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Background

An effectively functioning immune system is essential for human health and wellbeing. Nutrition is one of the major exogenous factors modulating different aspects of immune function. Currently, no single marker is available to predict the effect of a dietary intervention on different aspects of immune function. International Life Sciences Institute Europe commissioned a group of experts from academia, government and the food industry to prepare a guidance document. A draft of this paper was refined at a workshop involving additional experts. First, the expert group defined criteria to evaluate the usefulness of immune function markers. Next, five theoretical scenarios were drafted describing potential changes in the values of markers compared to a relevant reference range. Finally, all elements were combined, providing a framework to aid the design and interpretation of studies assessing the effects of nutrition on immune function.

Step 1: Criteria for selection and ranking were developed, based on Albers et al. 2003:

Step 2 / Table 1: Over 75 markers were ranked according to the criteria (illustrating example of allergy):

Step 4: Graphical representation of the five different scenarios for the modulation of immune function markers relative to the reference range.

Step 4: Markers were grouped by relationship to immune function (yes/no) and clinical relevance (yes/associated/unknown).

Step 5: Five potential scenarios of marker modulation were defined:

1) Modulation within a reference range
2) Modulation from outside the reference or control range back into the range
3) Modulation within the reference range back into the range
4) Prevention of modulation from within the reference or control range to outside the range
5) Modulation from a less favorable reference range into the reference range of a comparator group with a more favorable immune function.

Step 5: A framework for interpretation was developed:

A “flowchart” was devised to aid the interpretation of changes observed in combinations of immune markers, taking into account the type of marker and the changes observed relative to a defined reference range. Within this framework, the 5 scenarios in Step 4 above were considered. The need to consider the quality of individual studies and consistency of effects, is still emphasized, as well as the need to base ultimate conclusions on the totality of evidence. Working through the logical steps indicates that selected combinations of markers can be used to reach clear conclusions as to whether an observed modulation of immune function could be regarded as beneficial within the functional domain of allergy mitigation.

Conclusions

It was concluded that there is no gold standard or single marker for immune function. When selecting markers, the following should be considered: 1) the target population, 2) the exact physiological function of the immune system involved and 3) the health benefit of interest. Ideally, markers selected should include those indicating clinical relevance and involvement in immune function by themselves, or a combination of markers indicating clinical relevance which are plausibly linked to immune function. It was also concluded that challenge tests and function assays provide stronger results than ‘status markers’. Interpretation of marker changes should consider the targets identified and should be in relation to the relevant reference range, as illustrated in the 5 ‘scenarios’. The stepwise approach presented offers a rationale for selection and interpretation of marker modulation for future trials examining the impact of nutrition on overall allergic response.

References


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