Structured reporting of T cell assay results

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Introduction

Recently, the final versions of the Minimal Information about T cell assays (MIATA) guidelines were published following a vetting process among peers. Here we summarize the rationale and background of the project and propose how to implement structured reporting of T cell experiments. Successful adoption by peers bears the potential, in the long-term, of enhancing the development of new immunomodulatory therapeutics.

Assays for the analysis of cell-mediated immunity belong to the essential repertoire of many laboratories involved in a variety of immunological sub-specialties, including oncology, infectious diseases, autoimmunity, transplantation immunology, and others. Flow cytometry-based as well as Elispot assays have been developed to investigate a wide range of analytes on a single-cell level and were refined for sensitive, reliable, and polyfunctional analysis. Over the years, the assay evolution occurring in institutions worldwide has led to optimized assays, but has left the scientific community with countless permutations of assay protocols and local standards. At the institutional level, the two main challenges are to define the biomarker assay which fits best to the investigational medicinal product in development, and to control the performance of applied analytical assays. From the community-wide perspective, the biggest challenge arises from the question of how to reliably interpret and compare results generated by different labs.

In this dynamic setting, the Cancer Immunotherapy Consortium of the Cancer Research Institute (CIC-CRI) and the Immunoguiding Program of the Association for Cancer Immunotherapy (CIP-CIMT) initiated proficiency panel programs for the most commonly used T cell assays involving a large number of heterogeneous labs from different backgrounds (1). These panels revealed that results from testing the same samples can vary significantly between labs (2, 3). Hence, the heterogeneous landscape of T cell immune assays not only is reflected by the use of different protocols, but also translates into wide-spread variability in assay results. Data obtained from these large-scale proficiency panels enabled the identification of critical variables in assay design and conduct that can influence assay results (Figure 1).

Crucial findings from these efforts were summarized in harmonization guidelines for the community (3-6). In subsequent panels, the implementation and adherence to such harmonization guidelines were successful in improving the accuracy of assay results overall and reducing the variability among labs (7). However, it was noted early on that most publications on T cell-related immune monitoring data lack structured reporting of all the critical protocol variables that may influence assay results, which may prevent easy interpretation of reports and limit comparability of data generated across institutions.

To address this issue, the Minimal Information About T Cell Assays (MIATA) project was initiated to define reporting guidelines, mirroring similar Minimal Information (MI) projects that were initially developed for high-throughput genomic assays and successfully applied for a variety of other assays (2, 8, 9). Importantly, MIATA was started and carried out as a broad effort to reach consensus on the minimal information necessary to efficiently and transparently describe how T cell assays were performed such that peers can confidently understand and interpret the presented data. While this was the project's driving force, another question of similar significance to be asked was: what and how much are scientists willing to share? Consequently, the MIATA project included an intense vetting process with two public consultation periods and two open workshops, with constant outreach to the community, over the time frame of three years (10). A dedicated website (11) was created that comprehensively displays every step, comment, and participant contributing to the project. With the input of more than 120 peers from academia and industry, as well as from regulatory background, the MIATA guidelines were recently finalized (12). The guidelines are divided into five modules and additional sub-modules which relate to the information concerning the sample, the specific assay protocol, the data acquisition, and analysis, as well as the lab environment—all process parameters identified earlier to be critical variables that can influence assay results. The guidelines are also visible on the MIATA website.

How to implement MIATA at an institution

Clearly, the mere existence of guidelines will not automatically lead to more structured reporting of experimental procedures...
Implementation of MIATA in the field

The key for success of MIATA will lie in its broad adoption and regular use by the scientific community at large. The implementation process will need to involve two major players: the scientists reporting on T cell assays and the journals including editorial teams and reviewers. The authors of this commentary envision a bottom-up activity from the T cell aficionados, rather than a top-down approach in which journals enforce adherence as a mandatory measure.

Incentives that encourage authors to follow MIATA guidelines may help support such a bottom-up approach. First, acknowledgement of MIATA compliance by journals may provide important validation for authors who have chosen to report their assay information in accordance with the MIATA framework. Second, by listing adherent manuscripts on the MIATA homepage, the MIATA designation may serve to increase awareness and alert more readers to such publications, leading to increased numbers of downloads in the short-term and possibly more citations in the long-run. The latter will benefit authors and publishers alike.

For the realization of these incentives, journals will need to allow explicit and visible use of the acknowledgement for those publications that fulfill the MIATA criteria. Offering the choice of using MIATA without enforcing it should be the way to proceed.

Certainly, the question arises about who verifies manuscripts for compliance with MIATA guidelines. A detailed answer could be at the discretion of the respective journals. A simple answer could be that authors may indicate within their manuscript if they adhere to MIATA (passive label assignment). Alternatively, dedicated reviewers may confirm adherence and assign the label actively. Once a manuscript is accepted and has been reviewed and confirmed to be MIATA-adherent, the author(s) or the journal can notify the MIATA core team, which will list the published paper online and include a link to the actual paper/journal.

As mentioned earlier, the journals, including editorial teams and reviewers, will be an integral part of the successful adoption of MIATA by authors and, in turn, among the community at large. The provision of an optional choice, such as within the instructions for authors or editorial policies, to report in accordance with the MIATA framework, could support the adoption rate.

A similar process already took place for the reporting on microarray data, which started with the free choice adoption of the MIAME guidelines (14) and led to the integration of MIAME in authors' instructions by some journals who have adopted it. In other words, microarray data cannot be published in these journals without MIAME compliance, a result achieved from bottom up, but not forced down upon the community.

Discussion

While much effort within the community is needed to successfully implement MIATA, recent developments allow an optimistic view. An increasing knowledge exists about MIATA. The initial MIATA announcement has been cited more than 80 times, and the first adherent papers have been published (9). Many important stakeholders in different fields of immunology were and are enthusiastically involved in the project, and large organizations in Europe and the USA support the project's goal. This is largely because MIATA is part of bigger and complex efforts to provide tools to the community that can improve T cell assays and to guide the development of new immunotherapies (17). These efforts further include structured proficiency panel programs, assay harmonization, standardized response determination methods, availability of reference samples, automation of analysis procedures, and more. In the case of immuno-oncology, MIATA integrates well into a paradigm that encompasses peculiar features of immunotherapies that target the immune system and other, classical therapies that target the tumor (18).

Abbreviations

MIATA, Minimal Information About T Cell Assays
References


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