Monitoring immune modulation by nutrition in the general population: Identifying and substantiating health effects

Optimal functioning of the immune system is crucial to human health, and nutrition is one of the major exogenous factors modulating different aspects of immune function. In regard to this, there is a need for guidance on the assessment and interpretation of immune modulation by nutrition. ILSI Europe's Nutrition & Immunity and Probiotics Task Forces jointly organised an Expert Group (EG) to develop guidelines for the use of immunomodulation markers applied in nutrition intervention studies in the general population. Three health domains were selected based on the EFSA 2011 Guidance Document: defence against pathogens, control of low-grade (metabolic) inflammation and avoidance or mitigation of allergy. The EG recommendations have been published in the British Journal of Nutrition.

Step 1: Criteria for selection and ranking were developed, based on Albers et al 2005:

**Ranking Categories:** Biological relevance, Biological sensitivity, Feasibility, Practicality

**Ranking Levels:** Proven (+++), Strong (++), Medium (+), Low (0)

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

<table>
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<th>Function</th>
<th>Marker</th>
<th>Clinical relevance</th>
<th>Biological sensitivity</th>
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Step 3: Markers were grouped by relationship to immune function (yes/no) and clinical relevance (yes/associated/unknown).

Step 4: Various potential scenarios of marker modulation were defined:

- **Modulation within a reference range**
- **Modulation from outside the reference range back into the range**
- **Modulation from within the reference range to outside the range**
- **Prevention of modulation from within the reference or control range to outside the range**
- **Modulation from a less favourable reference range into the reference range of a comparator group with a more favourable immune function.**

Step 5: A framework for interpretation was developed:

A "flow-chart" 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 EG 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’.

References:

Keywords: biomarkers, immune function, validation, guidance, criteria