EDITORIAL

CRISPR, cell lines and organoids: New entrants in next generational lab medicine

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Pathology, while diverging into newer dimensions has always remained at the forefront of science in terms of incorporating newer methodologies for emerging technologies and informatics. While we will never know who could be the first person using tangible evidence in terms of data, but we did see laboratories transforming from pipetting methods and manual efforts to sophisticated software defined algorithmic systems to the incorporation of diversified contemporary molecular methods to demystify the tiniest details about the pathological processes in life forms. Knowledge is growing, reshaping into non-conventional methodologies with time, which require both accuracy and precision more than ever before in the clinical arena. "Clinical Laboratory" is now requiring expertise, specified bioinformatics skills mixed with the pathologist being informed in latest updates on their subjects. The subject of "laboratory joining hands with clinics" was a past slogan which is now needing an update into "Laboratory guiding clinics".[1] The continuous onslaught of data has resulted in specialized subjects like "data sciences", which have now become the hardcore foundation for next-generational clinical laboratories.[2]

The evolving theme of "Personalized Medicine" has bestowed more challenges for the pathologist, where the clinical laboratory would be required to generate data as per host's specific genetic and epigenetic compatibilities. Host donor compatibility in organ donation for prevailing therapeutics are current challenges where prevailing healthcare systems struggle. Recent developments in molecular sciences including genome engineering of patient's defect in metabolic and non-metabolic diseases with research being trickled to host's 3-D culture systems i.e., organoids which will overcome massive chunk of issues like organ donation rejection, reducing cost of HLA and allied compatibilities, creating disease specific models for research like COVID-19 and allowing tailored therapeutics for healthcare clientele.[3] Recently, CRISPR/Cas bioengineering of genome, have shown a credible potential to assist laboratories in exploring some of the current problems in the field of pathogenesis by helping study disease models and therapeutic efficacy of drugs.[3] The use of human cancer cell lines has allowed not just the development of cancer model, but assessment in real-time of the efficacy of chemotherapeutic medications for oncology patients, which can result in timely evaluation of therapeutic therapy resistance.[4] From oncology to psychiatry and autoimmune disease 3-D models of disease i.e., organoids are also being made available which are bound to replace the so termed "lethargic" conventional system to assess drug resistance in various metabolic diseases with accuracy and precision.[5] Shahjalal et al with limitations have developed islet cell organoids having the possible objective of utilizing them as replacement for organ donation, and hopefully over time this can lead us to address the issue of donor shortage due to mismatched donations.[6] All these technological advancements highlight the significance to adopt current technologies to address the diagnostic requirements of next-generational medicine.

Technology limitations, optimization and bench to clinical translation will be the future challenges our labs are going to face. Provided continual improvements, there remains a mammoth gap to be bridged requiring an up-gradation of knowledge base to modification of lab infrastructure in order to house the required tools for developing advanced technologies. Currently, there is a dire need to converge the rapidly emerging laboratory techniques into some degree of order in terms of regulatory compliance throughout the globe. Ivanov et al have highlighted the immense information outflow from next-generational sequencing as questionable, with need for appropriate customization.[7] Similarly, the recently most utilized genome editing techniques like CRISPR/Cas methods also face issues like off-target mutations and low efficiencies.[8] The latest version of 3-D organoids are also in need of optimization through oversight by commercial patronage and standardization to ensure optimal utilization. Astashkina et al have pointed towards the lack of these culture techniques to provide requisite data on drug toxicity profiles.[9] These shortcomings will be addressed over time as clinical usage has already commenced in certain advanced set ups.

Futuristic preparedness of the clinical laboratory for these newer lab technologies inclusive of molecular techniques,

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genome editing methods, use of organoids as cell culture for identifying drug effectiveness and genetic classification will become a routine practice. Pathologists and laboratory technologists will be required to update their knowledge in these emerging lab arenas. Knowledge base at this time is mandatory for laboratory leadership as they will be required to incorporate these newer life saviours into their arsenals. There will be a shift from current testing which will probably evolve as point of care testing for newer lab modalities like sequencing techniques, drug resistance testing for oncology patients and routine use of in vitro pathogenesis evaluation by using organoids and cell lines, CRISPR/Cas like bioengineering methods to create gene knockouts and dCas models, maintenance of bio banks and possibly development of organoids replacing human transplantation.[3-5] Timely incorporation of such technologies will not only help patients but will also bring business to laboratories.

It is the opinion of the authors that future laboratory requirements will be different from today relying more upon the latest innovational lab techniques and methods with more focus on standardization, accuracy, precision and turnaround time. Although the clinical laboratories of today face myriad challenges, they must strive hard to build up the needful technical expertise to integrate with creative and translational research for providing robust service delivery and for fulfilling future business needs. Continuous research and development should be a feature of any laboratory.

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