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Urine—an untapped goldmine for biomarker discovery?

GAO YouHe

National Key Laboratory of Medical Molecular Biology, Department of Physiology and Pathophysiology, Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences/School of Basic Medicine, Beijing 100005, China

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The past decade witnessed a few biomarkers discovered and validated; however, biomarker research as a whole has not been fruitful as expected. A majority of our efforts has been focused on blood, the dynamic tissue directly connecting every part of the body. Nevertheless, despite all the interest and endeavor spent on it, the blood has failed to deliver sufficient number of clinically valuable biomarkers. Is it possible that we have been barking up the wrong tree?

All cells in the body rely on a homeostatic microenvironment to survive and function. Blood, as the key provider of this internal environment for all tissues and organs, is naturally responsible to remain stable and balanced so as to protect organs from exposing to disturbing factors. In contrast, as a filtrate of the blood, urine bears no need or mechanism to be stable. Any change that is introduced into the blood either internally or externally tends to be cleared by the liver, kidney and/or other organs via a variety of mechanisms in order to maintain the homeostasis of the blood. In contrast, urine is the place that most of the wastes in blood are dumped into, and thus tolerates changes to a much higher degree. Biomarkers are the measurable changes associated with a physiological or pathophysiological process. Therefore, they are more likely to be magnified and detectable in urine than their counterparts in blood.

Despite the advantage of urine as a better biomarker source, urine biomarker research can be intimidated by the fact that changes in urine are much too complicated to sort out factors associated with any particular pathophysiological condition, especially in human samples. Besides the disease to be studied, many factors may also contribute to the overall changes and interfere with data analysis. The higher the complex level of these interfering factors, the larger number of samples is needed in a study, which poses a great challenge in the research involving human objects. Nevertheless, due to the non-invasive nature of urine sample collection, as well as minimal technical and ethical issues involved in the procedures, urine is among the most easily accessible biological samples ever collected from patients or healthy volunteers. Long-term storage and archiving of urine samples can be achieved by adsorbing urinary proteins on a piece of membrane and storing them dry in a vacuum pouch. This simple, economical, and scalable approach enables comprehensive and systematic collection of biological samples from all patients, potentially as part of their medical records. With these samples available along with their corresponding clinical information, it will be much easier to conduct large-scale biomarker research and population-wide validations, which in turn will lead to generation of high-quality biomarkers.

Because of the close relationship between urine and the urinary system, I speculate that the first group of urinary biomarkers established is likely to be in the nephrology field.

Medical record documentation dramatically changed the medical practice and clinical research in the last century as it had laid the foundation for analyzing various medical cases on both individual and population levels. It is fairly reasonable to speculate that prospective collection and

email: gaoyouhe@pumc.edu.cn

storage of urinary proteins will be valuable in disease-associated biomarker discovery and assessment by providing the resource for decoding the biological information stored in urine retrospectively. With the analytical technologies developing at an unprecedented speed, studies on the stored samples will presumably be more productive, cost-effective, and faster in the near future. The more researchers and clinicians involved in digging this goldmine of biomarkers, the faster we will see advances in the field of personalized medicine in this century.