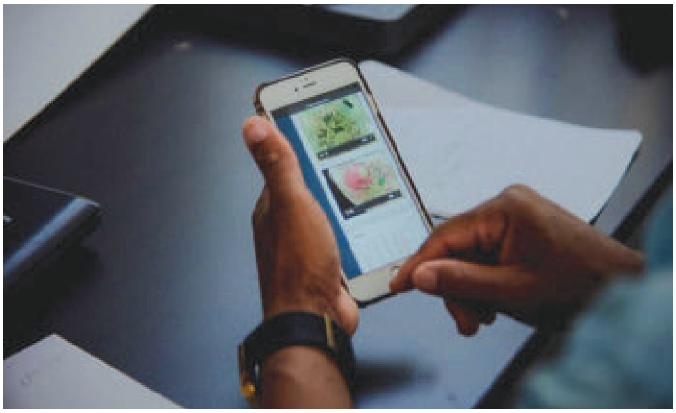
Living Informatics

Filling the Gap in Preclinical Data Collection and Analysis

The advent of modern bioinformatics has greatly enhanced pharmaceutical R&D. While drug developers and CROs have adopted innovations in translational bioinformatics and clinical research informatics, there remains an overlooked technology gap in preclinical *in vivo* research. Into the breach steps living informatics, a new area of biomedical informatics that brings the fruits of the home digital revolution to preclinical research labs.

Created through the convergence of life sciences, digital technology, and large-scale interpretive methods, living informatics is a continuous process of gathering large amounts of data from living systems through the use of sensors, systems, big data, and related technologies and disciplines. Recent advances in cloud-based technologies that enable the collection and analysis of vast quantities of *in vivo* data considered unimaginable just five years ago make living informatics possible. At that time, high-throughput data processing was fraught with risk and operational difficulties, not to mention considerable expense. Living informatics empowers scientists to focus on the research and discovery of novel drug candidates, as opposed to standard routine processes. Drug developers can make timely, informed decisions about which compounds will have a greater probability of success, and then accelerate development of those compounds while reducing overall R&D costs.

With living informatics, researchers are able to continuously monitor and transmit real-time activity, physiology, and behavior data.



With an online research application, a researcher monitors animal disease and well-being and can access data 24/7 from a mobile device. © Damien Maloney

AUTOMATING THE PHYSICAL AND DIGITAL INFRASTRUCTURE

In June, the first living informatics platform in preclinical *in vivo* research launched. This facility incorporates advances in animal research technology, including a highly automated physical and digital infrastructure comprising thousands of rodent cages equipped with intelligent sensors and a high-definition camera network. This high-tech facility enables continuous monitoring and recording of rodent motion, respiration, physiology, and behavior, as well as environment and husbandry, providing researchers with answers to scientific questions and auditable records of rich data for ongoing analyses. It is fully accredited by AAALAC International and received an AAALAC commendation for upholding the 3Rs.

Living informatics offers several advantages over traditional *in vivo* research, including processing of massive datasets, high throughput profiling of multiple compounds in parallel, sensitivity to subtle animal signs and behavior, and human-animal interactions that are less error-prone and far less stressful. Digital platforms can process terabytes of continuous, objective, and transparent data from each research subject; traditional approaches, by contrast, gather much less data, usually amounting to less than a kilobyte, and the data themselves are subjective. Moreover, the sensors, high-definition video, and other technological features embedded in the systems are similar to those used in common consumer goods such as the iPhone and the FitBit.

DISEASE RESEARCH

One of the most vivid examples of the power of living informatics is a model that combines physiological measurements with advanced analytics to produce a highly sensitive readout of rheumatoid arthritis (RA) induction, as well as clinically

relevant measures of therapeutic response. This index was validated through a series of experiments that induced RA in rats. The experiments also demonstrated that the model accurately tracks disease severity and prophylactic treatment efficacy when compared to conventional measurements. During the validation process, the model followed the industry standard to record traditional disease metrics, and then used machine learning to establish the correct parameters for its automated metrics. This approach obviated the need for manual methods of measurement, which are more subjective and error-prone, and which can be highly variable from one technician to another.

In addition to arthritis, the living informatics principles can be applied to advance preclinical research in lupus, multiple sclerosis (MS), lymphoma, liver fibrosis, leukemia, glioblastoma, chronic pain, and other disease areas in which the utility of available models has been limited by low sensitivity and manual means of observation and measurement. In these areas, living informatics can characterize a rate of disease onset several days before traditional measurement systems can pick up such a signal.

This system has also observed similar results in MS, a disease in which animal models are typically hyperinduced, i.e. researchers exaggerate the disease to such a degree that the signs and symptoms are clearly visible for scoring purposes. The problem is that such high amplification is not a true reflection of MS presentation in humans. Consequently, therapeutic compounds advancing from such animal studies do not necessarily correlate with human disease patterns, and thus are less precisely calibrated for clinical studies. The model can unobtrusively record and measure MS signs and symptoms in animals before the traditional scoring period even begins, obviating the need for hyperinduced research subjects. Use of this technology also increases the likelihood that compounds emerging from preclinical research are better mapped for actual MS disease progression, potentially leading to better drugs for clinical studies.

CONCLUSION

Living informatics platforms are highly adaptable to the changing needs of the pharma/biotech industry. As the field matures, and as greater numbers of drug developers adopt modern bioinformatics to animal studies, new meaningful payoffs in the form of cleaner, more robust, and more actionable data are expected to be seen, information that could lead to better, more precisely calibrated therapies reaching the clinic.

Joe Betts-Lacroix, *a proven entrepreneur and inventor, holds scores of granted and pending patents in fields ranging from biophysics and safety systems to antennas, thermal systems, user interfaces, and analog electronics.*