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Editorial: Biomarkers, Biospecimens and the Immunome

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Biomarkers are measurable parameters of the human body that serve as indicators of underlying biological or pathological processes. Despite the spectacular technological advances that have allowed the scientific community to measure an ever-expanding list of body parameters with greater sensitivity and specificity that aver before, these advances have not translated into greater numbers of clinically useful biomarkers, including those related to the measurement of immunological function itself or the measurement of immunological function as a means to detect or quantitate the effects of other diseases.

Biomarkers guide patient management in a multitude of settings including screening, diagnosis, prognosis, treatment choice and treatment monitoring. They also serve as primary sources of efficacy and safety data required by the Food and Drug Association for the approval of new therapies and medical devices. Despite the widespread and ever-growing need for new biomarkers and the deep investments made in their development by funding agencies and industry, the failure rate for biomarker development is extraordinarily high. Despite tens of thousands of reports of putative new biomarkers in the peer-reviewed literature, only a handful are qualified for drug development or approved for clinical use by the FDA and only about 100 biomarkers have proven clinically useful and reliable enough to be used in routine medical practice [1].

Biospecimens are the starting materials for the vast majority of biomarker measurements, including those relevant to the immunome. Overall, biomarker development has an extremely poor track record for success. Given the high degree of variability in the way that human biospecimens are collected, handled, stabilized, stored and transported, it is worth asking whether human biospecimens used for biomedical research and product development might be a significant source of the irreproducibility that is presently rife within this field of research [2]. In turn, could pre-analytical variation in human biospecimens be a major contributor to biomarker development failures?? It is not a question that investigators ask themselves often enough, but the "garbage in, garbage out" paradigm is as true for biomedical research as it is for data science.

Poor or unknown quality of biospecimens used for biomarker development is a doubled-edged sword. On the one hand, if the analysis test is itself in development, as is usually the case, variable results from various iterations of the analysis platform cannot be reasonably interpreted as being linked to variation in the technology if the test materials (biospecimens) are highly variable and beset with artifactual bias. This makes improvement in the analytical validity (analytical performance) of the platform more challenging. On the other hand, if the analysis platform is valid and reliable, the clinical validity (how the measurement relates to the clinical outcome of interest) of the measured biomarker becomes difficult or impossible to determine if pre-analytical variation in the biospecimens creates artifact that varies in type and amount from one sample to the next and overrides or obscures the correlation of the biomarker measurement with the clinical outcome.

There are two parts to the "biospecimen issue" that need to be considered by translational scientists. The first is the molecular quality of the sample and whether or not the sample being used for analysis is "fit for purpose" or of high enough molecular quality to yield valid results on the analysis platform being used. In this context, the definition of "quality" or "fit-for-purpose" depends on the relative stability or lability of the biomolecular class of interest, and how specimen collection, handling, processing, stabilization, storage and transportation variables (all of these are considered to be "pre-analytical" variables) might affect that class of molecule in that particular specimen type. DNA, for example, is a relatively stable molecule but may still undergo damage or degradation in specimen handling. Phosphoproteins, in contrast, are highly labile and may be completely altered in specimens by pre-analytical procedures that are not optimized to preserve them. Immunoglobulins are relatively stable components of the immunome, but the essential immunome includes a vast number of cells, genes, transcripts, regulatory molecules, and proteins that may not enjoy this same level of molecular stability [3]. Unfortunately, there is very little published data on the effects of pre-analytical variables of different types on these immunomic biomolecules, and investigators are relegated to studying these on their own to "optimize" specimens for their research project goals or, worse, ignoring the issue altogether.

The second aspect of the "biospecimen issue" that must be addressed is the molecular composition of the specimen at the time of analysis and to what degree pre-analytical steps may have artifactually altered that in ways that that have nothing to do with an underlying biological function that an investigator may be studying. In short, pre-analytical variables may change the biology of the biospecimen in ways that create artifactual or uninterpretable results, or both. Biopsecimens, whether liquid (blood) or solid (tissue), contain viable cells that react to the changes in their environment and the related stresses of procurement, handling, and stabilization (fixing or freezing) protocols. Depending on the setting, these stresses may be extreme. In the case of surgical specimens, for example, the biospecimen is exposed to multiple powerful drugs used pre- and intra-operatively, intra-operative ischemia (warm ischemia) associated with devascularization prior to resection, and cold ischemia related to time at room temperatures while awaiting stabilization to name only three types of "stress". Such variables can and do induce changes in the molecular composition of tissues as they react to these changes in their environment. The pre-analytical procedural and environmental variables to which human biospecimens are routinely subjected when collected within the healthcare system are both numerous and diverse. Worse, they are varied in variable ways from day to day, procedure to procedure, institution to institution. Thus, the variation is largely uncontrolled and undocumented. If this weren't enough of a challenge

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for immunomes researchers, many operative procedures, such as bowel surgery, my both introduce infection risk and disruption of normal anatomy and biology that control the microbiome. These, in turn, impact the immunome and must also be kept in mind when interpreting results from immunomic analyses of surgical specimens.

Despite the near universal acceptance of the truth in the aphorism "garbage in, garbage out", relatively little attention is paid to the quality and quality control of biospecimens used by the scientific community for biomarker research, in general or immunome research, in specific. Despite the technological advances that can compensate for some amount of quality shortfall in biospecimens to be analyzed, it is still worth emphasizing that the quality of the molecular analysis data will never be higher than the quality of the target analytes in the starting materials. There is still no such thing as "garbage in, diamonds out".

Fruitful search for and development of reliable biomarkers will require a greater understanding of the nonlinear complexity of the biological machinery and pathological perturbations of cells, tissues and organs involved in the human immune system. Biospecimens may be our window into that complexity, but they are not inert, passive objects of analysis. They are, themselves, complex adaptive systems. We must embrace the complexity and seek solutions. We cannot eliminate artifact, nor do we currently understand much about collection and handling artifact on different species of immunomic biomolecules in different kinds of samples. The most reasonable initial step in addressing this challenge is to employ standard operating procedures for collection and handling of specimens that minimize or eliminate procedural variation and document deviations from the standard. Currently, procedural variation creates artifacts that are both uncontrolled and unrecorded. This is untenable.

References

1. Poste G. Bring on the Biomarkers. *Nature* (2011) 496: 156-157.
2. Mullard A (2011). Reliability of 'New Drug Target' Claims Called into Question. *Nature Reviews Drug Discovery* 10: 643-644.
3. Ortutay C, Siermala M, Vihinen M (2007). Molecular Characterization of the Immune System: Emergence of Proteins, Processes and Domains. Immunogenetics 59: 333-348.