concept of "digital twins" for developing personalized hybrid brain models.

Using neuroimaging data from Alzheimer's disease, the project's scientists are building a model based on the networks and dynamic landscape of the individual brain. The objective is to design and test personalized neuromodulation protocols capable of restoring healthy dynamics. Neurotwin is expected to deliver model-driven breakthroughs in basic and clinical neuroscience.

The last of Metcalfe's seven trends to watch is the expanding use of the noninvasive diagnostic technology, ultrasound, an "underrated technology" with many other possibilities beyond diagnostics. Its other uses extend to breaking up tumors, opening up the blood-brain barrier to enable the delivery of drugs to the brain and immunomodulation.

Over 160 clinical disorders leveraging ultrasound are in various stages of research, and 34 have been approved around the world, including seven in the US.

All this shows the value of keeping an eye on the fringe. "The fringe is oftentimes the next trend. We just need to shorten the time it takes to get from the lab bench to the bedside," Metcalfe said.

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By **Jo Shorthouse**

17 Nov 2021

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