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Editorial

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Network Medicine: Harnessing the Potential of Digital Biomarkers

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It is with much enthusiasm that the Journal of Network Medicine and Targeted Therapies is launched. The timing is appropriate as the field advances at a steady rate, fuelled by developments both in our understanding of disease etiology and new technologies which are capable of diagnosing and interrogating disease. The advent of network medicine has been much heralded a consequence of and reflections on the often complex inter-relationships between various omics based components in disease pathways [1]. Similarly, the desire for targeted therapies speaks to the goal of personalized/precision medicine, and objective to circumvent bystander toxicity often associated with systemic therapeutic approaches [2]. Considerable progress has been made with regard to our capabilities to analyze genomic, proteomic, metabolomic and immunogenic profiles, and in the detection of circulating biomarkers. Miniaturization of these technologies and incorporation in medical devices and consumer products continues apace, and clinical validations are underway in a number of therapeutic areas. A watershed moment with regard to disease biomarkers occurred in 2016 with the publication of guidelines from the FDA-NIH working group [3]. The living document (referred to by the acronym 'BEST' derived from Biomarkers, EndpointS and other Tools) codifies several different categories of the biomarker, which will help guide development of future medical devices, and also drugs with companion diagnostics (Dx/Rx). The development of advanced technologies for the detection and monitoring of biomarkers has also fuelled much interest in the prospect for 'closed loop' drug delivery systems. A perhaps perfect embodiment of personalized medicine, this was first explored in the *diabetes mellitus* space, where precise correlations between biomarker (blood glucose) and drug effector (injected insulin) have been established [4]. Ultimately an automated closed loop system has been developed, approved and introduced to the market place [5] and this will stimulate additional efforts in other therapeutic areas. A major opportunity also lies in the mass deployment of new consumer-based devices with ever more sophisticated health monitoring capabilities. Though concerns have been highlighted relating to the consistency and accuracy of these devices [6] they offer potential to record a battery of digital monitoring biomarkers, including heart rate, PO_2 level, blood pressure, activity, gait, and sleep cycles. When used in a longitudinal manner in concert with therapy, they also offer the potential to quantify treatment effectiveness. Incorporation of such devices in clinical studies, where conventional biomarkers are also monitored, has successfully validated the potential of digital biomarkers for prognostic assessment in wellness and cardiometabolic disease [7]. Studies such as this will spur development of myriad clinical applications, e.g. novel clinical feedback loops, and are also likely to actively engage health providers by offering patient incentive mechanisms not previously accessible. This said, there exist some challenges for the widespread introduction of digital biomarker platforms into clinical practice, including security concerns and ethical considerations [8]. There is also the conundrum that the early adopters of this technology (the so-called 'fit-rich') may not be those who stand to benefit the most from its application [9]. Device cost reduction through economies of scale, consumer education on the use of the technology and incentives programs from health providers will all contribute to the growth of this sector, as the age of the digital biomarker becomes fully realized. Looking forward, one can anticipate major opportunities for the pharmaceutical and biotechnology industry to incorporate such technology and device-based approaches to disease management. In pioneering studies, the Verily Corporation launched an initiative known as the 'baseline' study wherein healthy volunteers are provided with a smartwatch whose multiple sensors upload data to the cloud periodically [10]. The objective is to track subjects as they progress from healthy into diseased states, validating specific biomarkers and uncovering others. Such approaches offer the potential to re-vision the pharma/biotech industry by focusing

on wellness instead of illness, in the vein of a lifestyle company. With the strategic deployment of sensors, either via wearable/handheld devices or coupled with *ex vivo* biopsy, the technology could provide the digital Dx for which the pharma/biotech corporation has a counterpart Rx in its portfolio. The recent growth in miniaturized sensing equipment now provides many viable options for rapid analysis of tears, saliva, sweat and urine in addition to conventional (liquid) biopsies and microbiome (16s rRNA) analysis. Many of these systems have direct interfaces to smartphones to allow data capture and storage. Taken together, one can thus imagine major developments on the horizon in terms of digital mapping of personal health. As witnessed in the personal computing sector, different platforms are likely to emerge, and consumer (patient) preferences based on cost, performance, reliability, aesthetics, and usability will drive the market. It is thus entirely expected that major advances will be made at the interfaces of disease management, high-performance computing, and device engineering. The field of network medicine evolved through computational studies of systems biology, and we are likely to reap similar impact and reward in the areas of disease diagnosis and treatment. As such, the Journal is ideally positioned to stimulate and track this dynamic field as it evolves.

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