

Off-target (heterologous/non-specific) effects of vaccination

Les Pensières
Fondation Mérieux Conference Center
Veyrier-du-Lac - France

8-10 June 2015

Steering Committee:

- Peter Aaby
 - Michael Greenberg
 - Ofer Levy
 - Jacques Louis
 - Mihai Netea
 - Valentina Picot
 - Frank Shann
 - William Warren
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- Cindy Grasso meeting coordinator

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Background

The immunological landscape is changing dramatically. We have recently learned that immune memory can be re-educated, that innate immunity can have “memory,” that certain lymphocytes can exhibit innate-like responses and that vaccines may have broader specificities that vary with age and sex. What was learned in classical immunological textbooks is being recast as we go from murine immunology to human immunology and as big data are collected and analysed. Recent clinical, immunological and epidemiological studies show that vaccines can provide greater protection than their intended purpose. For example, BCG, smallpox, measles, oral polio and, yellow fever vaccines may reduce disease and/or mortality from infections other than tuberculosis, smallpox, measles, polio and yellow fever, respectively, and some vaccines have shown promise against certain cancers and even autoimmune disorders.

The types of questions about the off-target effects of vaccines to be considered during the workshop are:

- How does trained immunity influence the off-target effects of vaccination?
- How does vaccine-induced off-target immunity vary with age and sex?
- What effect does inter-pathogen cross-reactivity have on the off-target effects of vaccines?
- How do environmental antigens (such as the microbiome) influence cross-reactivity?
- Are there negative consequences of the off-target effects of vaccines?

In addition to addressing fundamental questions of immunological mechanisms, the workshop will consider the following practical application-driven questions:

- How does understanding the off-target effects/trained immunity change our view of host defense and immunological memory?
 - Could off-target effects lead to a new class of vaccines, or repurpose existing ones?
 - What is the best way to determine whether the off-target effects are real and important or not?
- What data would be required (immunological, clinical, epidemiological, other) in order to assess the causal relationship?
- How could these “off label” observations be used to obtain new “on label” indications?

The intent of the workshop is to take a holistic approach to these questions drawing from the fields of immunology, systems biology, epidemiology, bioinformatics, public health, regulatory science and more. The workshop is designed to not only advance the science of vaccinology, but also to raise the key question that if indeed the off-target effects are real and measurable, how could the world imagine using these vaccines for their previously unintended purposes, and what additional actions would be required. The outcome of the seminar would ideally result in an assessment of the gaps in our knowledge and a proposed research agenda.



Scientific programme

Monday 8 June 2015

16:30 - 17:30	Registration	
17:30 - 17:45	Welcome address	Fondation Mérieux
17:45 - 18:20	Key-note address: Bacillus Calmette-Guérin immunotherapy for bladder cancer: overview of an “off-target” effect of BCG immunotherapy	Gary D. Steinberg
18:20 - 18h30	Discussion	

Session 1

Off-target effects of vaccination: defining the concept-range of off-target effects - Case studies

Chair: Stanley Plotkin

18:30 - 18:50	The WHO review of the non-specific effects of vaccination	Terry Nolan
18:50 - 19:10	Discussion	
19:30	Welcome Dinner	

Tuesday 9 June 2015

Session 1 Continued

08:30 - 08:50	Live vaccines and off-target effects: BCG and measles vaccines	Peter Aaby
08:50 - 09:05	Discussion	
09:05 - 09:25	Inactivated vaccines and off-target effects: DTP and interaction between live and inactivated vaccines	Henrik Ravn
09:25 - 09:40	Discussion	



Scientific programme

Session 2

Priorities and Implications

Chair: Jacques Louis

09:40 - 10:00	What would be required to provide convincing evidence of off-target effects of vaccination?	Stanley Plotkin
10:00 - 10:15	Discussion	
10:15 - 10:45	Coffee break	
10:45 - 11:05	Requirements for new trials to examine off-target effects of vaccination	Paul Fine
11:05 - 11:20	Discussion	

Session 3

Basic biological mechanisms accounting for the off-target effects of vaccination

Chair: William Warren

11:20 - 11:40	Epigenetic reprogramming by listeria monocytogenes	Melanie Hamon
11:40 - 11:55	Discussion	
11:55 - 12:15	Trained immunity: impact for non-specific effects of vaccination	Mihai Netea
12:15 - 12:30	Discussion	
12:30 - 14:00	Lunch	
14:00 - 14:20	Ontogeny of the immune system : implications for the response to vaccination	Ofer Levy
14:20 - 14:35	Discussion	
14:35 - 14:50	Cross-reactivity of immune responses: the role of the microbiome	Yasmine Belkaid
14:50 - 15:05	Discussion	
15:05 - 15:25	Long-term innate immune memory via effects on bone marrow progenitors	Helen Goodridge
15:25 - 15:40	Discussion	
15:40 - 16:10	Coffee break	



Scientific programme

Session 4

How should the next generation of clinical trial and epidemiological studies be designed to provide convincing evidence of off-target/non-specific effects of vaccination?

Chair: Michael Greenberg

16:10 - 16:30	How could the childhood immunization programme be optimized in low- and high-income countries taking into account both specific and off-target effects of vaccines ?	Frank Shann
16:30 - 16:45	Discussion	
16:45 - 17:05	Implications of beneficial off-target effects for upcoming eradication campaigns (measles and polio)	Ane Fisker
17:05 - 17:20	Discussion	
17:20 - 17:40	Vaccinations against smallpox and tuberculosis are associated with better long-term survival	Christine Stabell-Benn
17:40 - 17:45	Discussion	
17:45 - 18:05	Can trials in Africa study both off-target effects and determinants of severe morbidity/mortality?	Nelly Amenyogbe
18:05 - 18:20	Discussion	
19:30	Dinner	

Wednesday 10 June 2015

Session 4 Continued

08:30 - 08:50	Discovery and validation of homologous T cell epitopes in pathogens and humans: what implications for vaccines?	Annie de Groot
08:50 - 09:05	Discussion	
09:05 - 09:25	Developing a new live pertussis vaccine with beneficial off-target effects	Natalie Mielcarek
09:25 - 09:40	Discussion	
09:40 - 10:00	Designing infant immunization studies to model and characterize off-target effects using “big data” OMIC approaches on small volumes of biosamples	Ofer Levy



10:00- 10:15	Discussion
10:15 - 10:45	Coffee break

Repurpose vaccines for off-target effects: the perspectives of donors, regulatory and public health authorities and industry

Chair: Paul Fine

10:45 - 11:05	Regulatory implications and challenges	Jesse Goodman
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11:05 - 11:20	Discussion
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11:20 - 11:40	Open data, knowledge management and identification of new uses of old vaccines	Barend Mons
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11:40 - 11:55	Discussion
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11:55 - 12:15	An industry perspective	Michel Dewilde
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12:15 - 12:30	Discussion
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12:30 - 14:00	Lunch
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14:00 - 15:30	Workshop : The Way Forward, General Discussion. End of meeting	Facilitators: Frank Shann William Warren Terry Nolan
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