Report of Subgroup-1 on Immunity and Control of Leishmaniases through Immunological Intervention

Following a general review of the status of control of leishmaniasis through immunological interventions, the participants listed below met to consider the needs and gaps and make evidence-based recommendations to:

Scientists
Granting agencies and
Health Authorities.

It was evident in the plenary sessions that we do not have the tools to control leishmaniasis through immunological intervention. This is in spite of tremendous knowledge on immunology of leishmaniasis and host-parasite interactions, dozens of antigens that have been discovered during the past decades that are protective in animal models, genetic manipulation of the parasite has been possible for over 15 years and the genome of *Leishmania* has been sequenced. Why then, don't we have any vaccines for human use? This is probably because of some insufficiencies in knowledge, in particular, the immune surrogate markers of protection. Also most probably, it is due to the scarcity of the move from fundamental discoveries to development and industrial applications.

It is clear that "development" work for human leishmaniasis has not kept pace with "discovery research". Several reasons could be given for this: 1- Lack of a perceived market for a human leishmaniasis vaccine

(whether prophylactic or therapeutic), hence large international vaccine industries can not invest the required funds and time for their development (>$100M and over 10 years). 2- Discovery research has been funded far more than development by granting agencies over the past several decades. It is estimated that for 30 laboratories (minimum) receiving about US$500,000 /year over 35 years, there have been an estimated >$500 Million, for discovery research vs less than $10 M for development (i.e., preclinical and clinical studies - not counting Gates Foundation's contribution of $49 M for one recombinant vaccine recently). 3- Discovery research is by-and-large conducted in universities and research institutions, where scientists are not interested nor are experts in "development".
Considering these points the gaps were identified and the following recommendations were made to the 3 targets mentioned above:
Recommendations to:
The Scientific Communities

- Concentrate on human immunology to define surrogate markers of immunity using new advanced technologies
- Promote longitudinal studies in natural settings to better understand the natural history of leishmaniasis and mechanisms of protection in humans
- Proceed to clinical trials as soon as possible with known protective antigens. This is required to identify surrogate markers and validate animal models.

Granting agencies:

- Fund preclinical development of selected protective antigens identified over the years
- Promote development for vaccine clinical trials in endemic foci
- Develop new tools for the study of host factors involved in treatment failure

- Enhance connectivity/collaboration/networking focused on problem solving
- Set up more organizations to take discoveries into clinical development in endemic countries

Health authorities (particularly in endemic countries)

- Support and participate in field studies toward development of immunological interventions
- Promote advocacy for leishmaniasis vaccines

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