

Omics Research: Are You Doing It Right?

Presenting itself challenging, unlocking the fundamentals of a quality Omics research requires a multidimensional approach that considers study designs and downstream analysis. However, these may only just be the beginning.

Omics Research: A Systematic Approach

Systems Biology aims to understand biology as a whole through methodical examination of the structure and the dynamics of cellular and organismal function. Powered by high-throughput omics technologies and computational surge, cellular map of diverse interactions, signalling and regulation networks are decoded using high-resolution 'omics' platform, encompassing genomics, proteomics, transcriptomics and metabolomics. An example would be the Human Genome Project, that correlates multi-omics data to various health-related phenotypic observations to create life-changing clinical applications.

In the past 10 years¹, the genomic research landscape has significantly changed as a flurry of high-throughput sequencing (HTS) technologies such as short read massive parallel (e.g. Illumina), single-molecule real time (e.g. Pacific Biosciences) and Nanopore-based (e.g. Oxford Nanopore Technologies) sequencing emerged. Modern day data-driven system biology now stands on 2 main pillars: data generation through high throughput omics technologies and data modelling through advance bioinformatics and computational biology approaches. Massive and comprehensive data at the system level are first catalogued, followed by modelling and translating into accessible and visual forms in order to gain insightful scientific interpretation².

“ The technologies are robust enough now that anybody can collect these kinds of data. You still need to be pretty expert to figure out how to analyze it and combine them ... you'd probably want to talk to an expert so you do it right – at least so you know what the issues are. ”

Michael Snyder, Ph.D., Director, Center for Genomics and Personalized Medicine at Stanford University

HTS: A Small Element of A Bigger Story

As more and more researchers apply HTS in their research, misconceptions arise assuming that generating results that are readily publishable in a high-impact journal is just as easy as sending tissue materials for HTS, often accompanied by standard automated analyses offered by major service providers. In reality, executing quality omics research would require **study designs to be personalised** according to problem statements, hypotheses and objectives, in order to determine the right samples, positive/negative controls, treatments, collection methods and the exact DNA/RNA to be used. Another success key is in sample preparation which crucially ensures the quality of the DNA/RNA extracted while also choosing the right sequencing library preparation method. This is to capture the valid piece of DNA/RNA information before investing in HTS, so that the data obtained could inform us about actual biological events happening in the cells. After careful sample preparation, accurate sequencing technology has to be selected with respect to specific research aims: e.g. short or long read technology, the coverage required, cost-effectiveness in balancing funds spent and whether the data obtained are in line with the objectives. Lastly, this should be followed by good and technically sound data analyses.

Downstream Analysis: The Real Truth

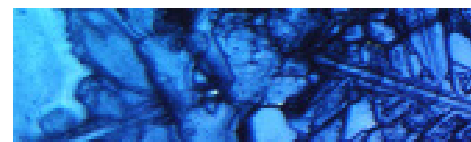
In 2011, the research cost for omics study was predicted to shift from “sequencing” to “sample collection and experimental design” and “downstream analysis”, indicating the importance of the latter in the future³. However, current market supply as provided by major bioinformatics service providers utilizes high automation in data analyses without realising that such procedures cannot be applied directly to all

cases. To understand this, one has to acknowledge that organisms are intrinsically different from each other, either inter-kingdom (e.g. animal versus plant, bacteria versus kingdom etc.) or down to inter-genus or inter-species levels. Therefore, no single analysis strategy, set of parameters or laboratory method can be applied to all types of samples or all kind of research backgrounds and it is crucial for any researcher to be aware of these significant differences .

Actual, **robust bioinformatics analyses must comprise of “machine time” and “human time”**. One may automate “machine analysis” as a fast and cheap outsourcing job, but good research practice would need to be complemented with “human analysis”, as experts compare and choose suitable software tools, learn how to install/configure and execute the results, put in cleaned data and optimise, estimate the effects of fine-tuning the parameters and how it will affect the accuracy of the data. Such knowledge, resource, and infrastructure intensive gathering would require specialized experience and expertise. At this instance, it may be worthwhile to consider collaborating with Contract Research Organizations (CRO), to not only overcome the growing challenges of storing, analysing, and interpreting HTS data, but also in terms of appropriate study designs and curated downstream analysis. These independent research organisations offer more precise and targeted R&D functions for the research industry and are capable of filling in these gaps.

Omics Research: A Big Picture Approach

The advent in next-generation technology and the exponential decline in sequencing costs have indeed opened up an array of opportunities in functional genomics research; enabling the deciphering of



genetic codes of all organisms. Undoubtedly, NGS technologies are pivotal in enabling the jumpstart of tremendous cutting-edge discoveries and applications such as in the field of precision medicine and oncology⁴, food safety⁵, veterinary⁶, agriculture⁷ and fisheries⁸. Above all, one needs to look further than just the application of HTS technologies in an Omics research. Incorporate a more holistic and inclusive approach; consider other research parameters tailored to specific research objectives and pivot more importance towards experimental design, sample collection and effective downstream data analysis for a quality omics research or ponder collaborating with an experienced partner and make life-changing discoveries together.

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