



## Disruptive Innovation in Laboratory Medicine

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Over the last 5 decades, laboratory medicine has witnessed a remarkable wave of innovations that transformed the field from a peripheral to a central player in healthcare delivery. These advances enabled the introduction and performance of new tests on a large scale, some in a decentralized setting, in an accurate and a precise manner, thus leading to better diagnosis, more accurate prediction of disease prognosis, and improved patient management. This evolution was the result of both sustaining and disruptive innovation, the latter being a new concept, technology, product, or process that is at first inferior to an existing one but with time it improves, becomes superior to it, and eventually replaces it. Some examples of disruptive innovation in laboratory medicine include continuous flow analysis, dry reagents on dipsticks, pregnancy home testing, PCR, point-of-care testing, and use of MALDI-TOF mass spectrometry for pathogen identification. Although sustaining innovation steadily drives progress, paradigm shifts usually occur only with disruptive thinking. With the escalating cost of healthcare and the prediction that it will soon reach 20% of the annual GDP in the US, bold measures and disruptive approaches in delivering effective and economical clinical laboratory testing are more needed than ever. In this Q&A, a group of inventors, entrepreneurs, and cutting-edge scientists share their views on sustaining and disruptive innovation in laboratory medicine.

**Describe briefly the core technology or concept of your innovation.**

**Eric Topol:** Smartphones as the hub of medicine going forward, capable of performing routine laboratories (with suitable hardware additions), real-time,



cloud computing and validated algorithms.

**Eugene Chan:** We have developed the rHEALTH sensor, which is a small, portable device designed to take a single drop of blood and give a read-out for many different laboratory tests. This is a notable departure from existing delivery of healthcare, where there are central laboratories required to provide this information. The rHEALTH is designed to democratize biomedical information, allowing individuals, anywhere, to get access to their results.



Image Courtesy of XPRIZE

**Y.M. Dennis Lo:** I work in the area of noninvasive prenatal testing (NIPT). My group first reported in 1997 the presence of cell-free fetal DNA in maternal plasma. We then spent the next 18 years translating

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this discovery into a safe and robust system for NIPT.



In particular, we have demonstrated that fetal trisomy 21 can be detected with high sensitivity and specificity using maternal plasma. This technology is now used in over 60 countries and over one million pregnant women had been tested.



**Carl T. Wittwer:** My innovation has been directed at increasing the utility of PCR in molecular analysis by 1) decreasing the time to result from over an hour to 15 s, and 2) introducing melting analysis to eliminate downstream open-tube analysis. A sample-to-answer PCR diagnostic in about 2 min

has become feasible, enabling point-of-care molecular testing and reduction in pre- and postanalytical errors.

### *Is the line between sustaining and disruptive innovation always clear?*

**Eric Topol:** Yes, in my view, sustaining is incremental but disruptive is truly transformational—having a major and durable impact.

**Eugene Chan:** Not at all. Innovation is built on great bodies of knowledge in the field. In this manner, this knowledge is to be both respected and challenged. Sustaining innovation will take one existing concept and push it further; disruptive innovation takes several concepts and combines them into one seamless advance. Very often, in a particular field, there are a substantial number of sustaining innovations that are then punctuated with disruptive innovations. In the case of the rHEALTH, it builds upon existing advances in microfluidics, nanofabrication, photonics, and cytometry. We were able to successfully put several innovations together to address an important problem.

**Y.M. Dennis Lo:** I believe that in many examples, the essence of a disruptive innovation is so fundamental that one can readily see the core difference from the incremental innovations in a particular field. In the area that I have worked on, for many years researchers tried to look for

intact fetal cells that had entered into the maternal blood but were not able to make this approach work robustly. By looking outside cells, in the cell-free plasma fraction of blood, one can find a readily analyzable source of fetal DNA. This is the fundamental change in thought process that has created a paradigm shift in the field.

**Carl T. Wittwer:** Certainly more of a gradient than a line. Fifteen-second PCR could be considered just an incremental improvement, but it may make a big difference in how esoteric testing is performed. Including melting analysis as an analytical back end to PCR, eliminating gels, sequencing, etc. was more of a paradigm shift at the time. High-resolution melting analysis appears to be a sustaining incremental improvement of melting analysis, but it continues to enable new applications previously not considered.

### *How can you teach disruptive innovation?*

**Eric Topol:** By doing it and fostering younger people to think big.

**Eugene Chan:** I don't know if you can since each case is fairly unique. One way to teach it is through case studies, so I will give you ours. In creating the rHEALTH, several factors influenced us. We are in Cambridge, one of the innovation hubs in the US. It was important that we did it outside the conventional university system and in a company since this allows for close coordination, organization, and teamwork. In a somewhat counterintuitive manner, I decided that we should be somewhat removed from the noise in the field, avoiding conferences and routine reading of the literature. This ensured that my team would not fall into the trap of thinking like everyone else or thinking there were certain limits to solutions. I picked a problem that would be important a few years out to give ourselves some time. We relied completely on ourselves to generate the innovation and made sure we met high scientific standards that can be clearly validated externally, including peer review, XPRIZE competitions, and third-party testing of the technology.

**Y.M. Dennis Lo:** I think that we can tell stories of disruptive innovations to our students, even as early as in primary schools. As the students appreciate the diverse circumstances under which disruptive innovations can occur, some of them, hopefully, may be able to catch the eureka moment and to arrive at their own disruptive innovation.

**Carl T. Wittwer:** Expose students to history through books like Thomas Kuhn's *The Structure of Scientific Revolutions* and books on Steve Jobs. Disruptive innovation arises from dissatisfaction with current "solutions" and a

drive to find something better. It is difficult to teach didactically—but perhaps by example. You cannot predict disruptive innovation, or it would not be disruptive.

*Is there any way that governments or institutions or research agencies can create environments that would increase the chance of developing disruptive innovation?*

**Eric Topol:** If the government regulatory agency gets out of the way and fosters innovation, rather than holding it back, it would undoubtedly help. More funding is needed from NIH and other sources to actualize the extraordinary opportunities and vast, unmet needs in medicine.

**Eugene Chan:** The entire ecosystem matters. Government, institutions, companies, investors, and people are part of this ecosystem. This system needs to feed on itself and encourage risk taking, serendipity, and change. The cultural underpinnings of this system should not be ignored. Focus should be based on the quality of the idea. Great ideas should be embraced and rewarded.

**Y.M. Dennis Lo:** I think that to increase the chance of developing disruptive innovation, researchers should be nurtured in an environment that encourages risk-taking. Academics should not be overloaded with administrative or teaching duties, so that they have the time to think and discuss with colleagues. Researchers should be given plenty of opportunities to travel to other centers, to engage in conference activities, so that they can be exposed to new developments, especially those in other fields.

**Carl T. Wittwer:** Grants usually bring the innovator into the system and decrease their chance of innovating. Innovation is driven by need and a desire to change the status quo for the better. This is usually not consistent with the security of a grant and by playing ball with those whose purpose it is to maintain the current system. Perhaps this can be accomplished through small grants, such as the NIH-SBIR (Small Business Innovation Research) and STTR (Small Business Technology Transfer) that focus on demonstrating feasibility. How we view inventors in the media may have a greater effect. Are they mad scientists with evil goals? Are they greedy businessmen? Do you want to be a disruptor?

*Why does most innovation occur in small rather than large companies?*

**Eric Topol:** Large companies are notoriously monolithic and not agile. Smaller companies, typically startups, have

maximal plasticity, unrestricted thinking and imagination, and lack the suppression often seen in large companies.

**Eugene Chan:** Small companies are not occupied with existing problems. This frees them to pursue their first product, which in the beginning, is bound only by market needs. The rHEALTH work is being done with a small, tight group of individuals who are fully committed to its success. Unlike larger companies, they are not beholden to quarterly earnings reports.

**Y.M. Dennis Lo:** I think that one possible reason is that large companies have more “inertia” and often are unable to move rapidly to pursue new directions.

**Carl T. Wittwer:** Small companies are hungry and have to take risks to survive. Large companies have a greater interest in maintaining their current market share. Innovation in large companies is like trying to move the world with no fulcrum.

*To what extent do you think disruption is the right mode of innovation to be considering in the immediate future of laboratory medicine?*

**Eric Topol:** Laboratory medicine will undergo the biggest shakeup in its history over the next decade—from “central” laboratories to “mobile” laboratories owned and operated by consumers. Assays will be markedly reduced in cost using a tiny fraction of the sample amounts taken today. These will be welcome changes, both from the standpoint of availability of data to each individual seeking it, along with the economics of taking advantage of Moore’s Law with cheap chips.

**Eugene Chan:** Laboratory medicine is a unique field in itself. On one hand, like most of medicine, it is ripe for disruption. On the other hand, the standards by which technologies are accepted are the same. They need to meet performance, sensitivity, and specificity requirements for providing values that can be trusted by physicians and individuals. Disruption in laboratory medicine needs to pass this critical step. Getting physicians and laboratory medicine experts onboard is particularly important for these new technologies.

**Y.M. Dennis Lo:** While I am excited to be involved in disruptive innovations, I do understand that many medical practitioners and regulatory bodies are very conservative and hence the immediate future of laboratory medicine would predominantly be based on incremental advances.

**Carl T. Wittwer:** This is a weighted question. We (people and governments in a democratic society) are the biggest COMPANY of all and change, especially in med-

ical care, is slow. There are so many agencies (FDA, CLIA, etc.) whose job is to protect the public good, and so many competing financial interests, that the barriers to change become almost insurmountable. Given this extraordinary inertia against change, the disrupters who dare to suggest that things can be faster, cheaper, and better need encouragement. Disruption is an evolutionary change. It is necessary for survival. If the disruptive innovation is not considered an immediate challenge, it is less likely that it will make a difference. The risk is also acceptable, because if the disruptive innovation is poor or misguided, it will fade away.

***What advice do you have for young scientists/entrepreneurs that want to innovate?***

**Eric Topol:** Go for it. We need young innovators, digital natives, to lead the way.

**Eugene Chan:** Pick a problem of great human importance, work on it, be an expert at it, and some good will come out of it.

**Y.M. Dennis Lo:** Modern innovations frequently require concepts from multiple fields. Hence, I would strongly recommend to young scientists to have a broad training, preferably having experience abroad.

**Carl T. Wittwer:** Go for it! No one will believe in your idea more than you do. You do not need extensive financial backing or venture capitalists who do not share your vision. Produce working prototypes. Publish. Produce more prototypes. Get someone to use your prototypes. Publish.

***What is it that people are saying today that 30–40 years from now will sound plainly myopic?***

**Eric Topol:** How did we ever practice medicine at a mass population level without having granular, high-definition data for each individual?

**Eugene Chan:** Why was healthcare so expensive back then? It is so easy to get my diagnostic information today. There's no reason why we shouldn't have broad accessibility to our own medical information in a simple and easy manner.

**Carl T. Wittwer:** Highly efficient, centralized laboratories for human diagnostics have a cost/benefit ratio that decentralized efforts (point of care, etc.) will never reach.

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