

Editorial

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Theranos revisited: the trial and lessons learned

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Introduction

CCLM readers may wonder as to why we bring back an old story, the Theranos story, which peaked in intensity and interest around 2016 and then disappeared from most people's radar after the company's total collapse in 2019. The reasons we are bringing the Theranos story back is that in September 2021, the widely anticipated trial of Elisabeth Holmes, the Company's Founder and CEO, has started in San Jose, CA, USA, and the world's newspapers are there to report on the proceedings and the final outcome. Here is the link to a recent, and very detailed, report in Toronto's Globe and Mail national newspaper.

<https://www.theglobeandmail.com/business/article-theranos-founder-elizabeth-holmes-fraud-trial-to-test-the-limits-of/>.

Holmes is accused of defrauding investors and customers and, if convicted, faces up to 20 years in prison. She pleaded not guilty.

CCLM is not a news outlet and has no interest in criminal cases. However, the Theranos incident, despite its links to possible criminal activity, has also a lot to do with laboratory medicine and *in-vitro* diagnostics. Particularly, it will be of interest for laboratory medicine professionals to hear, if any,

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as yet unknown details of Theranos's activities in laboratory testing and of their business practices, namely, that development of methods and diagnostic systems must follow stringent and accurate pathways before their adoption in clinical practice. This could be useful, in hopes that new lessons could be learned by the diagnostic industry, professional organizations and laboratory medicine practitioners. At the end of this editorial, we will provide a list of such possible "lessons".

Theranos story

The Theranos story is probably the biggest story that has ever hit laboratory medicine. It involved a young entrepreneur, Elizabeth Holmes, who created a company with the aim of revolutionizing healthcare testing by using capillary blood and innovative small-size equipment, operated outside the traditional labs (such as in pharmacies) by non-specialists, and even, by the patients/customers themselves. The company reached about \$10 billion valuation at some point, making Holmes the youngest ever billionaire. We will not dwell into more details, since the story has been well-described already in newspaper articles, books, scientific publications and in television documentaries. Apparently, a movie is also in the making.

One of us (EPD) got involved with the Theranos story early in 2014 and published the very first Theranos-related scientific manuscript in *CCLM*, analyzing the Theranos testing model and claiming that there were minor, if any, revolutionary concepts about their technology [1]. After this initial publication, an investigative reporter from The Wall Street Journal, John Carreyrou, independently started revealing disturbing details of Theranos business practices [2, 3], now fully described in his best-selling book [4]. At about the same time, Dr. John Ioannidis, of Stanford University, criticized the secrecy of Theranos's scientific activities [5, 6]. Details can be found in the cited literature. It is noteworthy that as of today, Theranos did not publish any of its technology in a peer-reviewed journal.

After the first publication, one of us followed the Theranos story closely, and with his associates Michelle Li and Clare Fiala (then high-school students/volunteers in the lab) published a series of articles, chronicling the rise

and fall of Theranos from 2015 to 2019 [7–10]. The latest piece of the series summarizes the story and provides additional literature [11]. *CCLM* had the intuition to realize that this was a big, developing story in laboratory medicine and invested a lot of space publishing updates and editorials in *CCLM* [12].

Some personal accounts

There are many personal accounts and unpublished details about this story and some are worth mentioning. The story had a negative impact on our long-standing friendships and relationships with a lot of people, including the leadership and many members of the American Association for Clinical Chemistry (AACC), some of whom were appointed expert consultants in the board of Theranos. Some editorials we wrote on Theranos were submitted to *Clinical Chemistry* and other Journals but did not achieve high priority for publication. On one occasion, our work was labeled as “gossip”, more suited for a tabloid newspaper instead of a high-ranking scientific publication. Retrospectively, we believe that a number of leading Laboratory Medicine journals, including *Clinical Chemistry*, apparently grossly misjudged the hitherto secret new technology that Theranos claimed to have developed. The reasons for this misjudgment remain speculative.

Here, it is important to mention the unconditional support of the *CCLM* publisher and the Board of Editors, who had the courage to publish numerous reports on the story, along with their own editorials and press releases. Thus, *CCLM* became the journal with most papers published on Theranos.

One rather extraordinary event was a confidential letter written by an apparently laboratory medicine professional, addressed to the Editor of *CCLM*, asking him to retract all *CCLM* publications of one of us on Theranos, due to a possible conflict of interest (at that time EPD was consulting with a small company that was using small blood sample volumes for diagnostics). Not only this did not happen, but it triggered a response from the *CCLM* Board of Editors, defending our publications and our academic freedom of speech [13]. We believe that this action was crucial since, despite the effort, we were not silenced in voicing our serious concerns with this company.

Another confrontation related to the Theranos story was the decision of the AACC to invite Elizabeth Holmes to present in a dedicated session at the 2016 AACC annual conference. We, and many other AACC members,

contested this as favoritism, because it is highly unusual that industry is provided a forum to present their developments in such invited sessions on national or international meetings [9]. Unfortunately, this debate has led to newspaper press releases which misrepresented some of our quotes about the judgment of AACC leadership of that time. From this incident, we learned to be very careful with public media releases since the reporters have their own agendas and objectives.

While most of these misunderstandings and confrontations have now been cleared and professional relationships have been mostly repaired, we also learned that even if you are right in scientific debates, the way you present your case is of paramount importance. Do not over-state your case; under-state it, may be better!

Our original prediction that Theranos had nothing new and that it would eventually collapse, turned out to be true and our writings, and those of others on the subject, are a testimony to this assertion. We still wonder how experienced investors, invested hundreds of millions of dollars on an apparently naïve (but not necessarily criminally-minded) young inventor. Most of the credit for bringing down

Table 1: Lessons to be learned from the Theranos story.

General

- Secrecy is necessary in the development of novel technologies, but it also facilitates fraud.
- Therefore, the basic features of new technologies must be made available to the scientific community before they are commercialized.

Investors

- Use your common sense and seek knowledgeable advice early on.
- Ask critical questions.
- Prominent laymen on the Supervisory Board are no proof of quality. The absence of persons with relevant experience in the field should raise suspicion.

Professionals and professional organizations

- Do not praise novel technologies as long as you do not know their basic principles.
- Consideration of conflicts of interest should be more than lip service.

Regulators

- Keep an eye on unwarranted exploitation of loopholes in the rules.
- Prominent laymen on the Supervisory Board are no proof of quality.

Companies

- Be transparent and timely release peer reviewed data to the scientific community, the general public and Government regulators.
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Theranos was given to Wall Street Journal reporter John Carreyrou. The story led to a best-selling book [4] and to the filming of an HBO TV documentary (<https://www.hbo.com/documentaries/the-inventor-out-for-blood-in-silicon-valley>). Nevertheless we firmly believe that the articles published in *CCLM* were of utmost importance to restore scientific integrity and hopefully serve as an example of dearly needed continuing scientific discourse. Our *CCLM* scientific papers, indexed in PubMed, will likely stand the test of time and remind those interested on the legendary story on exactly what happened and who did what.

There are many lessons to be learned from the Theranos incident and these are summarized in Table 1 (reproduced and modified from our editorial [11]). These lessons may guide us to navigate better when the next Theranos-like story comes about to hit us. Already, such stories are actually developing now, as we recently reviewed [14].

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References

1. Diamandis EP. Theranos phenomenon: promises and fallacies. *Clin Chem Lab Med* 2015;53:989–93.
2. The Wall Street Journal, Carreyrou J. Hot startup Theranos has struggled with its blood-test technology. Available from: <https://www.wsj.com/articles/theranos-hasstruggled-with-blood-tests-1444881901> [Accessed 20 Mar 2018].
3. The Wall Street Journal, Carreyrou J. Theranos whistleblower shook the company — and his family. Available from: <https://www.wsj.com/articles/theranoswhistleblower-shook-the-companyand-his-family-1479335963> [Accessed 20 Mar 2018].
4. Pan Macmillan Publishing. Bad blood: secrets and lies in a Silicon Valley startup. Available from: <https://www.panmacmillan.com/authors/john-carreyrou/bad-blood> [Accessed 3 Apr 2018].
5. Ioannidis J. Stealth research: is biomedical innovation happening outside the peer reviewed literature? *J Am Med Assoc* 2015;313:663–4.
6. Ioannidis J. Stealth research and Theranos: reflections and update 1 year later. *J Am Med Assoc* 2016;316:389–90.
7. Li M, Diamandis EP. Theranos phenomenon – part 2. *Clin Chem Lab Med* 2015;53:1911–2.
8. Li M, Diamandis EP. Theranos phenomenon – part 3. *Clin Chem Lab Med* 2016;54:e145–6.
9. Diamandis EP. Theranos phenomenon – part 4: Theranos at an international conference. *Clin Chem Lab Med* 2016;54:e243–4.
10. Diamandis EP, Plebani M. Theranos phenomenon – part 5: Theranos’ presentation at the American Association for Clinical Chemistry Annual Conference 2016. *Clin Chem Lab Med* 2016;54:e313–4.
11. Fiala C, Diamandis EP. The meteoric rise and dramatic fall of Theranos: lessons learned for the diagnostic industry. *Clin Chem Lab Med*;56:1443–6. <https://doi.org/10.1515/cclm-2018-0353>.
12. Lackner KJ, Plebani M. The Theranos saga and the consequences. *Clin Chem Lab Med* 2018;56:1395–6.
13. Lackner KJ, Gillery P, Lippi G, Melichar B, Schlattmann P, Tate JR, et al. The Theranos phenomenon, scientific transparency and freedom of speech. *Clin Chem Lab Med* 2016;54:1403–5.
14. Fiala C, Diamandis EP. The outcomes of scientific debates should be published: the Arivale Story. *J Appl Lab Med* 2020;5:1070–5.